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Intensive care unit–acquired hypernatremia is an independent predictor of increased mortality and length of stay☆,☆☆

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Abstract

Purpose: The purpose of this study is to examine the impact of hypernatremia acquired after intensive care unit (ICU) admission on mortality and length of stay (LOS).

Materials and Methods: Data for this observational study were collected from patients admitted between January 1, 2008, and September 30, 2010 to 344 ICUs in the eICU Research Institute.

Results: Of the 207 702 eligible patients, 8896 (4.3%) developed hypernatremia (serum Na >149 mEq/L). Hospital mortality was 32% for patients with hypernatremia and 11% for patients without hypernatremia ($P < .0001$). Intensive care unit LOS was 13.7 ± 9.7 days for patients with hypernatremia and 5.1 ± 4.6 for patients without hypernatremia ($P < .0001$). Multivariate analysis showed that hypernatremia was an independent risk factor for hospital mortality with a relative risk (RR) of 1.40 (95% confidence interval, 1.34-1.45) and ICU LOS with a rate ratio (RtR) of 1.28 (1.26-1.30). The RR for mortality and RtR for ICU LOS increased with increasing severity strata of hypernatremia, but the duration of hypernatremia was not associated with mortality.

Conclusions: Hypernatremia developed following ICU admission in 4.3% of patients. Hypernatremia was independently associated with a 40% increase in risk for hospital mortality and a 28% increase in ICU LOS. Severity, but not duration of ICU-acquired hypernatremia was associated with hospital mortality.

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1. Introduction

Although the incidence of intensive care unit (ICU)–acquired hypernatremia (4%-8%) and its association with increased mortality and length of stay (LOS) have been described, the independent effects of increasing severity and duration of hypernatremia on mortality and LOS remain unclear [1-8]. With all else being equal, is the risk of mortality higher when the peak serum sodium concentration is 155 mEq/L compared with 150 mEq/L compared with 140 mEq/L? Once a patient reaches a peak serum sodium concentration, is the risk of mortality greater if they remain at that concentration for 2 days compared with 1 day? Although hypernatremia in the ICU has been investigated, questions such as these remain largely unresolved.

Prior studies have begun to address these and similar questions; however, due to various limitations, further research is needed to confirm and extend earlier findings. Increasing severity of hypernatremia has been shown to be associated with increased mortality but only with limited adjustment for confounding or with the effect of hypernatremia being quantified only using the maximum sodium value or 1 or 2 sodium thresholds [1-3]. The effect of the duration of hypernatremia was also studied by O'Donoghue et al [1], but they were unable to identify a detrimental effect of prolonged hypernatremia greater than 150 mEq/L in the ICU. Further research is needed to confirm that this observation was not due to a type II error. Prior research also examined hypernatremia present on admission or that developed early in the ICU stay, which may have been related to the primary cause of admission rather than the result of ICU care [1-3]. The time of hypernatremia onset is important because it has been suggested that ICU-acquired hypernatremia is most often iatrogenic, and as such should be preventable [4-6,9]. Furthermore, no large scale multicenter study has evaluated ICU-acquired hypernatremia in the United States. Detailed knowledge of the implications of hypernatremia for ICU patients may spur intensivists to be more proactive in the anticipation, detection, and prevention of ICU-acquired hypernatremia, potentially improving patient outcomes. The objective of this study was to quantify the effect of the severity and duration of ICU-acquired hypernatremia on hospital mortality and ICU LOS using a large clinical ICU database containing data from a broad representative segment of US ICUs.

2. Materials and methods

2.1. Study design and patient population

Data from patients admitted to 344 US ICUs (medical, surgical, mixed, cardiac, cardiovascular surgical, trauma, and neurologic) from January 2008 through September 2010 were included in the eICU Research Institute's (eRI) data repository. This multistate consortium is guided by agreements among 32 participating programs and eRI governance documents. Further detail regarding the structure and process of the eRI is presented elsewhere [10,11].

All adult patients discharged (alive or expired) with a valid Acute Physiology and Chronic Health Evaluation (APACHE) IV score (Cerner, Inc, Kansas City, MO) and ICU LOS more than 48 hours were eligible for inclusion in this retrospective cohort study. Patients with serum sodium greater than 149 mEq/L on admission (within 24 hours before admission through 48 hours post ICU admission), an ICU admission diagnosis of diabetic ketoacidosis or hyperosmolar state, or serum glucose greater than 400 mg/dL on admission were excluded from the cohort. See Fig. 1 for cohort selection.

All data elements are stored with a uniform data structure across all eICU programs. Data are either documented directly in the clinical information system or captured via Health Level Seven International (HL7) interface messages during clinical care and mapped to standard data concepts. Data collected for this study included demographics (age, sex), clinical characteristics (APACHE IV score, source of admission, admission diagnosis, teaching hospital status, temperature, serum sodium, serum glucose, serum lactate, serum creatinine, duration of mechanical ventilation), ICU-acquired complications (acute kidney injury, respiratory failure, sepsis, and upper gastrointestinal hemorrhage [see Appendix for definitions]), outcomes (hospital and ICU mortality, hospital and ICU LOS). The eRI database was analyzed, and reidentification risk was certified as meeting safe harbor standards by Privacert, Inc (Pittsburgh, PA). The study protocol was submitted to the University of Maryland Baltimore Institutional Review Board and was deemed exempt under 45 CFR 46.101(b).

2.2. Statistical analysis

Data processing and statistical analysis were performed by the Pharmaceutical Research Computing Center within the Department of Pharmaceutical Health Services Research at the University of Maryland School of Pharmacy. The condition of interest, ICU-acquired hypernatremia, was defined by serum sodium greater than 149 mEq/L that developed more than 48 hours after admission to the ICU. The primary analysis investigated the association of ICU-acquired hypernatremia with hospital mortality and ICU LOS. Secondary analyses studied the association of the severity and duration of hypernatremia with hospital mortality and ICU LOS. Bivariable analysis was performed using χ^2 tests for categorical values and the Student t test for continuous values. $P < .05$ was considered significant.

Hospital mortality was studied using a modified Poisson distribution to provide relative risk (RR) of death (rather than odds ratios) [12], and ICU LOS was studied using a generalized estimating equations (GEE) model with a negative binomial distribution and log link to provide rate ratios (RtR). Robust error variance estimation was used for

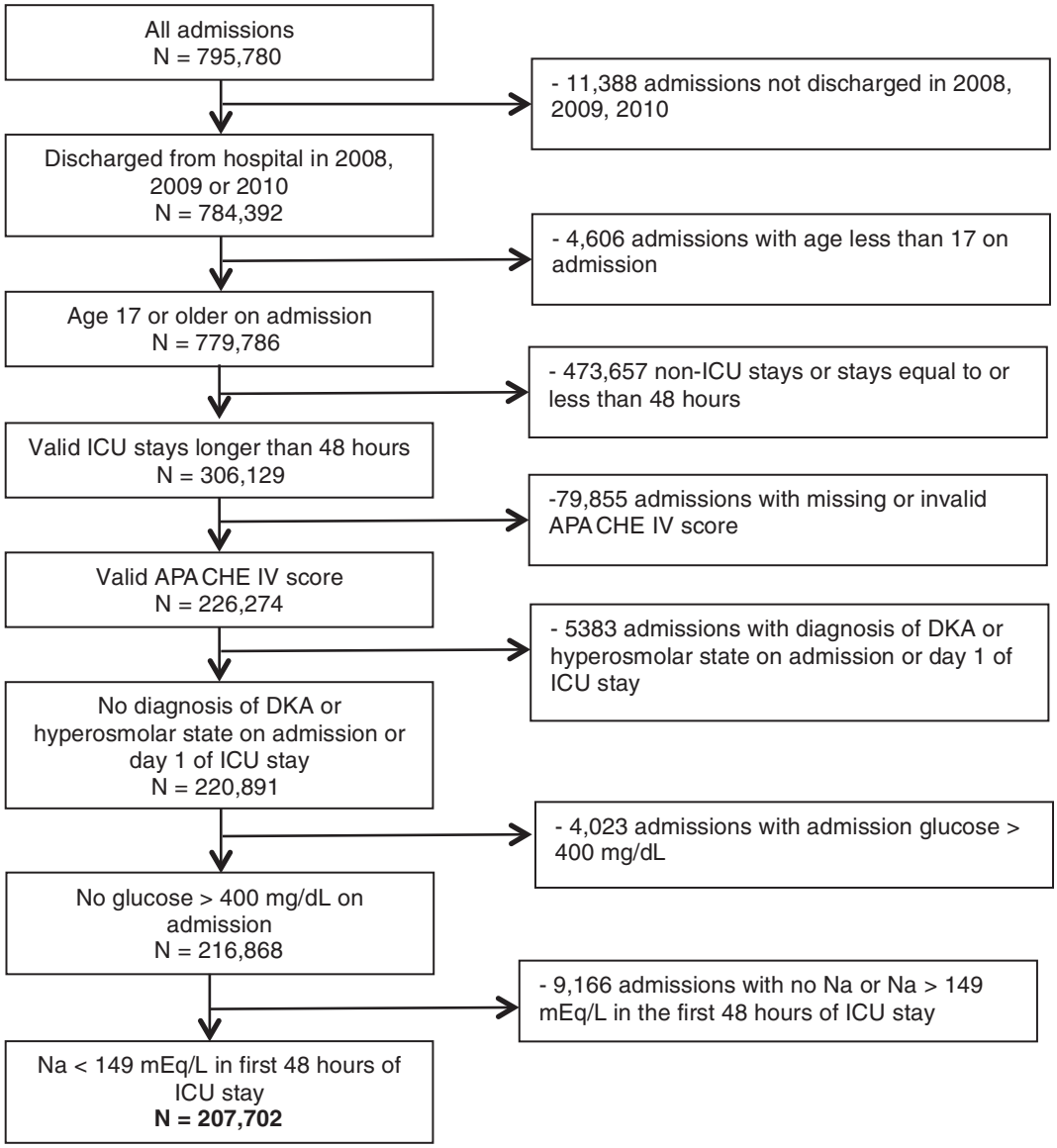

Fig. 1 Cohort inclusion diagram.

both multivariate analyses. Length of stay was truncated at 30 days to minimize the effect of outliers in the multivariate analyses.

Multivariable models were built to estimate the association between ICU-acquired hypernatremia, mortality, and ICU LOS, adjusting for potential confounders. Variable selection was based on clinical judgment as well as a model building strategy that tested the effect of including selected potential confounders on hypernatremia. Potential covariates and confounders with ICU-acquired hypernatremia were identified a priori using clinical knowledge and literature. Potential variables were included if they were known or suspected to impact the risk of hypernatremia or mortality. Factors that demonstrated differential distribution on univariate analysis were included in the multivariate models with the exception of serum lactate, which was only available in 20% of patients. These included age, sex, APACHE IV score, whether care was received at a teaching hospital, operative admission, highest glucose value, duration of temperature of 101°F or higher, highest temperature, ventilator days, ICU-acquired complications (acute kidney injury, acute respiratory failure, sepsis, and upper gastrointesinal hemorrhage), and highest serum creatinine.

A sensitivity analysis was performed that excluded patients with the following neurologic *International Classification of Diseases, Ninth Revision*, diagnostic codes: 225 (benign neoplasm of the brain), 239.6 (unspecified brain neoplasm), 320 to 349 (diseases of the central nervous system), 430 to 438 (cerebrovascular disease), and 850 to 854 (intracranial injury). This was done to address concerns that therapeutic hypertonic saline use or the development of central diabetes insipidus in this group would bias results. A second senstivity analysis was performed to study the effect of ICU LOS on the multivariate analysis by excluding patients with ICU LOS less than 6 days.

Table 1 Baseline patient characteristics

Characteristics	Hypernatremia acquired in ICU (n = 8896)	No hypernatremia during ICU stay (n = 198 806)	*P*
Age, mean (SD)	64.9 (15.8)	64.8 (16.3)	NS
Male, n (%)	5,270 (59.2)	106 572 (53.6)	<.0001
APACHE IV score, mean (SD)	76.8 (26.8)	59.5 (24.6)	<.0001
Admission source, n (%)			<.0001
Emergency department	4062 (45.7)	90 860 (45.7)	
Operating room/recovery room	1329 (14.9)	39 479 (19.9)	
Same hospital (floor, SDU, chest pain center, other ICU)	2533 (28.5)	47 890 (24.1)	
Direct admit	510 (5.7)	13 029 (6.6)	
Other hospital	462 (5.2)	7548 (3.8)	
Admission laboratories/physiology, mean (SD)			
Serum sodium (mEq/L)	138.7 ± 5.0	137.5 ± 4.6	<.0001
Serum glucose (mg/dL)	158.9 ± 63.8	148.4 ± 58.5	<.0001
Serum creatinine (mg/dL)	1.7 ± 1.4	1.6 ± 1.7	<.0001
Serum lactate (mg/dL)	2.9 ± 2.6	2.4 ± 2.4	<.0001
Temperature (°F)	98.3 ± 2.0	98.1 ± 1.6	<.0001

NS indicates nonsignificant.

All analyses were performed using SAS 9.2 software (SAS Institute, Cary, NC).

3. Results

The cumulative incidence of hypernatremia on admission through the first 48 hours of the ICU stay was 2.5% (data not shown). Of the 795 780 patients evaluated, 207 702 met the cohort entry criteria, and of those, 4.3% developed ICU-acquired hypernatremia. Baseline patient characteristics are presented in Table 1. Patients in the ICU-acquired hypernatremia group were more likely to be male and were more severely ill on admission based upon APACHE IV score. They were less likely to be admitted following an operative procedure and had significantly higher serum sodium, serum glucose, serum creatinine, serum lactate, and temperature on admission.

Table 2 Unadjusted outcomes, ICU events, and complications

Characteristics	Hypernatremia acquired in ICU (n = 8896)	No hypernatremia in the ICU stay (n = 198 806)	*P*
Maximum serum sodium (mEq/L), mean (SD)	153.0 (3.7)	140.5 (4.0)	<.0001
Time to the first sodium >149 mEq/L (d), mean (SD)	6.5 (4.9)	N/A	
Duration of sodium >149 mEq/L (d), mean (SD)	2.0 (2.0)	N/A	
Covariates			
Received care in a teaching hospital, n (%)	2486 (28.0)	45 236 (22.8)	<.0001
Operative admission diagnosis, n (%)	1425 (16.0)	40 379 (20.3)	<.0001
Maximum serum creatinine (mg/dL), mean (SD)	2.3 (1.8)	1.8 (1.9)	<.0001
Maximum serum lactate (mmol/dL), mean (SD)	3.5 (3.6)	2.7 (3.0)	<.0001
Maximum serum glucose (mg/dL), mean (SD)	279 (115.3)	211 (92.0)	<.0001
Maximum temperature (°F), mean (SD)	101.4 (1.7)	100.1 (1.5)	<.0001
Duration of temperature ≥101 °F (h), mean (SD)	41.8 (60.4)	19.3 (30.0)	<.0001
Days of mechanical ventilation, mean (SD)	8.7 (8.9)	1.8 (3.9)	<.0001
Acute renal failure as complication, n (%)	1191 (13.4)	4337 (2.2)	<.0001
Repiratory failure as complication, n (%)	464 (5.2)	1707 (0.9)	<.0001
Sepsis as complication, n (%)	570 (6.4)	2468 (1.2)	<.0001
UGI hemorrhage as complication, n (%)	131 (1.5)	555 (0.3)	<.0001
Outcomes			
ICU mortality, n (%)	1823 (20.5)	10 726 (5.4)	<.0001
Hospital mortality, n (%)	2820 (31.7)	20 779 (10.5)	<.0001
ICU LOS (d), mean (SD)	13.7 (9.7)	5.1 (4.6)	<.0001
Hospital LOS (d), mean (SD)	22.0 (17.5)	12.0 (12.2)	<.0001

UGI indicates upper gastrointestinal.

Table 3 Multivariate analysis

Variable	RR hospital mortality (95% CI)	RtR ICU LOS (95% CI)
ICU-acquired acute respiratory failure	1.91 (1.78-2.04)	1.51 (1.48-1.54)
ICU-acquired acute kidney injury	1.87 (1.79-1.95)	1.26 (1.23-1.28)
Sodium >149 mEq/L	1.40 (1.34-1.45)	1.28 (1.26-1.30)
ICU-acquired sepsis	1.39 (1.31-1.47)	1.17 (1.14-1.19)
Highest temperature	1.12 (1.11-1.12)	1.08 (1.08-1.08)
Teaching hospital	1.07 (1.04-1.10)	1.01 (1.00-1.01)
Highest creatinine	1.05 (1.05-1.06)	1.01 (1.01-1.01)
Age	1.02 (1.02-1.02)	1.00 (1.00-1.00)
APACHE IV	1.02 (1.02-1.02)	1.00 (1.00-1.00)
Ventilator days	1.01 (1.01-1.01)	1.07 (1.07-1.08)
Highest glucose	1.00 (1.00-1.00)	1.00 (1.00-1.00)
Duration of temperature ≥101°F	1.00 (1.00-1.00)	1.00 (1.00-1.00)
Female sex	0.99 (0.96-1.01)	1.00 (0.99-1.01)
ICU-acquired upper gastrointestinal hemorrhage	0.97 (0.85-1.10)	1.25 (1.19-1.31)
Operative admission	0.52 (0.50-0.54)	0.95 (0.94-0.95)

Table 2 presents patient characteristics during their ICU stay and outcomes. In this group of ICU patients with an ICU LOS more than 48 hours, most who developed hypernatremia did so in the first week of their ICU course and remained hypernatremic for 1 to 2 days. Hypernatremic patients had significantly higher maximum serum creatinine, serum lactate, serum glucose, and temperature during the ICU stay. They were also more likely to have ICU-acquired acute kidney injury, respiratory failure, upper gastrointestinal hemorrhage, and sepsis.

The unadjusted hospital mortality for patients who developed ICU-acquired hypernatremia was higher than that for those who were hypernatremic in the first 48 hours of the ICU stay (28%, data not shown) and was nearly triple that of patients who never experienced hypernatremia. Patients who developed ICU-acquired hypernatremia also had nearly triple the ICU LOS than those who did not develop hypernatremia.

Multivariate analysis (Table 3) demonstrated that ICU-acquired hypernatremia was associated with a 40% increased risk of hospital death. Only ICU-acquired respiratory failure and kidney injury increased the RR for hospital mortality to a greater degree. Patients with ICU-acquired hypernatremia had a 28% longer ICU LOS, with only ICU-acquired respiratory failure having a larger RtR. Both the RR for hospital mortality and the RtR for ICU LOS increased with increasing categories of maximum sodium when referenced to serum sodium between 135 and 145 mEq/L (Table 4). Patients with an operative admission diagnosis had a reduced risk for hospital mortality and reduced length of ICU stay.

Table 4 Multivariate analysis using maximum serum sodium

Maximum sodium (mEq/L)	RR hospital mortality (95% CI)	RtR ICU LOS (95% CI)
135 ≤ Na	1.42 (1.37-1.48)	0.88 (0.87-0.89)
135 < Na < 145	1.0 (reference)	1.0 (reference)
145 ≤ Na ≤ 149	1.28 (1.25-1.32)	1.19 (1.18-1.20)
149 < Na ≤ 155	1.46 (1.40-1.53)	1.36 (1.34-1.38)
Na > 155	2.17 (2.01-2.35)	1.38 (1.34-1.42)

*Adjusted for age, sex, APACHE IV score, whether care was received at a teaching hospital, operative admission, highest blood glucose value, duration of temperature of 101°F or higher, highest temperature, ventilator days, ICU-acquired complications (acute kidney injury, acute respiratory failure, upper gastrointestinal hemorrhage, and sepsis), and highest serum creatinine.

A significant relationship between the duration of ICU-acquired hypernatremia and mortality was not observed. Among the 8821 patients with at least 1 serum sodium concentration above 149 mEq/L, the RR of hospital mortality for every 24 hours above 149 mEq/L was 1.01 (95% confidence interval [CI], 1.00-1.02). Among the 6651 patients with at least 1 serum sodium concentration above 150 mEq/L, the RR of hospital mortality for every 24 hours above 150 mEq/L was 1.00 (95% CI, 0.98-1.02). Among the 1502 patients with at least 1 serum sodium concentration above 155 mEq/L, the RR of hospital mortality for every 24 hours above 155 mEq/L was also nonsignificant at 0.98 (95% CI, 0.94-1.03).

The sensitivity analysis excluding patients with the neurologic diagnoses did not show any significant differences regarding hospital mortality and ICU LOS when compared with the entire cohort. The results of the senstivity analysis of the cohort of patients with ICU LOS of 6 days or longer also did not show any significant differences when compared with the entire cohort.

4. Discussion

In the largest study of ICU-acquired hypernatremia to date, we demonstrated that hypernatremia greater than 149 mEq/L developed more than 48 hours after ICU admission in 4.3% of a heterogeneous population of 207 702 patients cared for in 344 ICUs across the United States. The

cumulative incidence of ICU-acquired hypernatremia in this study was at the lower range of prior studies, 4% to 8% [1,2,4-7]. However, in this population of patients with ICU LOS more than 48 hours, hypernatremia was more frequent than other ICU-acquired conditions (acute kidney injury [2.7%], respiratory failure [1.0%], sepsis [1.5%], upper gastrointestinal hemorrhage [0.3%]) for which there are common prevention strategies. In this study, hospital mortality for hypernatremic patients was 32%, and ICU LOS was 14 days, which is similar to previously published studies [1-3,6-8]. The median time to development of hypernatremia was 5 days in this study, which is similar to that of Darmon et al [2], but longer than the 3-day lag seen by O'Donoghue et al [1]. The median duration of hypernatremia in this study was 1.3 days, which is similar to the previously published durations [3,4,6,7] with the exception of the 18-hour duration seen by O'Donoghue et al [1].

Intensive care unit–acquired hypernatremia appears to be a similar clinical entity in the United States, Europe, and Australia [1-8]. Most of the variance among study results are likely due to the definition of ICU-acquired hypernatremia used (specifically, the defined time after which the condition was ICU-acquired and the level of hypernatremia required), whether means or medians were presented, and patient characteristics such as the percentage of patients who were admitted postoperatively. In this study, we defined hypernatremia as a serum sodium of greater than 149 mEq/L to allow comparison with most ICU-acquired hypernatremia literature from Europe and Australia [1,2,4-8], although we also present outcomes for milder ICU-acquired hypernatremia. We specifically planned to study only hypernatremia that developed as a complication during ICU care and thus included only that which developed 48 hours after ICU admission. Most if not all other studies have included hypernatremia, which developed earlier in the ICU course [1-8,13]. We found hypernatremia to be an independent predictor for mortality and LOS after controlling for illness severity and other ICU-acquired conditions and complications. Hypernatremia was associated with a 40% increase in risk for hospital mortality and a 28% increase in ICU LOS. The RR for hospital mortality and the RtR for ICU LOS increased with increasing severity of hypernatremia, but the duration of hypernatremia was not associated with mortality. This appears to confirm the lack of an association between the duration of hypernatremia and mortality as described by O'Donoghue et al [1]. Even a mild degree of hypernatremia (145 mEq/L $\leq$ Na $\leq$ 149 mEq/L) was associated with a 28% increase in risk for mortality and a 19% increase in ICU LOS.

In the multivariate analysis, being a surgical patient was associated with a lower risk for mortality and shorter LOS. This mortality finding was consistent with prior studies [1,7]. This may be explained by the fact that surgical patients, especially elective, often do not have the systemic derangements and severity of illness that is common in medically critically ill patients. As expected, severity of illness, fever, hyperglycemia, and other ICU-acquired complications (acute kidney injury, respiratory failure, upper gastrointesinal hemorrhage, and sepsis) were associated with increased mortality risk. All, but severity of illness, were associated with increased LOS. This can be explained by LOS being shortened by early death in more severely ill patients as seen in the APACHE IV cohort [14].

Intensive care unit patients are especially prone to hypernatremia due to their exposure to diuretics, hyperglycemia, and risk for acute and chronic renal dysfunction. In addition, nasogastric drainage, diarrhea, and fever are common in critical care patients. The risk of hypernatremia is increased when such factors are combined with critically ill patients' compromised capacity to maintain their own water intake due to sedation, mechanical or noninvasive ventilation, and altered mental status. In summary, ICU patients may be dependent on their care team to maintain appropriate water and sodium balance. It has been proposed that the development of hypernatremia is often iatrogenic, in that appropriate fluid and sodium management could prevent hypernatremia [4-6,9]. This has not been studied prospectively but offers the possiblity that increased vigilance with early detection and treatment of rising sodium levels with electrolyte-free water would allow prevention of hypernatremia and based on our findings, potentially decrease hospital mortality and ICU LOS.

With hypernatremia, failure to maintain an osmotic equilibrium leads to cellular dehydration, which may cause cellular and organ dysfunction. The development of hypernatremia is associated with neurologic, immunologic, endocrine, and musculoskeletal dysfunction [7,8,13,15]; however, neurologic compromise is often the most prominent organ dysfunction. It is becoming more evident that acute brain dysfunction in the form of delirium is associated with increased mortality and LOS [16]. It is tempting to hypothesize that the worsened outcomes seen in hypernatremic patients are related to acute brain dysfunction or delirium [13]. However, hypernatremia was not found to be a risk factor for the 11% of surgical ICU patients who developed delirium in a 2001 Turkish study [17]. Further investigations regarding the possible relationship between hypernatremia, delirium, and mortality would increase our knowledge of these disease processes.

There are several limitations to this study. As with any retrospective observational study, it is impossible to control for every source of bias. However, this study adjusted for potential confounding by restricting the analysis to patients free from hypernatremia until well after admission, by adjusting for severity of illness on admission using APACHE IV and by adjusting for hypernatremia-specific confounders as well as complications occurring later in the ICU stay, which are known to affect mortality and LOS. Another limitation is that we were not able to adjust for fluid and electrolyte management, diuretic, or hypertonic saline administration (although our findings were unchanged when a subset of neurologic patients were excluded). Finally, we were not able to adjust for delirium and acute brain

dysfunction, which is a possible mediator for hypernatremia's effects on mortality and LOS.

5. Conclusions

Intensive care unit–acquired hypernatremia developed in a significant percentage of ICU patients and was independently associated with a 40% increase in hospital mortality and a 28% increase in ICU LOS. Our findings suggest that the risk of mortality increases with severity of hypernatremia, but not with increasing duration at respective serum sodium concentrations. Opportunity for prevention of hypernatremia may exist through increased vigilance, early detection of an increasing trend in serum sodium, and treatment with electrolyte-free water. A prospective study evaluating this premise, which addresses fluid, water, and sodium balances as well as the relationship between hypernatremia, acute brain dysfunction, and delirium, is warranted.

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Appendix A. Definitions of ICU-acquired conditions

1. ICU-acquired respiratory failure

Patient ICU stays are counted as having ICU-acquired respiratory failure if they meet the following criteria:

Patient stays are excluded from consideration for ICU-acquired respiratory failure if any of these criteria are present: a primary admission diagnosis associated with respiratory failure and a diagnosis of respiratory failure that occurs less than or equal to 48 hours after ICU admission.

The patient has a new diagnosis indicating respiratory failure that occurs more than 48 hours after ICU admission AND the patient has evidence of mechanical ventilation more than 48 hours after ICU admission.

2. ICU-acquired renal injury

Patient ICU stays are counted as having ICU-acquired renal injury if they meet the following criteria:

The patient has evidence of renal injury more than 72 hours after ICU admission that was not present during the first 72 hours of the ICU stay. Evidence of new renal injury comes from documentation of diagnoses and laboratory values.

Patients are excluded from consideration for ICU-acquired renal injury if any of the following criteria are present: any diagnosis related to acute renal failure or dialysis documented with the first 72 hours of the ICU stay, medical history of chronic renal failure, or a baseline serum creatinine value greater than 530.4 μmol/L (6 mg/dL).

Patients are included by diagnosis criteria if there is any diagnosis related to acute renal failure or dialysis documented more than 72 hours after ICU admission.

Patients are included by laboratory criteria if the patient has either (1) a creatinine value greater than or equal to 2 times the baseline creatinine AND greater than 141.4 μmol/L (1.6 mg/dL) or (2) a creatinine value that increased greater than 176.8 μmol/L (2 mg/dL) over the baseline value.

3. ICU-acquired upper gastrointestinal hemorrhage

Patient ICU stays are counted as having ICU-acquired upper gastrointestinal (GI) hemorrhage if they meet the following criteria:

The patient has evidence of an upper GI hemorrhage more than 48 hours after ICU admission that was not present during the first 48 hours of the ICU stay. Evidence of a new upper GI hemorrhage comes from documentation of diagnoses and laboratory values.

Patients are excluded from consideration for ICU-acquired upper GI hemorrhage if any of the following criteria are present: admission diagnosis of upper GI hemorrhage or an active diagnosis of upper GI hemorrhage within the first 48 hours of the ICU stay.

Patients are included as having an ICU-acquired upper GI hemorrhage if they had an active diagnosis of upper GI Hemorrhage occurring more than 48 hours after ICU admission, and there was evidence of active hemorrhage defined by at least 1 U of blood transfused or at least 10 g/L (1 g/dL) drop in hemoglobin level within 36 hours of the diagnosis.

4. ICU-acquired sepsis

Patient ICU stays are counted as having ICU-acquired sepsis if they meet the following criteria:

The patient has evidence of sepsis more than 48 hours after ICU admission that was not present during the first 48 hours of the ICU stay.

Patients are excluded from consideration for ICU-acquired sepsis if they had either an admission diagnosis of sepsis or an active diagnosis of sepsis within the first 48 hours of the ICU stay.

Patients are included as having ICU-acquired sepsis if they had a diagnosis of sepsis that occurred more than 48 hours after ICU admission.

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