Iran J Burn Wound Res
ISSN: 3060-8414

2025, Volume 1, Number 2

Research Paper

Variability in serum sodium concentration and its prognostic significance in severe burn injuries: A retrospective study

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ABSTRACT

Article info:
Received: 3 Jun 2025
Accepted: 30 Jun 2025

Keywords:
Burns
Hypernatremia
Hyponatremia
Prognosis
Water-electrolyte imbalance

Dysnatremia is a common electrolyte disturbance in severe burn patients and may significantly impact prognosis. This study investigated the association between serum sodium variability and mortality in adults with extensive burn injuries. In this retrospective cross-sectional study, 300 adult burn patients with burns involving more than 20% of total body surface area (TBSA) and at least second-degree depth were included. Patients were admitted to Velayat Burn and Plastic Surgery Center (Rasht, Iran) between March 2018 and March 2020. Serum sodium was measured daily during hospitalization. Hypernatremia and hyponatremia were defined as serum sodium >145 mmol/L and <135 mmol/L, respectively. Sodium variability was quantified as the standard deviation (SD) of daily sodium measurements. Multivariate logistic regression was used to identify independent predictors of in-hospital mortality. Of the 300 patients (mean age: 47.5 ± 13.5 years; mean TBSA: 39.8 ± 21.9%), 21.3% of the patients had hypernatremia, and 33 (11%) developed hyponatremia. Overall mortality was 36.7%. Non-survivors had significantly higher mean serum sodium levels (143.2 ± 8.9 vs. 138.6 ± 3.0 mmol/L; $P < 0.0001$) and greater sodium variability. Multivariate analysis identified age (Odds ratio (OR): 1.15; $P = 0.004$), TBSA (OR: 1.24; $P = 0.002$), mechanical ventilation duration (OR: 1.38; $P < 0.001$), inhalation injury (OR: 23.5; $P = 0.003$), and sodium variability (OR: 1.12; $P = 0.004$) as independent predictors of mortality. Dysnatremia—particularly hypernatremia—and greater serum sodium variability are strongly associated with increased mortality in patients with severe burns. These findings underscore the prognostic importance of sodium monitoring and suggest that minimizing sodium fluctuations may improve outcomes in critically ill burn patients. Further prospective studies are warranted to validate these associations and inform clinical management strategies.

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https://iranjburns.com/
https://doi.org/10.61882/ijbwr.1.2.22

1. Introduction

Burns are one of the most expensive traumatic events due to wound healing and complications that lead to long-term hospitalization and high costs for the healthcare system [1], accounting for an estimated number of 180,000 deaths annually [2]. Prevention of burn injury is a priority; however, once an injury has occurred, the primary goal should be to prevent further injury progression and ensure patient survival [3]. Burns have extensive local and systemic effects [2], and one of these side effects is a disturbance in plasma sodium levels [4,5]. Sodium is the primary active extracellular electrolyte in the body. The serum sodium level is generally regulated through water homeostasis at the cellular level and adjusted via thirst, antidiuretic hormones, and renal activity. Changes in plasma sodium levels are known as dysnatremia [6]. Dysnatremia is common in severely ill patients, such as burn patients, and is associated with poor outcomes, including prolonged hospital stay and increased mortality; nevertheless, not enough attention has been paid to dysnatremia in burn patients [7]. A lot of factors contribute to dysnatremia in severely burned patients.

One of the contributing factors is that severely burned patients need extensive fluid resuscitation to survive the acute phase of burn shock. Microvascular integrity is compromised, and a plasma-like fluid leaks into the interstitial space, resulting in edema. The time after injury at which capillary integrity is restored differs among individuals [5,8]. Indeed, one of the most important causes of hypernatremia is skin damage, especially burns. Proteins lose their three-dimensional shape at temperatures higher than 44 degrees Celsius (equivalent to 111 degrees Fahrenheit), and as a result, cell and tissue damage occur following burns [4]. Many of the consequences of burns result from direct damage to the skin tissue and its subsequent dysfunction, including the inability to prevent evaporation and water loss, as well as control body temperature. Disruption of the cell membrane causes the movement of sodium and potassium ions in the direction of their concentration gradients, leading to the occurrence of electrolyte disturbances [9].

Furthermore, in extensive burns (TBSA >30%), a severe inflammatory reaction occurs with tissue edema and severe capillary leakage, leading to inadequate circulating volume [9,10]. During this time, the plasma volume must be maintained to ensure adequate oxygen delivery to vital organs and peripheral tissues. After acute phase fluid resuscitation and recovery of cellular integrity, the circulating fluid volume must be normalized. Extensive water and electrolyte shifts can occur, and dysnatremia may develop [5]. Dysnatremia has a lot of side effects for burn patients.

Disturbances in serum sodium levels, or dysnatremia, can increase neurohormonal activity, lead to organ dysfunction, and worsen the underlying disease, resulting in severe and potentially irreversible consequences, including death. Understanding and managing sodium disturbances is crucial to improving outcomes, preventing complications, reducing hospitalization days, and alleviating healthcare workload. This study aimed to examine the association between dysnatremia (both hypernatremia and hyponatremia) and in-hospital mortality among adult patients with severe burn injuries admitted to Velayat Burn Hospital in northern Iran.

2. Materials and Methods

This retrospective cross-sectional analytical study included 300 adult patients aged over 18 years, with thermal or chemical burns involving more than 20% of the TBSA and at least second-degree depth, admitted to the Velayat Burn and Plastic Surgery Center in Rasht, Iran, between March 2018 and March 2020.

Patients were excluded if they had preexisting renal failure (including dialysis), liver disease (cirrhosis, hepatitis), inflammatory conditions (e.g., inflammatory bowel disease (IBD), osteoarthritis), acute conditions (e.g., pancreatitis, infection, myocardial infarction (MI)), malignancy, malnutrition, nephrosis, sepsis during admission, or incomplete data. Of 614 screened patients, 300 met eligibility criteria and were included in the analysis.

Demographic and clinical variables extracted included age, gender, marital status, cause of burn, burn depth (categorized as partial-thickness and full-thickness burns), TBSA, inhalation injury, abbreviated burn severity index (ABSI) score, serum sodium levels, duration of intensive care unit (ICU) and hospital stay, ventilator use, and mechanical ventilation days. The ABSI score was calculated based on age, sex, TBSA, burn depth, and inhalation injury. Data were collected from medical records after obtaining proper permissions. Due to the retrospective design, only variables that were consistently recorded were used. Daily body weight and intravenous (IV) fluid volumes were largely missing and thus excluded.

To be included in sodium variability analysis, patients needed at least three serum sodium measurements during hospitalization. Sodium was measured on admission and daily at 6:00 AM. Normonatremia was defined as 135–145 mmol/L, hypernatremia as >145 mmol/L, and hyponatremia as <135 mmol/L. All serum sodium values were obtained from the hospital's central laboratory. Standard burn resuscitation was performed using the Parkland formula and lactated Ringer's solution; hypertonic saline was not used. Blood glucose levels were maintained between 80 and 150 mg/dL. To correct dysnatremia, patients received intravenous 0.9% sodium chloride or 5% Sodium Chloride (NaCl) for hyponatremia, and half-saline with water replacement—either orally or parenterally—for hypernatremia, based on clinical judgment and physician consultation. Sample size was calculated using G*Power, based on Sen et al.'s findings, assuming an odds ratio of 1.35 and a mortality rate of 13.4%, yielding a minimum required sample of 300 (power = 95%, α = 0.05). All eligible patients from the two years were included, providing a census-based cohort.

2.1 *Statistical Analysis*

Quantitative variables were reported as mean ± standard deviation; qualitative data were presented as frequencies and percentages. Sodium variability was defined as the standard deviation of daily serum sodium levels and analyzed as a continuous variable.

For comparisons, Fisher's exact and Chi-square tests were used for categorical data; Mann–Whitney U and independent sample t-tests were used for continuous variables. A multivariable logistic regression model was constructed using variables identified as significant in univariate analysis to determine independent predictors of in-hospital mortality. Stepwise selection was used, though its limitations (e.g., inflated Type I error) were acknowledged. Key predictors, including sodium variability, TBSA, ABSI, and the number of mechanical ventilation days, were analyzed as continuous variables. Complete case analysis was used, with <5% missing data across the main variables.

3. Results

3.1 *Patients' demographic and clinical characteristics*

The mean age of the patients was 47.48 ± 13.46 years. Out of 300 patients examined in this study, 64 (21.3%) developed hypernatremia, and 33 (11%) developed hyponatremia. Other demographic and clinical characteristics of patients are presented in Table 1.

3.2 *Relationship between demographic and clinical characteristics of patients with hypernatremia*

The results of the study showed that factors such as age, marital status, cause of the burn, outcome, inhalation injury, burn depth, TBSA, ABSI score, length of hospital stays, length of ICU stays, mechanical ventilation, and use of ventilator had a significant relationship with the occurrence of hypernatremia (P <0.005). Still, the variable of gender did not have a substantial relationship in the two groups, with hypernatremia and non-hypernatremia (P = 0.131). Demographic and clinical characteristics of patients associated with hypernatremia are presented in Table 2.

3.3 *Relationship between demographic and clinical characteristics of patients with hypernatremia and survivorship*

The non-survivors in this study were older (54.85 ± 12.63 vs. 43.21 ± 12.03 years; P = 0.00001) and had a greater TBSA score (58.26 vs. 29.03; P < 0.0001) and an ABSI score (11.42 ± 2.34 vs. 7.24 ± 1.67; P < 0.0001). Additionally, they had a longer mean duration of mechanical ventilation (6.53 ± 4.67 days vs. 1.24 ± 2.36 days; P < 0.0001) and ICU stay (8.09 ± 5.87 days vs. 3.17 ± 3.63 days; P < 0.0001) compared to survivors. Although gender was significantly associated with mortality in univariate analysis (P = 0.033), it was not an independent predictor in multivariate regression (P = 0.915). In contrast, variables such as age (OR = 1.15; P = 0.004), TBSA (OR = 1.24; P = 0.002), duration of mechanical ventilation (OR = 1.38; P < 0.001), inhalation injury (OR = 23.5; P = 0.003), and serum sodium variability (OR = 1.12; P = 0.004) remained significant in multivariate analysis. Additionally, the mean frequencies of hypernatremia and hyponatremia were significantly higher in non-survivors compared to survivors (21.3% and 9.3% vs. 0% and 2%; P < 0.0001). Overall, non-survivors had significantly higher mean serum sodium levels than survivors (143.15 meq/L vs. 138.61 meq/L; P < 0.0001). Moreover, hypernatremia was more frequent than hyponatremia among non-survivors (21.3% vs. 9.3%; P < 0.01) (Table 3).

Table 1. Baseline Demographic and Clinical Characteristics of Adult Burn Patients Included in the Study

Parameter	Category	n (%) / Mean ± SD
Gender	Male / Female	153 (51%) / 147 (49%)
Age (years)	21–40 / 41–60 / 61–80 / 81–100	99 (33%) / 146 (48.7%) / 53 (17.7%) / 2 (0.7%)
	Mean ± SD	47.5 ± 13.5
Marital Status	Single / Married	92 (30.7%) / 208 (69.3%)
Cause of Burn	Flame / Scald / Explosion	191 (63.7%) / 66 (22%) / 43 (14.3%)
Outcome	Survivors / Non-survivors	190 (63.3%) / 110 (36.7%)
Inhalation Injury	Yes / No	94 (31.3%) / 206 (68.7%)
Burn Depth	Partial-thickness / Full-thickness	42 (14%) / 258 (86%)
TBSA (%)	Range 11–100	Mean: 39.8 ± 21.9
ABSI Score	Range 4–≥12	Mean: 8.8 ± 2.8
Hospital Stay (days)		7.4 ± 5.6
ICU Stay (days)		5.0 ± 5.2
Mechanical Ventilation (days)		3.2 ± 4.2
Ventilator Use	Yes / No	159 (53%) / 141 (47%)
Sodium Disorder Category (n, %)	Normal / Hyponatremia / Hypernatremia	203 (67.7%) / 33 (11%) / 64 (21.3%)
Mean Sodium (meq/L)		140.3 ± 6.3

Table 2. Baseline Demographic and Clinical Characteristics of Burn Patients With and Without Hypernatremia (n = 300)

Variable	Without Hypernatremia (n = 236)	With Hypernatremia (n = 64)	P-value
Age, years (mean ± SD)	45.6 ± 12.7	54.5 ± 14.0	<0.001
Age group, n (%):			
– ≤40 years	89 (37.7)	10 (15.6)	
– >40 years	147 (62.3)	54 (84.4)	0.001
Sex, n (%):			0.131
– Male	115 (48.7)	38 (59.4)	
– Female	121 (51.3)	26 (40.6)	
Marital status, n (%):			0.002
– Single	80 (33.9)	12 (18.8)	
– Married	156 (66.1)	52 (81.2)	
Cause of burn, n (%):			<0.001
– Flame	109 (46.2)	31 (48.4)	
– Scald	57 (24.2)	9 (14.1)	
– Explosion	24 (10.2)	19 (29.7)	
Inhalation injury, n (%):	48 (20.3)	46 (71.9)	<0.001
Burn depth, n (%):			0.015
– Partial-thickness	39 (16.5)	3 (4.7)	
– Full-thickness	197 (83.5)	61 (95.3)	
Total body surface area, % (mean ± SD)	34.7 ± 18.3	58.3 ± 24.2	<0.001
ABSI score (mean ± SD)	8.1 ± 5.2	8.8 ± 6.6	<0.001
Hospital length of stay, days (mean ± SD)	7.0 ± 5.2	8.8 ± 6.6	0.031
ICU length of stay, days (mean ± SD)	4.2 ± 4.7	7.7 ± 5.7	<0.001
Mechanical ventilation, days (mean ± SD)	2.3 ± 3.8	6.3 ± 4.4	<0.001
Ventilator use, n (%):	99 (41.9)	60 (93.8)	<0.001
In-hospital mortality, n (%):	46 (19.5)	64 (100.0)	<0.001

Table 3. Comparison of Clinical Characteristics between Survivors and Non-Survivors (n = 300)

Variable	Survivors (n = 190)	Non-Survivors (n = 110)	P-value
Age, years (mean ± SD)	43.2 ± 12.0	54.9 ± 12.6	<0.001
Age group, n (%):			<0.001
– ≤40 years	84 (44.2)	15 (13.6)	
– >40 years	106 (55.8)	95 (86.4)	
Sex, n (%):			0.033
– Male	88 (46.3)	65 (59.1)	
– Female	102 (53.7)	45 (40.9)	
Marital status, n (%):			<0.001
– Single	75 (39.5)	17 (15.5)	
– Married	115 (60.5)	93 (84.5)	
Cause of burn, n (%):			<0.001
– Flame	155 (81.6)	36 (32.7)	
– Scald	57 (30.0)	9 (8.2)	
– Explosion	24 (12.6)	19 (17.3)	
Inhalation injury, n (%):	13 (6.8)	81 (73.6)	<0.001
Burn depth, n (%):			<0.001
– Partial-thickness	37 (19.5)	5 (4.5)	
– Full-thickness	153 (80.5)	105 (95.5)	
TBSA, % (mean ± SD)	29.0 ± 11.1	58.3 ± 23.6	<0.001
ABSI score (mean ± SD)	7.2 ± 1.7	11.4 ± 2.3	<0.001
Hospital stay (mean ± SD)	6.4 ± 4.3	9.3 ± 6.8	0.046
ICU stay (mean ± SD)	3.2 ± 3.6	8.1 ± 5.9	<0.001
Mechanical ventilation (days)	1.2 ± 2.4	6.5 ± 4.7	<0.001
Ventilator use, n (%):	56 (29.5)	103 (93.6)	<0.001
Sodium disturbance, n (%):			<0.001
– Normal	156 (82.1)	47 (42.7)	
– Hypernatremia	6 (3.2)	58 (52.7)	
– Hyponatremia	28 (14.7)	5 (4.5)	
Mean sodium level (meq/L)	138.6 ± 3.0	143.2 ± 8.9	<0.001

3.4 Sodium variability as an independent predictor of mortality

Although gender showed a significant association with mortality in univariate analysis (P = 0.033), it was not an independent predictor in multivariate regression (P = 0.915). In contrast, variables such as age, marital status, cause of burn, inhalation injury, burn depth, TBSA score, ABSI score, duration of mechanical ventilation, ICU stay, and ventilator use were significantly associated with mortality in univariate comparisons (P < 0.0001). To identify independent predictors of in-hospital mortality, a multivariate logistic regression analysis was performed. The results demonstrated that increased age (OR = 1.149, P = 0.004), higher TBSA (OR = 1.236, P = 0.002), prolonged duration of mechanical ventilation (OR = 1.384, P < 0.001), inhalation injury (OR = 23.533, P =

0.003), and greater plasma sodium variability (OR = 1.118, P = 0.004) were all significant independent predictors of mortality. Specifically, increased serum sodium variation, measured as the standard deviation of daily sodium values, was associated with a higher risk of death (OR = 1.118, 95% Confidence Interval (CI): 1.035–1.206, P = 0.004) (Table 4).

4. Discussion

This study evaluated the prognostic impact of dysnatremia and serum sodium variability in patients with severe burns. We found that 21.3% of patients developed hypernatremia and 11% developed hyponatremia—findings consistent with previous studies on electrolyte disturbances and sodium variability in critically ill and burn patients [11–13], as well as with broader literature reporting hypernatremia in 11% and hyponatremia in 3.9–14.5% of hospitalized patients [5,14–18]. Stewart et al. similarly reported hypernatremia and hyponatremia in 9.9% and 6.8% of burn patients, respectively [19]. In burn patients, hypernatremia typically results from increased water loss through injured skin and sepsis [5,14], while hyponatremia is associated with intravascular volume shifts into damaged tissues [20,21]. These electrolyte imbalances are common in critical illness and have been consistently associated with increased morbidity and mortality [22,23]. Our findings reaffirm this association, with dysnatremia—especially hypernatremia—more prevalent among non-survivors. Hypernatremia occurred in 21.3% of non-survivors versus just 3.2% of survivors. Previous ICU studies have shown that 4–26% of critically ill patients develop hypernatremia, with associated mortality rates ranging from 30% to 48% [24–27]. Severe hyponatremia has also been linked to adverse outcomes [28], although its role in burn patients remains less well-characterized. The higher rates of dysnatremia and mortality observed in our study, compared to Stewart et al. [19], may stem from differences in sodium threshold definitions, burn severity (mean TBSA of 39.8% vs. 9%), and patient age (47.5 vs. 36.3 years) —both of which were independent predictors of mortality in our analysis.

Mechanical ventilation was another strong predictor of hypernatremia and mortality, consistent with prior research. Mackie et al. and Arora et al. reported higher sodium levels in ventilated burn patients due to insensible fluid losses [29,30]. Our findings echoed this: ventilated patients had significantly higher rates of hypernatremia ($P < 0.0001$), and non-survivors had higher mean sodium levels (143.2 vs. 138.6 mmol/L).

Most notably, we identified sodium variability—measured as the standard deviation of daily serum sodium—as an independent predictor of mortality, aligning with studies by Shen et al. [11] and Lam et al. [31]. Namdar et al. also reported a high prevalence of hypernatremia (43.3%) and associated increased mortality [32]. Overall, hypernatremia may have a more deleterious effect than hyponatremia in burn patients, with mortality rates between 30% and 40% [33,34].

Multivariate logistic regression analysis revealed that for every 1% increase in TBSA, the odds of death rose by 23.6% (OR = 1.236), while each additional day of mechanical ventilation increased the odds of mortality by 38.4% (OR = 1.384). Sodium variability also independently increased mortality risk (OR = 1.118), highlighting the importance of minimizing electrolyte fluctuations in these patients. Other clinical variables, such as age, TBSA, and inhalation injury, were more common among patients with hypernatremia and non-survivors. These findings align with Lam et al., who found that patients over 40 years old, with TBSA ≥40%, and inhalation injury had significantly higher rates of hypernatremia and mortality [31]. These outcomes are likely due to extensive water loss, inflammatory responses, and altered renal handling of water during severe burns [35]. Although the ABSI score and variables such as gender, marital status, burn depth, and cause of burn were associated with mortality in univariate analysis, they were not independent predictors in the final model, likely due to confounding by stronger variables, including TBSA and mechanical ventilation duration. This study has several limitations that should be taken into account when interpreting the findings. First, its retrospective design limited the analysis to routinely documented medical records. As a result, essential variables such as daily body weight, precise fluid balance, and the volume and administered intravenous fluids were unavailable, potentially introducing residual confounding.

Table 4. Multivariate Logistic Regression Analysis Identifying Independent Predictors of In-Hospital Mortality in Burn Patients

Variable	B	OR (Exp B)	95% CI (Lower–Upper)	P-value
TBSA (%)	0.212	1.236	1.083 – 1.411	0.002
Mechanical Ventilation (days)	0.325	1.384	1.163 – 1.647	<0.001
Sodium Variability (SD of meq/L)	0.111	1.118	1.035 – 1.206	0.004
Age (years)	0.139	1.149	1.045 – 1.263	0.004
Inhalation Injury (Yes)	3.158	23.533	2.903 – 190.794	0.003
Gender (Female)	-0.080	0.924	0.214 – 3.982	0.915
ABSI Score	-1.059	0.347	0.103 – 1.164	0.087
Marital Status (Married)	-0.737	0.479	0.073 – 3.121	0.441
Cause of Burn (Flame)	0.082	1.085	0.177 – 6.662	0.930
Cause of Burn (Scald)	0.462	1.588	0.332 – 7.588	0.562
Cause of Burn (Explosion)	-1.418	0.242	0.025 – 2.357	0.222
Burn Depth (Full-thickness)	-0.018	0.982	0.107 – 8.976	0.987

OR: Odds Ratio, CI: Confidence Interval, SD: Standard Deviation

Second, the study did not assess the timing or progression of acute kidney injury or its interaction with serum sodium variability. Additionally, patients with preexisting sepsis or renal dysfunction were excluded, which may limit the applicability of these findings to more critically ill or complex burn populations.

Third, as a single-center study conducted at a tertiary burn hospital in northern Iran, the results may not be generalizable to other healthcare settings with different patient profiles, treatment protocols, or resource availability. Furthermore, although most key variables—including serum sodium, TBSA, ABSI score, and ventilation duration—were complete for the majority of patients, a small proportion (<5%) of missing data was handled through complete case analysis, which may introduce selection bias.

Finally, stepwise logistic regression was used to identify independent predictors of mortality. While commonly applied, this method carries a risk of overfitting and inflated Type I error. Future research should consider using penalized regression approaches (e.g., least absolute shrinkage and selection operator (LASSO)) and external validation in large, multicenter prospective cohorts to confirm these findings and enhance their generalizability.

This study demonstrates that dysnatremia—particularly hypernatremia—is a common and clinically significant electrolyte disturbance in adults with severe burn injuries. Hypernatremia was notably more prevalent among non-survivors and associated with increased ICU stay, longer mechanical ventilation, and higher mortality. Notably, serum sodium variability emerged as an independent predictor of in-hospital mortality, underscoring the prognostic value of maintaining stable sodium levels throughout the burn care process. Other independent predictors included TBSA, age, inhalation injury, and duration of mechanical ventilation. These findings underscore the importance of close monitoring and prompt correction of sodium abnormalities in critically ill burn patients. Efforts to minimize fluctuations in serum sodium, alongside optimal fluid management and respiratory support, may improve patient outcomes. Further large-scale, prospective, multicenter studies are warranted to validate these associations and determine whether tighter control of sodium variability can reduce mortality in this high-risk population.

Acknowledgment

The authors are grateful to the Deputy of Research and Technology at Guilan University of Medical Sciences and the Velayat Burn and Plastic Surgery Center.

Authors' contributions

S.R. and S.A. designed the project, developed the data collection, and wrote the manuscript. M.M.R. was responsible for the patient's treatment. A.A. was responsible for data analysis, and S.D., L.P., and M.T. participated in the recruitment and data collection. All authors read and approved the final version of the manuscript.

Conflict of interest

No potential conflict of interest was reported by the authors.

Ethical declarations

The ethics committee of Guilan University of Medical Sciences approved the study protocol (IRB approval: IR.GUMS.REC. 1399.281).

Financial support

This study was conducted as part of a Doctor of Medicine thesis and received funding from Guilan University of Medical Sciences.

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