# Prevalence of Hypernatremia Among Medically Hospitalized Patients and The Related Clinical Outcomes

Juhaina Salim Al-Maqbali<sup>1,2\*</sup>, Intisar Hamood Al Yaqoubi<sup>3</sup>, Rayan Khalfan Al Jabri<sup>4</sup>, Afnan Ahmed Al Farsi<sup>5</sup> and Abdullah M. Al Alawi<sup>3,6</sup>

<sup>1</sup>Department of Pharmacology and Clinical Pharmacy, College of Medicine and Health Science, Sultan Qaboos University, Muscat, Oman

Received: 9 July 2024

Accepted: 4 May 2025

\*Corresponding author: <u>Juhaina@squ.edu.om</u>

## DOI 10.5001/omj.2025.97

#### Abstract

Objectives: Hypernatremia is frequently observed, and its prevalence varies widely depending on hospital clinical settings. Hypernatremia was found to be an indicator of mortality and morbidity in critically ill patients. This study aimed to examine the prevalence, health implications, and predictors of hypernatremia in hospitalized patients for medical illness. *Methods:* A retrospective study included hospitalized adult patients (≥18 years) at a tertiary hospital. Two measurements of serum sodium were documented: upon admission, and at the time of discharge. Hypernatremia was defined as a sodium concentration exceeding 145 mmol/L. Results: During admission, 424 patients met the inclusion criteria, and 34 patients (8.02%, 95%Cl: 5.78-11.02%) had hypernatremia. There were 189 women (44.58%), and the median age was 59 (IQR: 40.5 -73) years. Aging was associated with severe hypernatremia (p<0.01) and patients with severe hypernatremia had lower concentrations of potassium and albumin (p<0.01). Patients who received normal saline (0.9%) during hospitalization, which led to a significant improvement in sodium concentration at discharge compared to the concentrations upon admission (141 vs 149.5 mmol/L; p<0.01). Patients with hypernatremia experience a considerably higher risk of inpatient mortality (p=0.024). Serum albumin concentration had a negative association with the likelihood of hypernatremia (adjusted odds ratio (aOR): 0.92;95% CI:0.881 - 0.962; p < 0.01) and negative association with the likelihood of inpatient mortality (aOR: 0.82; 95% CI: 0.791 - 0.871, p<0.01). Conclusions: Hypernatremia is prevalent in the elderly and those with hypovolemia. It's often linked with hypokalaemia and hypoalbuminemia, and it may potentially lead to adverse health outcomes including increased inpatient mortality.

Keywords: Hypernatremia, hypokalaemia, hypoalbuminemia, hypovolemia, and inpatient mortality.

# Introduction

Sodium is the primary cation in the extracellular fluid (ECF) and is vital for maintaining the intravascular volume. Two biological mechanisms can alter sodium balance and hydromineral homeostasis. The first mechanism is determined by sodium chloride intake, leading to cell dehydration, inhibited sodium appetite, increased natriuresis, enhanced water intake, and reduced fluid excretion. The second mechanism involves hypovolemia, triggering

<sup>&</sup>lt;sup>2</sup>Department of Pharmacy, Sultan Qaboos University Hospital, University Medical City, Muscat, Oman

<sup>&</sup>lt;sup>3</sup>Internal Medicine Residency Training Program, Oman Medical Specialty Board, Muscat, Oman

<sup>&</sup>lt;sup>4</sup>College of Medicine and Health Science, Sultan Qaboos University, Muscat, Oman

<sup>&</sup>lt;sup>5</sup>Royal College of Surgeons in Ireland, D02 YN77 Dublin, Ireland

<sup>&</sup>lt;sup>6</sup>Department of Medicine, Sultan Qaboos University Hospital, University Medical City, Muscat, Oman

compensatory reactions like increased thirst and sodium appetite, especially for isotonic drinks, and antidiuretic and anti-natriuretic responses. Hypervolemia reduces water and sodium intake and increases diuresis and natriuresis.<sup>2</sup> Dysfunctions in these systems can lead to a medical condition known as dysnatremia, which includes either hyponatremia (low sodium concentrations) or hypernatremia (high sodium concentrations).<sup>3,4</sup> Hypernatremia is primarily caused by a deficit of water relative to solute. The key reason for hypernatremia is the disproportionate loss of total body water compared to solute loss. It's often associated with hypovolemia, which occurs in situations where the loss of water exceeds the loss of sodium.<sup>3,4</sup> Hypernatremia is characterized as a serum sodium concentration that exceeds 145 mmol/L.<sup>5</sup> In addition, alternative thresholds for determining the severity of hypernatremia have been suggested, such as concentration greater than 150 mmol/L or greater than 156 mmol/L.<sup>6</sup>

Hypernatremia is rare among previously healthy individuals but is often seen in patients in a hospital setting. The prevalence of this condition can vary greatly depending on the clinical settings, with a reported prevalence between 1% and 5%. However, within intensive care units (ICUs), the prevalence can increase to as high as 9-37%. <sup>7,8,9,10,11,12</sup> Risk factors for hypernatremia include excessive fluid loss, excessive sodium intake, conditions that disrupt thermoregulation, disorders such as diabetes insipidus and renal tubular damage. <sup>13,14,15</sup> There is an increased risk of hypernatremia in elderly patients with renal tubular damage associated with multiple myeloma, <sup>15</sup> the second most frequent hematological malignancy. <sup>16</sup> In AML, caused by the clonal expansion of myeloblasts in the peripheral blood, bone marrow, or other tissues patients, <sup>17</sup> hypernatremia can be due to Arginine vasopressin deficiency. <sup>18</sup> Hypernatremia can present a variety of symptoms from moderate and nonspecific, such as headaches, nausea, and lethargy, to severe neurological signs like seizures and coma. <sup>9</sup>

Electrolyte imbalances, including dysnatremia, are commonly seen in patients who present in emergency departments, and such imbalances often result in hospitalization. Several studies undertaken in emergency departments have examined risk factors for hypernatremia, including season and age. <sup>5,14,19</sup> The hot climate of the Gulf region increases the risk of dehydration-related hypernatremia, particularly in vulnerable populations like the elderly, due to excessive perspiration and insufficient fluid intake.

It's important to note that the detection of hypernatremia is critical as it can result in prolonged hospital stays, increased morbidity and mortality rates, as well as higher healthcare costs. Horover, dysnatremia has been identified as a predictor of mortality and morbidity in critically ill patients, Particularly in patients with acute kidney injury. A large retrospective study showed that patients with severe hypernatremia (sodium concentration exceeding 160 mmol/L) had almost a 50% in-hospital mortality rate. Other research has indicated an even higher in-hospital mortality rate of up to 75%. Hypernatremia can be life-threatening and rapid correction of severe hypernatremia can lead to neurological consequences; however this approach is debatable and optimal rates of correction must be decided based on individualized patient approach.

Most existing studies have focused on hypernatremia in the ICU setting, <sup>23</sup> and there is a scarcity of data assessing hypernatremia among patients hospitalized in medical wards. Additionally, there is a lack of knowledge regarding the factors that necessitate hospitalization due to hypernatremia among medical patients. The goal of this study was to examine the prevalence and health impacts of hypernatremia in patients hospitalized for medical illnesses in a tertiary hospital setting and to evaluate health outcomes associated with hypernatremia.

# Methods

This retrospective cohort study took place at Sultan Qaboos University Hospital (SQUH) from December 29, 2020, to September 12, 2021. It included adult patients (those aged 18 years and older) who were admitted and cared for in the General Internal Medicine Unit over the study period. The analysis used two measurements of serum sodium: one taken at the time of admission and one at the point of discharge. The study excluded patients younger than 18, those with a serum sodium concentration below 136 upon admission, those directly admitted to the High Dependency Unit (HDU) or Intensive Care Unit (ICU), and adult patients admitted under subspecialties outside of the General Internal Medicine Unit.

The study collected relevant demographic information such as age and gender, alongside medical history details including conditions like hypertension, diabetes mellitus (DM), chronic kidney disease (CKD), heart failure (HF),

ischemic heart disease (IHD), and chronic liver disease from the patient's electronic health records. Sodium concentrations upon admission and discharge were noted, and biochemical data, including electrolyte concentrations of calcium, potassium, phosphate, magnesium, and albumin, were collected. The initial volume status of the patient was recorded at presentation, along with the management details for hypernatremia. The primary diagnosis was classified using the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10).

The normal range for serum sodium concentration is between 136 mmol/L and 145 mmol/L. Hypernatremia is defined by a sodium concentration above 145 mmol/L and is classified into mild (146-150 mmol/L), moderate (151-160 mmol/L), and severe (≥161 mmol/L) categories. <sup>5,6</sup> To evaluate hospitalization outcomes, the prevalence of hypernatremia was determined by analyzing the sodium concentration recorded upon admission.

The study received approval from the Medical and Research Ethics Committee at the College of Medicine and Health Sciences, Sultan Qaboos University (SQU), Muscat, Oman (MREC #2866; SQU-EC/ 087/2022; dated August 28th, 2022). This research follows the ethical standards and principles detailed in the Declaration of Helsinki.

Given the retrospective nature of this study, the requirement for consent was waived by the Medical and Research Ethics Committee.

Sample size was based on primary outcome: prevalence of hypernatremia. We know from literature that the prevalence of hypernatremia is expected to range between 1% and 9%. Therefore, we determined that a sample size of 126 patients was necessary to identify the prevalence of hypernatremia in our setting by attaining a 95% confidence level and 80% statistical power. However, because we wanted to link hypernatremia to clinical outcomes, we further increased the cohort using a non-probability convenient technique, which relied on the availability of patients during the study period. The research inclusion criteria were used to screen all patients admitted to the designated wards which lead to including 424 patients.

Analysis was conducted utilizing the concentration of sodium measured upon admission. Relevant variables were compared between different concentrations of sodium and normal sodium groups. Categorical variables were presented using frequencies and percentages. The median and interquartile ranges (IQRs) were used to define variables following a continuous abnormal distribution, and the Kruskal-Wallis test was employed for univariate analysis. The Chi-Square test examined the associations between categorical variables among the sodium groups, while Fisher's exact test was used when cells had an expected frequency of less than five. The Wilcoxon Signed Rank Sum test was performed to determine the impact on sodium concentration after hypernatremia treatment (comparing admission to discharge). Only variables with a significance level (p) below 0.05 were considered in the binary logistic regression analysis, to identify potential independent characteristics associated with hypernatremia compared to normal sodium concentration and inpatient mortality. The study employed Kaplan-Meier survival estimates and log-rank tests to demonstrate the length of time before the occurrence of various clinical outcomes in patients with different concentrations of hypernatremia. The significance level for a two-tailed test was set at p < 0.05. Statistical analysis was conducted using STATA version 17.0 (StataCorp, 1985-2021, Stata Statistical Software, College Station, TX, USA).

#### Results

During admission, a total of 898 patients underwent screening. Out of the total, 346 patients were excluded from the study because their sodium concentration at admission was lower than 136 mmol/L. Additionally, 128 patients were omitted because they only had one sodium reading throughout their admission. Only 424 patients who met the inclusion criteria were included in the analysis. On the day of admission, 34 patients (8.02%, [95%CI: 5.78-11.02%]) had hypernatremia. Out of the patients included in the study, 4.72% (n=20/424) had mild hypernatremia, 2.36% (n=10/424) had moderate hypernatremia, and 0.94% (n=4/424) had severe hypernatremia.

**Table 1** presents the clinical and biochemical characteristics of the groups, classified according to the severity of hypernatremia (mild, moderate, and severe) and normal sodium concentrations. There were 189 women (44.58%),

and the median age was 59 (IQR: 40.5 - 73.0) years. Aging was associated with severe hypernatremia compared to the other groups with different sodium concentrations (p<0.01). Approximately half of the patients had a history of hypertension (47.17%), whereas none of the identified comorbidities were associated with differences in sodium concentrations among the groups. Additionally, patients with severe hypernatremia had lower concentrations of potassium and albumin compared to the other groups (p<0.01). We further investigated the evolution of patients' volume status upon admission. Out of the 34 patients diagnosed with hypernatremia, 21/34 (61.76%) were found to be hypovolemic. However, 30/34 patients received normal saline (0.9%) during their hospital stay, leading to a significant improvement in sodium concentration at discharge compared to the concentrations upon admission (141 (IQR:138-144) mmol/L vs 149.5 (IQR:147-154) mmol/L; p<0.01).

**Table 1**: Clinical and biochemical characteristics and medications profile of admitted patients stratified according to hypernatremia severity and normal sodium on day of admission (n=424).

Characteristics n (%) unless specified otherwise	Total n= 424 (100%)	Normal Sodium level 136– 145 mmol/L n=390 (91.98%)	Mild hypernatremia 146–150 mmol/L n=20 (4.72%)	Moderate hypernatremia 151-160 mmol/L n=10 (2.36%)	Severe hypernatremia 161-172 mmol/L n=4 (0.94%)	<i>p</i> -value
Female	189 (44.58%)	175 (44.87%)	5 (25.00%)	7 (70.00%)	2 (50.00%)	0.110
Age; IQR, years	59 (40.5 - 73)	58 (40 – 71)	65.5 (49.5 – 76)	74.5 (68 – 83)	78 (72.5 – 82)	<0.01
Comorbidities						
Hypertension (HTN)	200 (47.17%)	186 (47.69%)	7 (35.00%)	5 (50.00%)	2 (50.00%)	0.739
Ischemic heart disease (IHD)	69 (16.27%)	64 (16.41%)	2 (10.00%)	2 (20.00%)	1 (25.00%)	0.691
Heart failure	50	49	1 (5.00%)	0	0	0.672
(HF) Diabetes mellitus	(11.79%) 148	(12.56%) 136	8 (40.00%)	3 (30.00%)	1 (25.00%)	0.947
(DM) Chronic liver	(34.91%) 21	(34.87%) 18 (4.62%)	2 (10.00%)	1 (10.00%)	0	0.356
disease (CLD) Chronic Kidney disease (CKD)	(4.95%) 65 (15.33%)	62 (15.90%)	0	3 (30.00%)	0	0.079
Biochemical Profi		(13.9070)				
Calcium (Ca <sup>+</sup> );	2.24	2.24 (2.16	2.22 (2.07 – 2.30)	2.29 (2.24 – 2.39)	2.34 (2.27 -	0.153
IQR, mmol/l	(2.16 – 2.31)	- 2.31)	2.22 (2.07 – 2.30)	2.29 (2.24 – 2.39)	2.34 (2.27 – 2.38)	0.133
Potassium (K+); IQR, mmol/l	3.8 (3.4 – 4.1)	3.8 (3.5 – 4.1)	3.4 (3.2 – 4.1)	3.1 (2.7 – 3.5)	2.9 (2.8 – 3.45)	<0.01
Magnesium	0.80	0.80 (0.75	0.80(0.69 - 0.94)	0.79(0.66 - 0.80)	0.82 (0.76 -	0.557
(Mg+); IQR, mmol/l	(0.75 – 0.85)	- 0.84)	0.00 (0.0) 0.5 1)	0.77 (0.00 0.00)	1.03)	0.557
Phosphate	0.83)	0.99 (0.83	0.98(0.72-1.07)	0.99(0.76 - 1.21)	0.77 (0.62 -	0.597
(PO3+); IQR,	(0.81 –	- 1.17)	0.50 (0.72 1.07)	0.55 (0.70 1.21)	1.16)	0.277
mmol/l Albumin; IQR, mmol/l	1.17) 33.16 (27 – 40)	34 (28 – 40)	29.5 (24 – 34.1)	27.5 (20 – 33)	22 (18 – 26.5)	<0.01
Volume status ass	Volume status assessment					
	93	72	12 (60.00%)	5 (50.00%)	4 (100%)	< 0.01
Hypovolemic	(21.93%) 51	(18.46%) 50	0	1 (10.00%)	0	0.320
Euvolemic	(12.03%)	(12.82%)	· ·	1 (10.0070)	· ·	0.520

Overloade	vd.	37 (8.73%)	36 (9.23%)	1 (5.00%)	0	0	0.917
Overloade	tu	243	232	7 (35.00%)	4 (40.00%)	0	<0.01
Not assess	sed	(57.31%)	(59.49%)				
Treatmen	nt						
Normal (0.9%)	Saline	279 (65.80%)	249 (63.85%)	18 (90.00%)	8 (80.00%)	4 (100%)	0.027

**Table 2** represents the clinical outcomes associated with different concentrations of hypernatremia. Patients with mild to moderate hypernatremia experienced substantially higher incidences of inpatient mortality compared to patients with normal sodium concentrations (13.08% vs 35% vs 30%; p=0.024). All other measured clinical outcomes were not associated with differences in sodium concentrations. We included relevant parameters to the backward stepwise regression analysis to identify independent predictors for hypernatremia,

**Table 2**: Clinical outcomes of admitted patients stratified according to severity of hyponatremia (mild, moderate, and severe) and normal sodium (n=424).

Clinical outcomes n (%) unless specified otherwise	Total n= 424 (100%)	Normal Sodium level 136–145 mmol/L n=390 (91.98%)	Mild hypernatremia 146–150 mmol/L n=20 (4.72%)	Moderate hypernatremia 151-160 mmol/L n=10 (2.36%)	Severe hypernatremia 161-172 mmol/L n=4 (0.94%)	<i>p</i> -value
LOS; IQR, years	20.17 (7.53 – 45.91)	22.51 (7.30 - 55.39)	20.53 (11.97 – 37.71)	12.76 – 6.60 – 18.19)	6.66 (4.23 – 9.09)	0.369
Admission to HDU/ICU	158 (37.44%)	147 (37.79%)	8 (40.00%)	3 (33.33%)	0	0.555
CPR	49 (12.60%)	43 (12.01%)	4 (22.22%)	2 (22.22%)	0	0.318
Inpatient Mortality	61 (14.39%)	51 (13.08%)	7 (35.00%)	3 (30.00%)	0	0.024
90-day readmission	88 (20.75%)	79 (20.26%)	4 (20.00%)	3 (30.00%)	0	0.357
1-year mortality	44 (10.38%)	38 (9.74%)	3 (15.00%)	2 (20.00%)	1 (25.00%)	0.210

Serum albumin concentration had a negative association with the likelihood of hypernatremia (adjusted odds ratio (aOR): 0.92; 95% CI: 0.881 - 0.962; p<0.01). Hypovolemia, however, was associated with a positive likelihood of hypernatremia (aOR; 7.68; 95% CI: 3.578 - 16.497, p<0.01) (**Table 3**). Additionally, **Table 4** shows that albumin had negative association with the likelihood of inpatient mortality (aOR: 0.82; 95% CI: 0.791 - 0.871, p<0.01).

**Table 3**: Backward stepwise binary logistic regression model for independent factors associated with hypernatremia versus normal sodium (n=424).

Outcome tested in the model	Independent factors	aOR* [95% CI]	<i>p</i> -value
Hypernatremia group	Albumin; IQR, mmol/l	0.92 [ 0.881 – 0.962]	<0.01
	Volume status: Hypovolemic	7.68 [ 3.578 – 16.497]	< 0.01

<sup>\*</sup> Stepwise backward binary logistic regression model for an adjusted odds ratio (aOR) for the following factors significantly (p<0.05) associated with hypernatremia in the univariate analysis that includes age, potassium, albumin, hypovolemia volume status and not assessed volume status.

**Table 4**: Binary logistic regression model to identify if hypernatremia is independent factor for inpatient mortality (n=424).

Outcome tested in the model Inpatient mortality	Independent factors hypernatremia group	<b>aOR* [95% CI]</b> 1.01 [ 0.583 – 4.150]	<b><i>p</i>-value</b> 0.377
	Age; IQR, years	1.01 [0.992 - 1.027]	0.287
	Potassium (K+); IQR, mmol/l	1.07 [0.768 - 1.497]	0.680
	Albumin; IQR, mmol/l	0.82 [ 0.791 – 0.871]	<0.01
	Volume status: Hypovolemic	0.82 [ 0.791 – 0.871]	0.587
	Volume status: Not assessed	0.52 [ 0.217 – 1.213]	0.587

<sup>\*</sup>Binary logistic regression model for an adjusted odds ratio (aOR) for the following factors significantly (p<0.05) associated with hypernatremia in the univariate analysis that includes age, potassium, albumin, hypovolemia volume status and not assessed volume status.

**Figure 1** depicts a comparative analysis of the duration until readmission within a 90-day period among different sodium concentration groups. It was observed that patients with severe hypernatremia group were readmitted sooner within this time frame compared to other groups. Yet, this pattern did not meet the threshold for statistical significance (Hazard Ratio (HR): 1.41; 95% CI; 0.973-2.049, p=0.069). Similarly, **Figure 2** demonstrates the analysis of the time until death within one year. Patients with moderate hypernatremia displayed an earlier incidence of death within one year, though, it was statistically insignificant (HR: 1.49; 95% CI; 0.966-2.319, p=0.071).

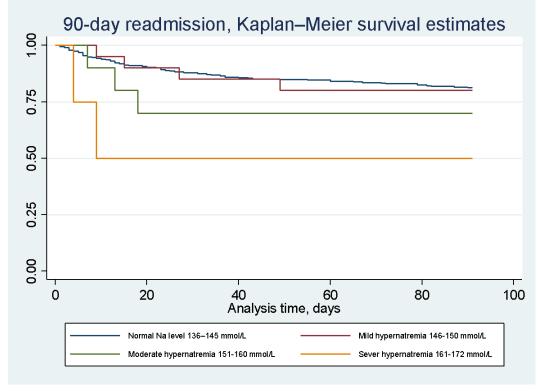


Figure 1: Analysis of time to 90-days readmission among the patients with different levels of sodium (n = 424).

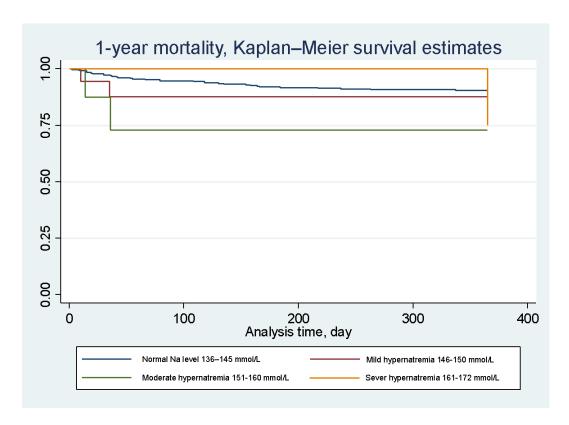


Figure 2: Analysis of time to 1-year mortality among the patients with different levels of sodium (n = 424).

## **Discussion**

This study is one of the few that has examined the prevalence and health implications of hypernatremia in patients admitted to medical wards. Hypernatremia prevalence was relatively high among the cohort, and it was associated with aging. Patients with hypernatremia presented to the hospital with hypovolemia and had lower concentrations of potassium and albumin. The treatment administered led to improvements in sodium concentrations, but they experienced a substantially higher incidence of inpatient mortality compared to patients with normal sodium concentrations. Furthermore, a decrease in albumin concentrations demonstrated an independent association with adverse health outcomes.

Hypernatremia is a common electrolyte disorder, with a prevalence fluctuating between 1-37% among various patient groups, including those admitted to the ICU.<sup>7,8,10</sup> In this study, the prevalence was 8.02%, it is within the range of prevalence of hypernatremia in literature, however, it is in the lower side, ranging from 1% to 37% depending on the study population and clinical setting, this could be the due exclusion of critically ill patients. Hypernatremia is notably common in ICUs, with studies reporting prevalence rates of 8.9% to 37.2%. <sup>12,24</sup> In our study, mild hypernatremia was observed in 4.72% of patients, in contrast to the 1%-13.1% reported in other studies. Moderate hypernatremia was observed in 2%-2.36% of patients, compared to 8.5% in other studies. Severe hypernatremia was present in less than 0.1%-4% of our patients as opposed to 4-15.3% noted in various other studies, including studies from United Kingdom. <sup>14,25</sup> These discrepancies might be due to the patient types and their settings in different studies. Some of those studies included patients from diverse specialties, who were in emergency rooms, outpatient settings, or even admitted to the ICU. In contrast, our study specifically focused on medical cases and included only patients admitted to medical wards. <sup>24,26</sup> Additionally, the association between aging and hypernatremia observed in our cohort has been corroborated by studies from Japan and the United States, which have highlighted the diminished thirst mechanism and reduced renal function in elderly populations as significant contributors to hypernatremia.

Hypernatremia tends to occur more frequently in elderly, frail individuals compared to younger ones. Our study demonstrates a statistically significant association between older age and hypernatremia; older patients exhibited a higher severity of hypernatremia. <sup>8,19</sup> This can be explained by the diminished thirst sensation in the elderly and the gradual decline of renal function with age, which reduces the kidney's efficacy in maintaining electrolyte and water homeostasis. <sup>27,28</sup> Our study investigated gender as a potential factor associated with hypernatremia. Consistent with earlier studies, our findings revealed no significant connection between gender and hypernatremia. <sup>19,29</sup> However, one study from Japan noted a significant association between female sex and an increased risk of hypernatremia in older community-dwelling individuals, with smaller muscle mass potentially mediating this relationship. <sup>30</sup>

While the existing literature provides limited insights into the association of comorbidities with hypernatremia, our study reported that 41.2% of patients with hypernatremia also had hypertension. Another study noted that around 54% of their patient population with hypernatremia were hypertensive. However, both studies found no significant association between hypernatremia and hypertension.<sup>31</sup> No such data was available in the literature about the correlation between other chronic medical conditions and hypernatremia, as this was not studied thoroughly previously. CKD was identified in 8.8% of hypernatremia patients in this study. In contrast, another study reported CKD presence in only 1% of its hypernatremia patients.<sup>32</sup> These discrepancies could be associated with varying stages of CKD, different treatments given, and possible dietary differences between the groups. Notably, baseline hyponatremia and time-dependent hyponatremia or hypernatremia are independently linked to an increased risk of all-cause mortality in patients with CKD.<sup>33</sup> Also, this study found that ischemic heart disease was present in 14.7% of patients with hypernatremia, heart failure was present in 2.9% of patients, and diabetes mellitus was observed in 35.3% of patients with hypernatremia. In another study, only 11% of hypernatremia patients were found to have diabetes.<sup>34</sup> This discrepancy in percentages may be attributed to differences in the prevalence of diabetes mellitus itself among the patients included in the studies. Interestingly, among hypernatremia patients, chronic liver disease was the least common comorbid condition, perhaps because hyponatremia is more typically associated with chronic liver disease. On the other hand, hypernatremia, though less common, is also linked to adverse outcomes in cirrhosis, often caused by hypotonic fluid losses due to osmotic diuresis or lactulose-induced diarrhea.<sup>35</sup> Also to emphasize that studies examining hypernatremia in the Gulf region remain limited, despite its clinical significance in hospitalized populations. The Gulf region, characterized by a predominantly hot climate, poses a higher risk of dehydration-related hypernatremia due to excessive water loss from perspiration and inadequate fluid intake, especially among vulnerable populations such as the elderly.

In this study, hypernatremia was significantly associated with hypokalemia and hypoalbuminemia. The relationship between hypernatremia and hypokalemia could be explained by the autoregulation of solutes in the plasma, as both are cations and both influence cellular transmembrane potentials. <sup>36</sup> Also, previous studies have noted a significant association between hypokalemia and hypernatremia, particularly in specific patient populations such as those with community-acquired pneumonia, cancer, and CKD. These conditions often coexist due to underlying disease processes or as side effects of treatments. <sup>37,38</sup> Regarding hypoalbuminemia, it is associated with hypernatremia, particularly in the context of critical illness, inflammation, and renal dysfunction. This mainly occurs due to the osmolar effect of sodium on plasma, which results in decreased albumin concentrations to maintain serum osmolarity. <sup>39</sup> Sodium homeostasis is associated with water homeostasis, and changes in volume status might result in various forms of dysnatremia.

In this study, hypovolemia was found in 61.8% of patients with hypernatremia, a statistically significant finding. Hypernatremia in hypovolemic patients occurs due to water loss through different mechanisms, including urinary loss, gastrointestinal loss, or even sweating and insensible loss with febrile illnesses, resulting in elevated sodium readings. Overcorrection or an inability to appropriately correct hypernatremia may result in permanent neurological injuries and death. Therefore, meticulously calculated fluid replacement is imperative in these patients to avoid such preventable damage. In our study, normal saline infusion was used to correct hypernatremia for most of the patients with hypernatremia.

Across various clinical settings, hypernatremia is consistently associated with poor outcomes, including higher mortality rates, longer hospital stays, and increased healthcare costs. This association is evident in patients with severe traumatic brain injury, subarachnoid hemorrhage, and COVID-19, as well as in general hospitalized populations. The severity of hypernatremia further influences the extent of these adverse outcomes, with moderate to severe hypernatremia posing a greater risk. 12,45,46 In this study, we found that both mild and moderate

hypernatremia were associated with increased mortality. However, this association was not evident in patients with severe hypernatremia due to the small number of patients with severe hypernatremia (n=4) in our study.

This study has many strengths. Unlike previous studies, it focused on medical patients admitted to non-critical areas. It was powered to assess the prevalence of hypernatremia and comprehensively examined various factors potentially associated with hypernatremia. Additionally, it evaluated health outcomes potentially linked to hypernatremia. However, the study's limitations include its retrospective nature, which has its challenges. Information on nutritional status and average water intake was not captured due to a lack of documentation, and capturing other information like hematological parameters was not possible. Lastly, the data on readmission and death were solely derived from SQUH only.

## **Conclusion**

Hypernatremia is a significant electrolyte derangement among hospitalized medical patients, but less prevalent compared to critically ill medical patients. Old age and hypovolemia are common among patients with hypernatremia. Additionally, hypokalemia and hypoalbuminemia are associated with hypernatremia, suggesting a common mechanism driving these body elemental disturbances. Hypernatremia might be associated with poor health outcomes, including increased inpatient mortality.

### References

- 1. Bie P. Mechanisms of sodium balance: total body sodium, surrogate variables, and renal sodium excretion. Am J Physiol Regul Integr Comp Physiol 2018;315(5):R945-r62.
- 2. Bernal A, Zafra MA, Simón MJ, Mahía J. Sodium Homeostasis, a Balance Necessary for Life. Nutrients 2023;15(2).
- 3. Hypernatremia QQ. Clin J Am Soc Nephrol 2019;14(3):432-434.
- 4. Sonani B, Naganathan S, Al-Dhahir MA. Hypernatremia. StatPearls. Treasure Island (FL): StatPearls Publishing Copyright © 2024, StatPearls Publishing LLC.; 2024.
- 5. Wootton E, Grossmann M, Warren AM. Dysnatremia in a changing climate: A global systematic review of the association between serum sodium and ambient temperature. Clin Endocrinol (Oxf) 2024;100(6):527-541.
- Oehler D, Immohr MB, Böttger C, Bruno RR, Sigetti D, Haschemi J, et al. Donor hypernatremia is associated with increased mortality after heart transplantation: A retrospective study. Clin Transplant 2022;36(12):e14803.
- 7. Mapata L, Richards GA, Laher AE. Hypernatremia at a Tertiary Hospital Intensive Care Unit in South Africa. Cureus 2022;14(2):e22648.
- 8. Bataille S, Baralla C, Torro D, Buffat C, Berland Y, Alazia M, et al. Undercorrection of hypernatremia is frequent and associated with mortality. BMC Nephrol 2014;15:37.
- 9. Feigin E, Feigin L, Ingbir M, Ben-Bassat OK, Shepshelovich D. Rate of Correction and All-Cause Mortality in Patients With Severe Hypernatremia. JAMA Netw Open 2023;6(9):e2335415.
- 10. Jansch C, Matyukhin I, Marahrens M, Lehmann R, Khader B, Ritter O, et al. Hypernatremia: Epidemiology and Predictive Role in Emerging and Established Acute Kidney Injury. J Clin Med Res 2023;15(8-9):399-405.
- 11. Yun G, Baek SH, Kim S. Evaluation and management of hypernatremia in adults: clinical perspectives. Korean J Intern Med (Korean Assoc Intern Med) 2023;38(3):290-302.
- 12. Arzhan S, Roumelioti ME, Litvinovich I, Bologa CG, Unruh ML. Outcomes of Hospital-Acquired Hypernatremia. Clin J Am Soc Nephrol 2023;18(11):1396-1407.
- 13. Kuru BK, Baydın A, Ocak M, Aksoy İ. Diagnostic and prognostic efficacy of optic nerve sheath diameter in patients with dysnatremia. Med Ultrason 2024.
- 14. Otterness K, Singer AJ, Thode HC Jr, Peacock WF. Hyponatremia and hypernatremia in the emergency department: severity and outcomes. Clin Exp Emerg Med 2023;10(2):172-180.

- Imashuku S, Kudo N, Kubo K. Severe hypernatremia and hyperchloremia in an elderly patient with IgG-kappa-type multiple myeloma. J Blood Med 2013;4:43-47.
- 16. Mohammed DA, Khallaf SM, El-Naggar MG, Abdel-Hameed MR, Bakry R. Interleukin-10: A Potential Prognostic Marker in Patients with Newly Diagnosed Multiple Myeloma. Resum Oncol 2021;17(1):38-41.
- 17. Sayed SA, Hassan EA, Abdel Hameed MR, Agban MN, Mohammed Saleh MF, Mohammed HH, et al. Ketorolac-fluconazole: A New Combination Reverting Resistance in Candida albicans from Acute Myeloid Leukemia Patients on Induction Chemotherapy: In vitro Study. J Blood Med 2021;12:465-474.
- 18. Rasi V, Riekhof F, Mahmoud M, Ejiofor S, Lentine KL. A Case of Hypernatremia in a Newly Diagnosed Patient With Acute Myeloid Leukemia: Lessons for Nephrologists. Cureus 2024;16(4):e59186.
- 19. Imai N, Sumi H, Shibagaki Y. Impact of age on the seasonal prevalence of hypernatremia in the emergency department: a single-center study. Int J Emerg Med 2019;12(1):29.
- 20. Ma Y, Zhang P, Hou M. Association of hypernatremia with mortality in patients with COVID-19: A systematic review and meta-analysis. Immun Inflamm Dis 2023;11(12):e1109.
- 21. Atlani M, Kumar A, Pakhare AP, Singhai A, Gadwala R. Potential Association of Hypernatremia With Mortality in Patients With Acute Kidney Injury and COVID-19. Cureus 2022;14(7):e27530.
- 22. Ates I, Özkayar N, Toprak G, Yılmaz N, Dede F. Factors associated with mortality in patients presenting to the emergency department with severe hypernatremia. Intern Emerg Med 2016;11(3):451-459.
- 23. Lindner G, Funk GC, Schwarz C, Kneidinger N, Kaider A, Schneeweiss B, et al. Hypernatremia in the critically ill is an independent risk factor for mortality. Am J Kidney Dis 2007;50(6):952-957.
- Arzhan S, Roumelioti ME, Litvinovich I, Bologa CG, Myers OB, Unruh ML. Hypernatremia in Hospitalized Patients: A Large Population-Based Study. Kidney360 2022;3(7):1144-1157.
- 25. Vedantam A, Robertson CS, Gopinath SP. Morbidity and mortality associated with hypernatremia in patients with severe traumatic brain injury. Neurosurg Focus 2017;43(5):E2.
- 26. Tsipotis E, Price LL, Jaber BL, Madias NE. Hospital-Associated Hypernatremia Spectrum and Clinical Outcomes in an Unselected Cohort. Am J Med 2018;131(1):72-82.e1.
- 27. Andreucci VE, Russo D, Cianciaruso B, Andreucci M. Some sodium, potassium and water changes in the elderly and their treatment. Nephrol Dial Transplant 1996;11(Suppl 9):9-17.
- 28. Luckey AE, Parsa CJ. Fluid and electrolytes in the aged. Arch Surg 2003;138(10):1055-1060.
- 29. Barma MA, Soiza RL, Donnan PT, McGilchrist MM, Frost H, Witham MD. Serum sodium level variability as a prognosticator in older adults. Scand J Clin Lab Invest 2018;78(7-8):632-638.
- 30. Tanaka S, Fujishiro M, Imatake K, Suzuki Y, Ishihara H, Tani S. Impact of Female Sex on the Susceptibility to Hypernatremia Among Older Community-Dwelling Individuals in Japan. Int J Gen Med 2022;15:777-785.
- 31. Wu D, Chen Y, Guan H, Sun Y. Association of abnormal serum electrolyte levels with hypertension in a population with high salt intake. Public Health Nutr 2019;22(9):1635-1645.
- 32. Hassanein M, Arrigain S, Schold JD, Nakhoul GN, Navaneethan SD, Mehdi A, et al. Dysnatremias, Mortality, and Kidney Failure in CKD: Findings From the Chronic Renal Insufficiency Cohort (CRIC) Study. Kidney Med 2022;4(12):100554.
- 33. Sun L, Hou Y, Xiao Q, Du Y. Association of serum sodium and risk of all-cause mortality in patients with chronic kidney disease: A meta-analysis and sysematic review. Sci Rep 2017;7(1):15949.
- 34. Snyder NA, Feigal DW, Arieff AI. Hypernatremia in elderly patients. A heterogeneous, morbid, and iatrogenic entity. Ann Intern Med 1987;107(3):309-319.
- 35. Bernardi M, Zaccherini G. Approach and management of dysnatremias in cirrhosis. Hepatol Int 2018;12(6):487-499.
- 36. Girndt M. (Electrolyte disorders). Internist (Berl) 2011;52(8):963-974, quiz 75.
- 37. Ratanasrimetha P, Workeneh BT, Seethapathy H. Sodium and Potassium Dysregulation in the Patient With Cancer. Adv Chronic Kidney Dis 2022;29(2):171-9.e1.

- 38. Huang H, Jolly SE, Airy M, Arrigain S, Schold JD, Nally JV, et al. Associations of dysnatremias with mortality in chronic kidney disease. Nephrol Dial Transplant 2017;32(7):1204-1210.
- 39. Kahn T. Hypernatremia with edema. Arch Intern Med 1999;159(1):93-98.
- 40. Nguyen MK, Kurtz I. Correction of hypervolaemic hypernatraemia by inducing negative Na+ and K+ balance in excess of negative water balance: a new quantitative approach. Nephrol Dial Transplant 2008;23(7):2223-2227.
- 41. Adrogué HJ, Tucker BM, Madias NE. Diagnosis and Management of Hyponatremia: A Review. JAMA 2022;328(3):280-291.
- 42. Hoffman H, Jalal MS, Chin LS. Effect of Hypernatremia on Outcomes After severe Traumatic Brain Injury: A Nationwide Inpatient Sample analysis. World Neurosurg 2018;118:e880-e6.
- 43. Kolmodin L, Sekhon MS, Henderson WR, Turgeon AF, Griesdale DE. Hypernatremia in patients with severe traumatic brain injury: a systematic review. Ann Intensive Care 2013;3(1):35.
- 44. Ruiz-Sanchez JG, Nunez-Gil IJ, Cuesta M, Rubio MA, Maroun-Eid C, Arroyo-Espliguero R, et al. Prognostic Impact of Hyponatremia and Hypernatremia in COVID-19 Pneumonia. A HOPE-COVID-19 (Health Outcome Predictive Evaluation for COVID-19) Registry Analysis. Front Endocrinol (Lausanne) 2020;11:599255.
- 45. Ni HB, Hu XX, Huang XF, Liu KQ, Yu CB, Wang XM, et al. Risk Factors and Outcomes in Patients With Hypernatremia and Sepsis. Am J Med Sci 2016;351(6):601-605.
- 46. Thongprayoon C, Cheungpasitporn W, Yap JQ, Qian Q. Increased mortality risk associated with serum sodium variations and borderline hypo- and hypernatremia in hospitalized adults. Nephrol Dial Transplant 2020;35(10):1746-1752.