

Acquired hypernatremia in a general surgical Intensive Care Unit: Incidence and prognosis

ABSTRACT

Purpose: Intensive Care Unit (ICU)-acquired hypernatremia (IAH) is a serious electrolyte disturbance that recently was shown to present an independent risk factor for mortality in critically ill patients. IAH has not been widely investigated in Surgical ICU (SICU) patients. No study has specifically investigated IAH epidemiology in the Kingdom of Saudi Arabia (KSA) in general SICU. The objectives of this study are to assess the epidemiological characteristics and prognostic impact of IAH on SICU mortality and outcome in KSA and compare it with international figures.

Materials and Methods: A retrospective observational study on a prospectively collected data of patients (14 years of age or older) admitted to SICU over 2 years, with normal serum sodium on admission and who developed IAH (serum sodium above 145 mmol/L) from day two of admission. Traumatic brain injury patients with therapeutic target sodium level above 145 mmol/L were excluded.

Results: Over 2 years study period, 864 patients were admitted to SICU. A total of 50 (5.8%) developed IAH and were included in the study. Twenty-eight (56%) patients were male. The median age was 47 (14-84) years. The mean (\pm standard deviation) Acute Physiology and Chronic Health Evaluation II score was 17 ± 6.5 . The incident density (the rate of occurrence of IAH per 100 days care for SICU admission for the first episode) was 0.71. Risk factors include mechanical ventilation, male sex, age ≥ 50 years, postgastrointestinal surgeries, weekend and night admission. SICU mortality was 40%. The SICU and hospital median (range) length of stay was 8.3 (2-53) and 28.8 (3-95), respectively.

Conclusions: IAH is not uncommon in SICU patients and is associated with increased risk of SICU as well as hospital mortality.

Key words: Fluid replacement; hypernatremia; Intensive Care Unit; quality of care

Introduction

Hypernatremia is a disorder of water metabolism and is usually defined as a plasma sodium concentration above 145 mEq/L.^[1,2] The various physiological consequences of hypernatremia are life-threatening.^[3] The clinical consequences of hypernatremia include but are not limited to cardiac dysfunction, neurologic consequences, and

insulin resistance in addition to impaired gluconeogenesis. Osmolality is regulated within narrow ranges in the healthy individual, and even slight elevations in osmolality lead to the development of thirst and the secretion of antidiuretic hormone. Under normal conditions, thirst is the major defense mechanism against the development of hypernatremia.^[4] As a result, and in any case, it can only develop secondary to

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sodium gain or free water loss or a combination of both along with poor access to water.^[1]

In a general medical-surgical population of noncritically ill patients, the prevalence of hypernatremia has been estimated at up to 1%.^[5] Because of nature of their serious underlying diseases, patients in the Surgical Intensive Care Unit (SICU) are at the higher risk of developing ICU-intensive acquired hypernatremia (IAH).^[6] The incidence ranges from 8% in neurosurgical to 10-12% of cardiothoracic SICU patients.^[7-9]

In the single study available on dysnatremia in a cohort of general SICU patients, the incidence of IAH was found to be 18.6%.^[10] Major risk factors are mechanical ventilation, coma, and sedation.^[11] Inability to express thirst and inadequate fluid management by ICU physicians along with water loss, appear to be the causative triad, which make IAH largely preventable.^[2]

Although previous studies on IAH are important contributions to the literature, few focused on the critically ill general surgical patient. The incidence of IAH in such patients, as well as its effect on mortality, is not well described. We therefore undertook this study to describe the incidence of IAH and assess its effects on outcome among this cohort of patients admitted to SICU in a large university hospital. Because IAH is frequently preventable, it has been regarded as an indicator of the quality of ICU care by some authors.^[12,13] Since IAH is considered a preventable problem that is found to be an independent risk factor for mortality in critically ill patients (40-70%).^[8,14,15] We intended to have a simple description of incidence of IAH and its outcome in the SICU rather than looking at a detailed diagnosis of the group studied nor causes of the hypernatremia.

Materials and Methods

Data sources and study design

The study was approved by the institutional review board at King Khalid University Hospital (KKUH)-Riyadh. We conducted a retrospective observational study on a prospectively collected data to assess the epidemiological characteristics and prognostic impact of IAH in an SICU.

Study population

Critically ill medical and surgical patients in KKUH are cared for in separate units. The SICU in KKUH is a closed unit and can accommodate up to 14 patients. In addition to emergency surgery and elective high-risk noncardiac surgery admission to the SICU, it serves as the regional neurosurgical, trauma referral center as well vascular surgery center. All critically ill adult patients in our SICU are managed by qualified, dedicated critical care staff.

For this study, we utilized a population of patient who were identified as consecutive adults (14 years of age or older) admitted between January 1, 2012, and December 31, 2013, with IAH defined as a change in serum sodium concentration from normal level on admission to a level above 145 mmol/L following day one in the SICU.

Patient characteristics

Patient characteristics were identified (age, sex, admission location, weekend admission, night admission, and clinical admission diagnosis). The severity of illness at inception (within the 1st day of ICU admission) was assessed using the Acute Physiology and Chronic Health Evaluation (APACHE) II score.

Patients with IAH were classified into three categories, mild (serum sodium 145-149 mmol/L), moderate (serum sodium 150-154 mmol/L), and severe (serum sodium > 155 mmol/L). Persistent hypernatremia was defined as serum sodium > 145 mmol/L for longer than 48 h.

Statistical analysis

Collected data have been analyzed using descriptive and inferential tests. Descriptive tests expressed as counts and percentages. Continuous variables of the study population characteristics were described as mean \pm standard deviation (SD) or median (range, interquartile range [IQR]) depending on data distribution. Comparison between two categorical variables was made using the Chi-square test or Fisher's exact test as appropriate, and continuous data have been tested with ANOVA or Kruskal-Wallis depending on its distribution. A $P < 0.05$ indicated statistical significance. Statistical analysis has been done using IBM Corporation Released 2012. IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp. Armonk, NY, USA).

Results

During the 2 years study period (January 2012–December 2013), 864 patients were admitted to SICU. Patients with hypernatremia on admission and eight patients with traumatic brain injury, who received hypertonic and/or mannitol therapy to keep their sodium level above 145 mmol/L, were excluded. The most abnormal (maximum) laboratory values in each 24-h period (00:00-23:59 h) were recorded. Fifty patients (5.8%) were documented to have hypernatremia after 24 h of SICU admission (mild 27 (54%), moderate 13 (26%), and severe hypernatremia 10 (20%) patients). Twenty-eight (56%) patients were male, with 1.3:1 as a male to female ratio. The median (range) age was 47 (14-84) years; twenty-four (48%) patients had age \geq 50 years. The mean (\pm SD) APACHE II score was 17 ± 6.5 . The incident density (rate of occurrence of IAH per 100 days of care) for the first episode of SICU acquired

hyponatremia was 0.71/100 days of admission, based on a total of 7061 admission days. Study population characteristics are summarized in Table 1.

The most common admission diagnosis was postgastrointestinal surgeries (44%). Ten (20%) patients were postemergency surgery. Admission time was tracked, twelve (24%) patients were admitted during weekend and night time admission occurred in 36% of the time (18 of 50 patients). Out of all study population, 33 (66%) patients were ventilated at admission time; two of which had a “do not resuscitate” order in place, who died in the SICU.

Hyponatremia was persistent in 18 (36%) patients; of which 16 (89%) had sodium level ≥ 150 mmol/L. Nine out of 18 patients who had persistence hyponatremia died in SICU ($P = 0.37$). The redevelopment of hyponatremia after sodium correction did not have an effect on mortality (16 out of 50, 32%) compared to those who did not develop a second episode of IAH ($P = 0.48$).

The median (range) time from SICU admission to the development of hyponatremia was 71 (range [24-541], IQR [38-146]) h. Figure 1 illustrates the distribution of occurrence of IAH in the SICU 24 h after admission. Fifty percent of cases occur on day 2 and 3 of SICU admission. The remaining 50% of IAH cases span over the next 6 days. Median (range) time

Table 1: Characteristics of patients with surgical Intensive Care Unit acquired hyponatremia

Characteristics	Patients with IAH (n: 50)
Age median years (range)	47 (14-84)
Male, sex, n (%)	24 (48)
Admission diagnosis, n (%)	
GI surgery	22 (44)
Isolated TBI	6 (12)
TBI with multiple traumas	5 (10)
Orthopedic surgery (trauma)	5 (10)
Neurosurgery (nontrauma)	2 (4)
Others	10 (20)
Emergency operations, n (%)	10 (20)
Admitted via, n (%)	
Emergency room	12 (24)
Operation room	22 (44)
Hospital floors	15 (30)
Another hospital	1 (2)
Weekend admission, n (%)	12 (24)
Night admissions, n (%)	18 (36)
Ventilated at admission, n (%)	33 (66)
APACHE II score, mean (SD)	17 (6.5)
DNR care status, n (%)	2 (4)

IAH: ICU acquired hyponatremia; GI: Gastrointestinal; TBI: Traumatic brain injury; DNR: Do not resuscitate; APACHE: Acute Physiology and Chronic Health Evaluation

taken for hyponatremia correction was 24 (5-180) h. The average of the highest serum sodium level in hyponatremic patients who died was 158 mmol/L, which differ significantly ($P \leq 0.001$) compared to IAH group who survived (average serum sodium was 148 mmol/L).

Compared to mild and moderate IAH, severe IAH had a significant ($P < 0.001$) effect on SICU mortality and has had the longest correction time needed ($P < 0.03$). The SICU outcome, hyponatremia development time, correction time needed, incident of hyponatremia redevelopment, and the mean of hyponatremia between these three levels are summarized in Table 2.

SICU mortality was 40% (20 patients), and the overall hospital mortality was 46% (23 patients); thus, 3 patients died post-SICU discharge, all of them were not hyponatremic at discharge time. The SICU and hospital median (range) length of stay was 8.3 (2-53) and 28.8 (3-95), respectively. Out of 20 patients who died, 15 (75%) patients were hyponatremic at the time of death. Two patients were re-admitted to SICU within 48 h of discharge, both died while in the ICU.

Discussion

Our study is one of very few studies that focused on IAH in critically ill surgical patients. In this study, we showed that IAH can occur in general SICU patients early in the course of their critical illness and is associated with increased mortality. However, the incidence of 5.8% is lower than previous reports, 8% in neurosurgical, and 12% in cardiothoracic SICU patients. The striking result of our study is the strong association between level of IAH and ICU mortality of critically ill surgical patients. The average highest serum sodium level in hyponatremic patients who died was 158 mmol/L, which differ significantly ($P \leq 0.001$) compared to the IAH group who survived (average sodium 148 mmol/L). This is in consistence with previously published papers which support that IAH has an effect on mortality, independent of the underlying disease, or disease severity.^[14] IAH is strictly a hyperosmolar condition caused by

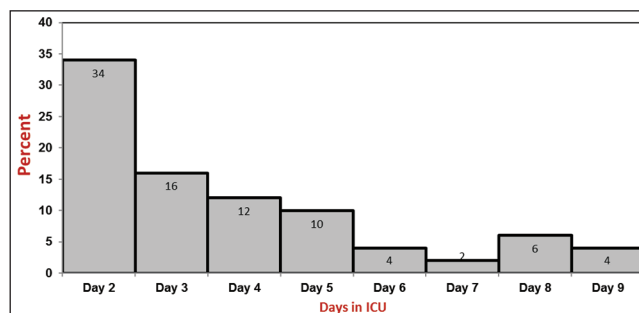


Figure 1: Time from Intensive Care Unit admission to onset of hyponatremia

Table 2: Characteristics of Intensive Care Unit acquired hypernatremia based on the degree of hypernatremia

Outcome	Mild (n = 27)	Moderate (n = 13)	Severe (n = 10)	P
ICU outcome, died, n (%)	6 (22)	6 (46)	8 (80)	<0.001
Time taken to hypernatremia development, hours, median (range)	54 (24-306)	104 (48-359)	59 (31-420)	<0.12
Time taken for correction, hours, median (range)	24 (5-72)	72 (12-156)	62 (24-180)	<0.03
Persistence hypernatremia, n (%)	2 (7.4)	9 (69)	7 (70)	<0.001
Redevelopment of hypernatremia after correction, n (%)	7 (26)	6 (46)	3 (30)	<0.07
Mean of hypernatremia, mmol/L, mean (SD)	147 (1.3)	152 (1.8)	160 (5.6)	<0.001

SD: Standard deviation

a decrease in total body water relative to electrolyte content. It is a “water-problem,” not a problem of sodium homeostasis. Critically ill surgical patients are often unconscious, intubated or sedated, and receive large volumes of infusions. Their “water intake” is mainly managed by the physician. As a result, this special cohort is prone to develop IAH. Although IAH from the use of hypertonic saline, mannitol, or bicarbonate solution in SICU patients is possible, it is more likely to occur from routine use of isotonic saline for replacement of the free water deficit in patients with excessive renal or nonrenal fluid losses and for medication administration.^[16] Several previously published studies have shown the relationship between inadequate intravenous (IV)-fluid therapy and the development of IAH indicating the suboptimal quality of care.^[11,15,17,18]

Of note, in this study, 50% of patients developed IAH within their 2nd and/or the 3rd day of SICU stay. Time taken for hypernatremia corrections differs significantly according to the degree of hypernatremia; longer time was needed for more severe IAH ($P < 0.004$). Despite a slightly lower incidence of IAH in our study, it persisted in 18 (36%) patients; of which 16 (89%) had sodium level ≥ 150 mmol/L. Nine patients (50%) of those who had persistence hypernatremia died before discharge from SICU. It is worth mentioning that the crude mortality rate in our SICU during the study period was 16%.

Prevention of hypernatremia would be a more advisable strategy than its treatment. Rising serum sodium should be considered a relative contraindication for further administration of saline and should prompt treatment with water either via a feeding tube or as a hypotonic IV solution.^[18] Likewise, in the SICU, it should be possible to recognize a trend toward hypernatremia and prescribe more hypotonic solutions. Use of hypotonic fluids is sometimes avoided by physicians because of the fear of hyponatremia.^[19] Developing strategies to prevent IAH could be more challenging than it first appears. The most effective way to reduce this risk is to allow patients to resume control and regulation of their own fluid and electrolyte balance as soon as it is safely possible. Although strict control by more frequent sodium measurements (for example every 6–8 h) may elucidate trends in serum sodium levels that then can be corrected easily,

further studies are needed to establish optimal strategies for prevention of IAH in SICU.

Our study provides few important contributions to the epidemiology of IAH in critically ill surgical patients in addition to the previously published work. First, our study extends the general applicability of the literature to a broader population of nonselect population of SICU patients compared with the previous studies on neurosurgical and cardiothoracic ICUs.^[7,8] Second, we identified certain patient characteristics that are associated with IAH in SICU. Identifying patients at risk may be difficult for clinicians preoccupied with more acute medical issues or other laboratory investigations. A single abnormal serum sodium level may be lost in a long list of laboratory values. Characteristics like mechanical ventilation, male, age ≥ 50 years, postgastrointestinal surgeries, and weekend and night admission were more common in those who had IAH. These could potentially be used to help clinicians identify patients at increased risk. Third, few IAH papers have reported their incidence density (ID) of IAH. ID is the most appropriate measure of the frequency of new development of any morbidity in a particular population over a period of time. It refers to a number of new cases per population in a given time period.^[20] This implies that the ID is constant over time. It assumes a single figure for the entire population over defined period of follow-up. When the follow-up period varies from person to person in a dynamic population (which is the case in any SICU) an epidemiological tool for calculating risk and incidence (like ID) is the most appropriate.^[21] In this study, our ID was 0.71/100 days of SICU admission, compared to 1.3/100 (in cardiothoracic ICU), and 7.4/100 (in combined medical and SICU) in a recent paper.^[9,10] Fourth, the association of IAH with SICU readmission within 48 h was not previously reported.

As such our observational study is valuable for generating hypotheses; no causal inference can strongly be made. It has several limitations. First, the design of our study, retrospective analysis of a prospectively collected data, implies limitation of factors (like the use of diuretics or fluid balance) available for further analysis. However, earlier studies showed that inadequate fluid management was

the main cause of IAH.^[17] Similarly, hyperglycemia was not included in the factors analyzed.^[22] As a result, it was not included as one of the potential confounding factors when evaluating the association between mortality and IAH. Finally, we cannot determine from our data whether the association between IAH and mortality reflects direct physiological effects of IAH or constituted a marker for suboptimal quality of care. It could be a contributing factor for that. Additional studies are needed to investigate this issue.

Conclusion

Our results confirm that the development of IAH is a common event early in the course critically ill surgical patients requiring SICU admission and is independently associated with prolonged SICU stay and mortality, making careful monitoring for and treatment of IAH an imperative action. It is interesting to find that increased mortality rate is associated with increasing degree of hypernatremia, however because the number are relatively small, hard conclusions are hard to make.

Since it is largely preventable complication in the SICU, efforts should focus on the prevention of IAH. Prompt identification of patients at risk for IAH and early adaptation of the fluid balance may diminish the risk. The efficacy of this approach and its impact on mortality remain to be determined. In hospitals that use any type of computer databases containing patient data and laboratory results, the incidence of IAH can be monitored periodically to assess the progress in the quality of care provided over time.

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Conflicts of interest

There are no conflicts of interest.

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