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Plasma sodium during the recovery of renal function in critically ill adult patients: Multicenter prospective cohort study

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ABSTRACT

Background: Sodium increases during acute kidney injury (AKI) recovery. Both hypernatremia and positive fluid balances are associated with increased mortality. We aimed to evaluate the association between daily fluid balance and daily plasma sodium during the recovery from AKI among critical patients.
Methods: Adult patients with AKI were enrolled in four ICUs and followed up for four days or until ICU discharge or hemodialysis initiation. Day zero was the peak day of creatinine. The primary outcome was daily plasma sodium; the main exposure was daily fluid balance.
Results: 93 patients were included. The median age was 66 years; 68% were male. Plasma sodium increased in 79 patients (85%), and 52% presented hypernatremia. We found no effect of daily fluid balance on plasma sodium (β −0.26, IC95%: −0.63–0.13; $p = 0.19$). A higher total sodium variation was observed in patients with lower initial plasma sodium (β −0.40, IC95%: −0.53 to −0.27; $p < 0.01$), higher initial urea (β 0.07, IC95%: 0.04–0.01; $p < 0.01$), and higher net sodium balance (β 0.002, IC95%: 0.0001–0.01; $p = 0.05$).
Conclusions: The increase in plasma sodium is common during AKI recovery and can only partially be attributed to the water and electrolyte balances. The incidence of hypernatremia in this population of patients is higher than in the general critically ill patient population.

1. Introduction

Intensive care-acquired hypernatremia is usually managed with a positive fluid balance [1]. However, extensive evidence indicates that overly positive fluid balances are associated with intensive care unit (ICU) morbidity and mortality [2-4]. Hypernatremia is common in patients admitted to the ICU and is an independent risk factor for in-hospital morbidity and mortality [5-11]. Common causes of hypernatremia in critically ill patients include lack of access to water, osmotic diuresis, and hypotonic losses [12].

Hypernatremia has also been reported during the recovery from acute kidney injury (AKI), likely within the context of sodium overload during the initial fluid resuscitation [13-15]. This phenomenon may be explained by an impairment in the kidney's urine concentration capacity [15,16]. However, current evidence on this subject is restricted to case reports, case series, and retrospective studies [12]. Additionally, patients recovering from AKI have a reduced capacity to concentrate urine and may not benefit from positive fluid balances [15,17].

In this prospective cohort study, we sought to describe: 1) the trends in plasma sodium in critical care adult patients recovering from AKI, and 2) the impact of fluid balances on plasma sodium. We hypothesized that there is an association between fluid balances and sodium trends during kidney recovery. As a secondary objective, we aimed to describe the incidence and risk factors for plasma sodium increase and hypernatremia during the recovery from acute kidney injury.

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2. Materials and methods

2.1. Design, setting, and population

In this longitudinal study, patients were consecutively enrolled from four mixed medical and surgical ICUs from Buenos Aires, Argentina, from March 2019 to February 2020. Enrolment was interrupted in March 2020 due to the COVID-19 pandemic. All patients over 18 years old admitted to the ICU with acute kidney injury or who developed their first acute kidney injury episode during an ICU stay were consecutively included. Acute kidney injury was defined according to KDIGO guidelines [18]. Exclusion criteria were based on coexisting conditions that could interfere with fluid and sodium management, such as: preexisting chronic kidney disease, pregnancy or puerperium, burns compromising over 20% of the total body surface, open abdomen with temporal closure technique, central nervous system pathology, acute or chronic treatment with antidiuretic hormone or antidiuretic hormone analogs.

This study was approved by all local ethics boards and was developed according to the *World Medical Association's Declaration of Ethical Principles for Medical Investigations in Humans of Helsinki* and its posterior amendments [19]. All data were de-identified at the moment of collection and were kept under complete confidentiality, with access restricted only to the principal investigator, following current legal regulations in Argentina: *National Law on Protection of Personal Data 25,326/00 (Habeas Data Law)* [20], and *Law on Patient's Rights, Clinical Records, and Informed Consent 26,529 /09* [21]. Since this observational study did not interfere with usual care, the need for informed consent was waived.

2.2. Patients' follow-up and measured variables

The main exposures of interest were daily net fluid balance and net cumulative fluid balance, calculated as the difference between enteral and parenteral intake of fluids and urine output (supplementary material eTable 1; Eq. 1). Insensitive fluid losses were not considered. The main outcomes of interest were daily plasma sodium and total sodium variation during the follow-up period (ΔNap), calculated as the difference between plasma sodium at index day and the last follow-up day (supplementary material eTable 1; Eq. 2).

Age, gender, cause of acute kidney injury, and Acute Physiology and Chronic Health Evaluation (APACHE) II [22] at the time of ICU admission were registered upon enrolment. Index day (day 0) was the day with the peak plasma creatinine during the acute kidney injury episode.

We also captured information on daily plasma measurements in morning routine lab workup, including plasma sodium, plasma potassium, plasma chloride, plasma urea, and plasma creatinine (measurement method and equipment used are detailed in the supplementary material eTable 2). Daily 24-h urine measurements such as urine sodium, urine potassium, urine urea, and urine creatinine (measurement method and equipment used are detailed in the supplementary material eTable 2) were also assessed. Measurements also included daily fluid intake and output (i.e., oral, enteral, and intravenous fluid intake between 8 a.m. and 7:59 a.m. the following day was registered as daily fluid intake; diuresis between 8 a.m. and 7:59 a.m. the next day was recorded as daily fluid output). Finally, we calculated daily numeric variables such as fluid balances (insensitive losses not considered), cumulative net change in plasma sodium, and cumulative net change in plasma creatinine (Supplementary material eTable 1; eqs. 2 and 3). Additionally, we calculated electrolyte-free urinary water clearance, sodium balances, and potassium balances (Supplementary material eTable 1. - eqs. 4–6).

Patients were followed up during the recovery of renal function. We defined renal function recovery as the period between the index date (day 0) and the return of plasma creatinine to baseline levels. All the aforementioned variables were measured daily until the recovery of the renal function, or one of the following censoring criteria was met: a) the occurrence of a new AKI episode defined as a new increase in creatinine according to KDIGO guidelines criteria [18]; b) requirement of renal replacement therapy; c) requirement of muscle mass resection (limb amputation, muscle group resection); d) ICU discharge.

2.3. Statistics

Summary statistics were reported as mean and standard deviation (SD) for normally distributed continuous variables; median and 25–75 interquartile range (IQR) for non-normally distributed variables; frequencies and percentages for categorical and dichotomous variables. To estimate the effect of the daily water balance on the daily serum sodium, we used a generalized linear mixed model (GLMM), including time as a covariate, with a normal probability distribution function, an identity link, and a random intercept to account for the repeated measures. Additionally, with generalized estimating equations (GEE), we evaluated the trends of serum sodium over time and the changes in trends associated with sex, age, and ICU mortality.

ΔNap was calculated as detailed in eTable 1 – eq. 2. Using ΔNap as the outcome variable, we fitted a linear regression model to evaluate the determinants of sodium variation during the follow-up period. Additionally, a one-way ANOVA was conducted using AKI etiology (septic, post-operative, or other) as the explanatory factor.

We calculated the percentage of missing data through data visualization and descriptive statistics and subsequently performed a generalized linear model analysis on data imputed through a 10-fold multiple imputation process. This sensitivity analysis included daily fluid balance and time as predictors, with daily plasma sodium levels as the outcome variable.

We defined 0.05 as the level of statistical significance. The summary estimates of the models were reported as the mean difference in the outcome for every predictor unit, alongside 95% confidence intervals (CI). All the analyses were performed with Stata 16.1 (Copyright 1985–2019 StataCorp LLC).

3. Results

Of 2876 patients screened for eligibility between March 2019 and February 2020, 542 patients met inclusion criteria, of whom 413 were excluded, mainly due to pre-existing chronic kidney disease (53.5%). Finally, 129 patients were enrolled, and 93 had complete data and were included in the final analysis (Fig. 1). More than half of the patients were males (67.7%), and the median age was 66 [IQR: 54.5–78.0] years old. The leading cause of acute kidney injury was sepsis (47.8%) (Table 1). According to the classification of the 2012 KDIGO guidelines [18], 41 patients (44%) reached stage 1 of AKI, 33 patients (36%) stage 2, and 19 patients (20%) stage 3. Peak urea concentrations and creatinine in the general patient population were 18 ± 8.7 μmol/l and 196 ± 86 μmol/l, respectively. The clinical and epidemiological characteristics of the study population, the biochemical variables, and the water and electrolyte balances are shown in Table 1.

A significant increase in plasma sodium was observed during the recovery of renal function (Fig. 2 A and B). The mean increase was 2.14 mmol/l of plasma sodium per day (95% CI: 1.82–2.47; $p < 0.01$). The plasma sodium increased in 79 of the 93 patients studied (85%). In this group, the mean ΔNap was 6.7 ± 3.9 mmol/l (Table 1). ΔNap levels >5, 10, and 15 mmol/l were observed in 56, 15, and 4% of the patients, respectively (supplementary eFigure 1). More than half of the patients (52%) reached sodium levels >145 mmol/l, while almost a third of the patients (27%) reached levels >150 mmol/l (Table 1).

The daily fluid balance was not associated with the daily plasma sodium (β −0.26, 95% CI: −0.63 - 0.13; $p = 0.19$) (Table 2). We did find a weak association between the urine output and daily plasma sodium (β 0.61, 95% CI: 0.15–1.1; $p \leq 0.01$). The four-day ΔNap was not associated with the cumulative fluid balance (β 0.04, 95% CI: −0.21–0.31; $p = 0.72$) (Fig. 3 and eTable 3 of the Supplementary material). The AKI

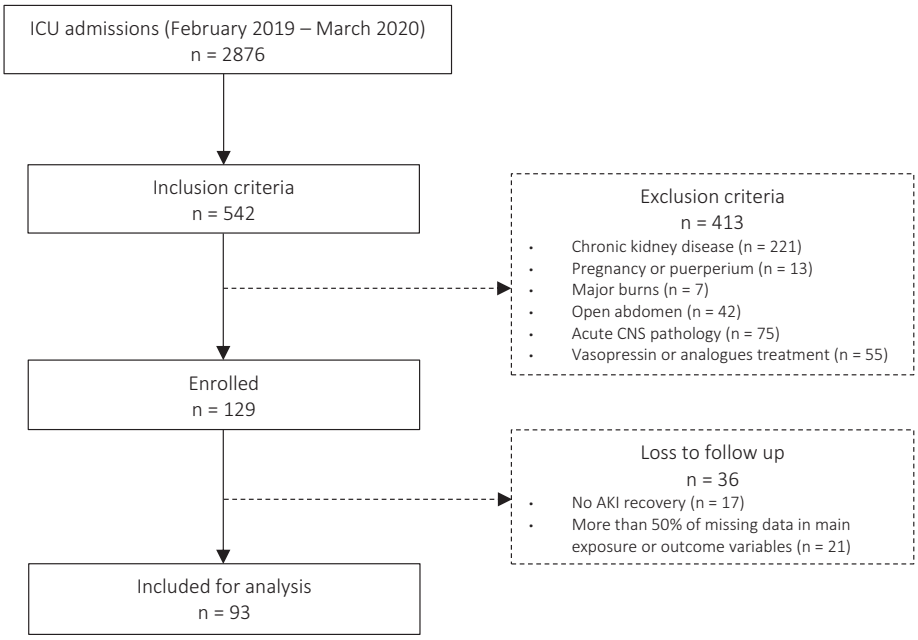

Fig. 1. Flow diagram for study participants.

Table 1
Demographic baseline characteristics and summary of the follow-up period.

Epidemiologic and clinical characteristics	
Age – years (median, IQR)	66 (55–78)
APACHE at ICU admission (mean, SD)	18.7 ± 7.3
Female sex – n (%)	30 (32)
Mortality – n (%)	11 (13)
AKI stage – n (%):	
- I	41 (44)
- II	33 (36)
- III	19 (20)
AKI etiology – n (%):	
- Sepsis	45 (48)
- Post-operative	22 (24)
- Other	26 (28)
Hypernatremia >145 mmol/l – n (%)	48 (52)
Hypernatremia >150 mmol/l – n (%)	25 (27)
4-day sodium net change – mmol/l (mean, SD)	5.3 ± 4.9
4-day urea net change mmol/l (mean, SD)	−2.4 ± 6.5
4-day creatinine net change (mean, SD)	−75 ± 68
Urine output ml/24 h (mean, SD)	2311 ± 1395
Fluid intake ml/24 h (mean, SD)	3008 ± 1268
Sodium intake mmol/24 h (mean, SD)	306 ± 171
Potassium intake mmol/24 h (mean, SD)	42 ± 44
Net fluid balance ml/24 h (mean, SD)	696 ± 1645
Net sodium balance mmol/24 h (mean, SD)	102 ± 261
Net potassium balance mmol/24 h (mean, SD)	−30 ± 64

etiology was not found to be a significant predictor of ΔNap (one-way ANOVA, F(2,91) = 1.28; $p = 0.28$).

No differences were observed in the baseline plasma sodium concentrations (eTable 4 of the Supplementary material) and in the trend of sodium increase between men and women (interaction term p-value: 0.16), between patients below or over 65 years old (interaction term p-value: 0.53), between survivors and non-survivors (interaction term p-value: 0.90), nor between different stages of AKI reached (interaction term p-value: 0.83). The fluid and electrolyte intake and output in the general population are summarized in Table 3 and eFigure 2 of the Supplementary material.

In the multivariate analysis, the independent predictors of ΔNap were a lower plasma sodium at day 0 (β −0.40, 95% CI: −0.53 to −0.27; $p < 0.01$), a higher plasma urea at day 0 (β 0.07, 95% CI: 0.04–0.01; p < 0.01), and a higher net sodium balance during follow-up (β 0.002, 95% CI: 0.0001–0.01; $p = 0.05$) (Table 4).

During follow-up, the daily mean concentration of cations in urine (sodium + potassium in urine) was lower than plasma sodium (Fig. 4). The median calculated urine osmolality was 283 mOsm/Kg (25–75 IQR: 228–344 mOsm/Kg) at day 0, which increased in the following days mostly due to urea contribution. The urine sodium and urine potassium remained relatively constant during the study period (Fig. 5).

We found 13% of missing at random data in the variable net daily fluid balance. The sensitivity analysis addressing this missing data with 10-fold multiple imputations also showed no association between net daily fluid balance and daily plasma sodium (supplementary eTable 5).

4. Discussion

This study found that adult critically ill patients with AKI present an increase in plasma sodium during the recovery of renal function. Our study also shows that a high percentage of patients present hypernatremia; and that these changes in plasma sodium cannot be fully explained by water and electrolyte balances.

Several studies have shown an association between ICU-acquired hypernatremia and increased mortality, longer hospital stays, and increased use of health resources [7,11,15,23-25]. The reported incidences range from 3 to 17%, depending on the population studied and the sodium threshold used to define it [7,23,26,27]. We considered a plasma sodium equal to or >145 mmol/l to define hypernatremia because levels higher than these have been associated with a worse prognosis [23]. Although AKI has been proposed as a risk factor for developing hypernatremia in the ICU [14], the incidence of hypernatremia in critically ill patients with AKI has not been studied. In this sense, our study is novel by showing that 52% of patients with AKI developed hypernatremia, and 27% reached levels higher than 150 mmol/l. These findings demonstrate a higher incidence of hypernatremia in critically ill patients recovering from AKI than that reported by studies conducted in heterogeneous populations of critically ill patients [7,23,26,27].

Several large population-based studies found that variations in plasma sodium, even within normal levels, were independently associated with ICU and in-hospital mortality [11,24,25,28]. We observed increases in plasma sodium >10, 15, and 20 mmol/l in 35, 14, and 7% of

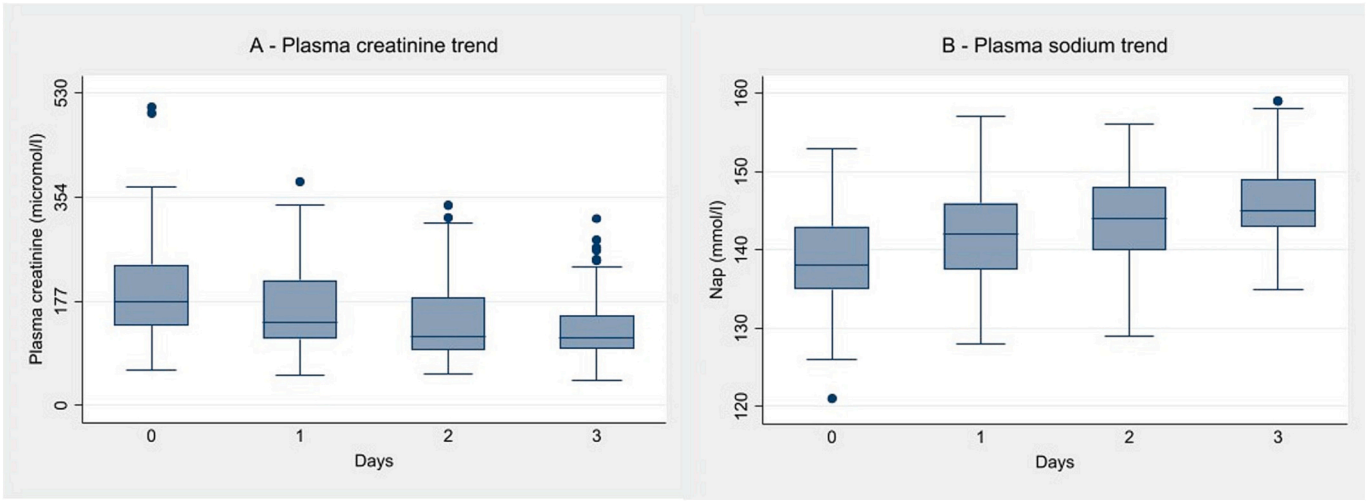

Fig. 2. Trends of plasma sodium (Nap) and plasma creatinine during follow-up.
A: Daily trends in plasma creatinine reflecting renal function recovery. B: Daily trends in plasma sodium reflecting the daily increase in its levels. (Nap = plasma sodium, micromol/l = micromol per liter, mmol/l = millimole per liter).

Table 2
Analysis of daily fluid balance on daily plasma sodium.

Predictor	Mean estimate change in daily Nap (95% CI)	*p* value
Net daily fluid balance (l/24 h)	−0.26 (−0.63–0.13)	0.19
Time (days)	2.18 (1.53–2.83)	< 0.01

Impact of net daily fluid balance on daily plasma sodium estimated through generalized linear model with time included as an independent variable. (Nap = plasma sodium).

patients, respectively. We also identified seven patients whose sodium increased dangerously, averaging 4 mmol/day. Similar increases were observed by *Sam* et al. in a retrospective cohort of 20 patients with advanced stages of AKI who developed hypernatremia in the post-AKI period. The authors found a daily increase in plasma sodium of 5–8 mmol/l per day, which meant a final rise of 17 mmol/l during recovery. These findings reinforce the importance of monitoring the plasma sodium slope in this group of patients [16].

Historically, ICU-acquired hypernatremia was considered an iatrogenic problem caused by a water deficit, excessive sodium intake, or a combination of both [1,29-37]. However, some authors suggest that other more complex factors may influence changes in sodium over time [38-43]. Our findings align with this last hypothesis, showing that the daily water and sodium balances do not fully explain the daily variation in plasma sodium. Nevertheless, we observed a weak association between the accumulated sodium balance during the recovery of renal function and sodium changes. Recently, a prospective study conducted in a heterogeneous population of critically ill patients showed that the cumulative balance of sodium during the first days of hospitalization was independently associated with the development of hypernatremia [15]. The authors argue that the renal inability to excrete sodium and the high sodium load during initial resuscitation account for this sodium increase. In line with these findings, we also observed an inability of the kidney to eliminate sodium with the excretion of persistently low concentrations of cations in urine despite the increase in plasma sodium levels. In this sense, restricting sodium intake after renal injury could be a positive intervention to prevent or avoid hypernatremia in this group of patients.

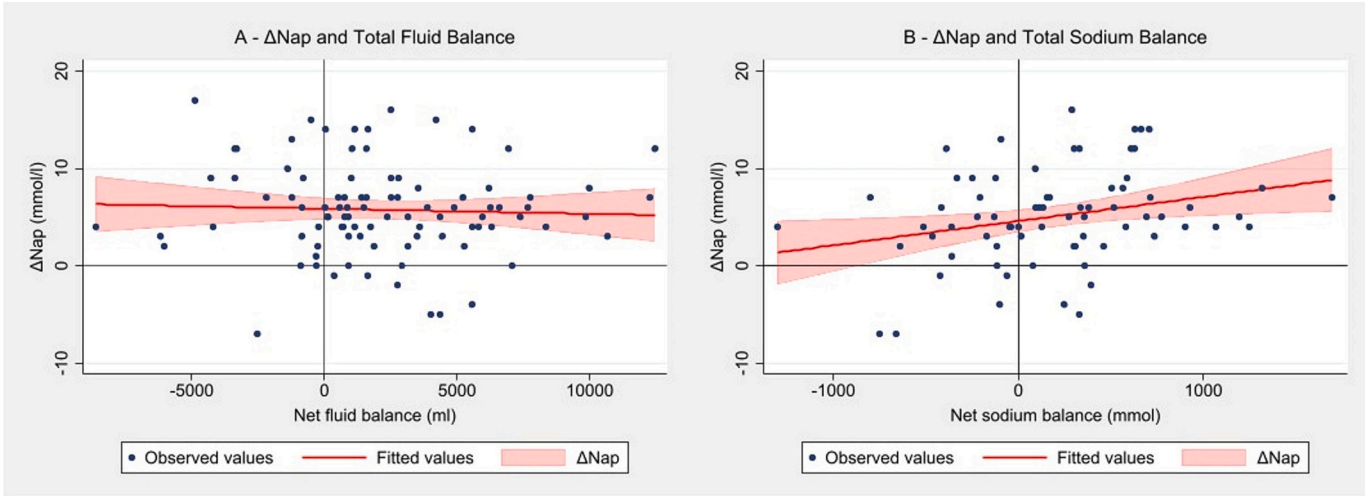

Fig. 3. Relationship between sodium variation and fluid and sodium balances.
A: Scatter plot of four-day plasma sodium net change (ΔNap) vs. four-day net fluid balance. B: Scatter plot of four-day plasma sodium net change (ΔNap) vs. four-day net sodium balance.

Table 3
Trends of the intake, output, and balances of both fluids and sodium during the follow-up.

	Day 0	Day 1	Day 2	Day 3
Fluid intake 24 h (ml) median, IQR 25–75	3167 (2555–4082)	2602 (2250–3599)	2786 (1917–3572)	2800 (1977–3776)
Sodium intake 24 h (mmol) median, IQR 25–75	330 (240–460)	286 (195–386)	252 (170–390)	241 (156–380)
Urine output 24 h (ml) median, IQR 25–75	1490 (925–2425)	2000 (1500–2900)	2200 (1500–2990)	2200 (1513–3225)
Urine sodium 24 h (mmol) median, IQR 25–75	53 (38–92)	67 (35–104)	73 (31–105)	90 (48–118)
Net fluid balance 24 h (ml) mean, SD	1599 ± 1547	674 ± 1702	422 ± 1588	392 ± 1503
Net sodium balance 24 h (mmol) mean, SD	191 ± 222	125 ± 257	93 ± 272	40 ± 261

Table 4
Multivariate analysis with 4-day sodium net change (ΔNap) as the outcome variable.

Predictor	Mean estimate change in ΔNap (95% CI)	p value
Net sodium balance (mmol/4-day follow-up)	0.002 (0.0001–0.001)	0.05
Plasma urea at day 0 (mmol/l)	0.068 (0.042–0.010)	<0.01
Plasma sodium at day 0 (mmol/l)	−0.400 (−0.525 to −0.274)	<0.01
Constant	56.584 (39.126–74.042)	<0.01

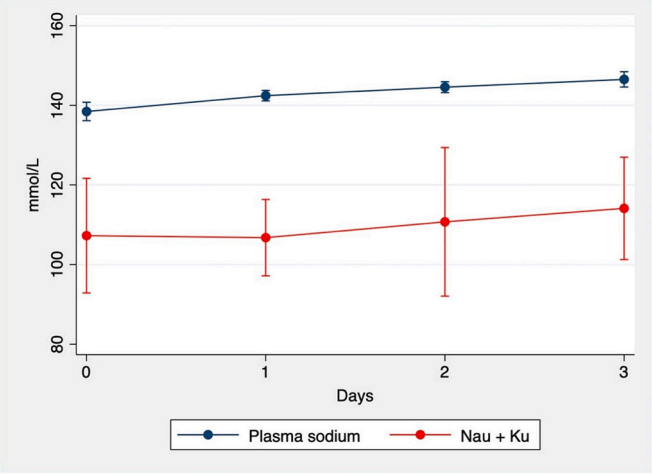

Fig. 4. Comparison of trends in plasma sodium and urine cations.
The daily mean concentration of cations in urine (Nau + Ku) was lower than the plasma sodium at all time points. Urine cations = Urine sodium + urine potassium; Nau = urine sodium; Ku = urine potassium.

In our study population, the plasma urea concentration at the onset of renal function recovery was an independent determinant of plasma sodium variability during the post-AKI period. The osmotic diuresis generated by urea and its competition with urinary cations for its

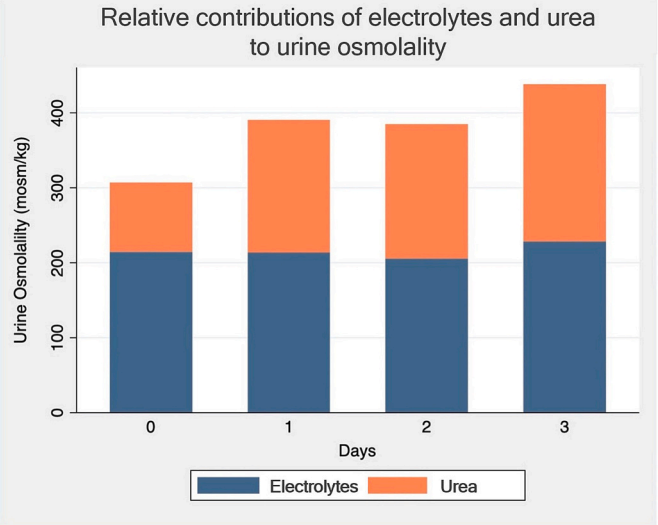

Fig. 5. Relative contributions of urine electrolytes and urine urea to the calculated urine osmolality.
Calculated urine osmolality trend and the relative components of its formula. The electrolyte component of urine (Nau, Ku, and their accompanying anions) remained relatively constant throughout the days, while the urine urea was the main contributor to the urine osmolality increase (mosm/kg = milliosmoles per kg; Electrolytes = urine sodium + urine potassium + anions; Urea = urine urea).

elimination could explain this association, which was more evident in those patients with higher plasma urea concentrations. In a cohort of critically ill patients who developed hypernatremia during AKI recovery, *Sam* et al. observed that the average urinary osmolarity measured was 373 ± 122.9 mmol/kg and that 42% of the urinary osmoles corresponded to urea and creatinine while sodium and potassium represented only 22% of the total urine osmolarity [16]. Although we calculated urinary osmolality instead of measuring it, the findings were similar to *Sam* et al.'s. The average osmolarity was 394 ± mmol/Kg, 46% of the osmoles corresponded to urea, and only 27% corresponded to urinary electrolytes. Additionally, we observed that the percentage of urea contribution to urinary osmolarity increased during the AKI recovery, while that of urinary electrolytes did not change. These findings, albeit speculative, suggest that sodium may act as a competitor with urea and other osmoles for excretion in urine. Given that urine osmolality during this period is relatively constant (either isoosmolar or slightly hyperosmolar compared to plasma) and considering urea constitutes 47% of the total urinary osmoles, there is limited capacity for sodium and potassium, along with their associated anions, to contribute significantly to urine osmolality. This hypothesis aligns with observations made by another researcher [16].

Unlike the behavior of urea, lower plasma sodium levels on day 0 showed a more significant increase in sodium during the recovery period. The low sodium levels of these patients may express greater disease severity with a more accentuated initial state of 'anti-diuresis.' At the time of recovery of renal function, the increase in diuresis and the renal inability to concentrate urine might expose these patients to a further increase in plasma sodium concentrations. However, the inverse relationship observed between sodium on day 0 and its subsequent variability was maintained after adjusting for APACHE. In any case, this finding should be interpreted with caution since, as it is an observational study, it is likely that those patients with lower plasma sodium levels at the beginning of the recovery of renal function have not been monitored as closely as patients with higher sodium levels, who may have received more interventions to prevent hypernatremia.

As we mentioned, the concentration of excreted cations (urine sodium + potassium) remained at all times below plasma sodium

concentrations, showing some renal difficulty in eliminating them, even in hypernatremia. This finding has already been suggested by different authors who posited this mechanism as the main culprit for developing hypernatremia in AKI recovery [44,45]. In this sense, the calculation of electrolyte-free water clearance has been suggested as the indicator that best explains the hypernatremia induced by osmotic diuresis in the recovery of AKI [46,47]. Electrolyte-free water clearance, when positive, indicates a larger loss of water than electrolytes in urine, which means an increase in plasma sodium. Conversely, when its value is negative, it indicates free water gain, which will tend to decrease plasma sodium. In the subgroup of patients where the electrolyte-free water clearance was calculated, we found that it was and remained positive throughout the study period. However, it was not associated with sodium changes. This non-significant outcome may be the result of a limited sample size. From a pathophysiological point of view, electrolyte-free water clearance should be monitored during renal function recovery to understand, prevent, and treat unwanted sodium increases. The administration of an amount of water equal to that excreted as electrolyte-free water should prevent further increases and help return its levels to normal.

Finally, the pathophysiological mechanisms are likely to generate the increase in sodium in the recovery of renal function and have their highest expression in patients with more severe forms of AKI. Indeed, the studies that found this association included patients with advanced stages of renal dysfunction [15,16]. Unlike the patients in those studies, 70% of our patients presented mild and moderate forms of AKI (KDIGO I and II), and only 30% developed severe forms (KDIGO III). Based on our findings, we can infer that the pathophysiological mechanisms that raise plasma sodium are present in both severe and mild AKI stages. This finding is relevant given that mild forms of AKI are the most frequent in critically ill patients [48,49].

Our study has several limitations. First, the recruitment had to be suspended due to the implementation of COVID-19 safety protocols in the ICUs, and it was not possible to reach our planned sample size during protocol development. However, we were able to observe trends and results similar to other studies. Second, many potential confounding variables considered a priori could not be measured (mechanical ventilation, fever, diuretic administration, corticosteroid treatment), so the associations between plasma sodium and water balances could not be adjusted for these variables. This limitation may imply that the magnitude of the observed associations would be different if these variables had been included in the analysis. However, as mentioned above, our study's trends and results align with other researchers' observations. Third, insensible sweat and fecal losses were not quantified and, therefore, were not considered in the calculations of water and electrolyte balances, which may have generated some imprecision in the estimation of the balances in some patients. Fourth, urinary measurements of electrolytes, urea, and creatinine, as well as their derived calculations, were not performed in all patients, which may have limited the statistical power in the analysis of the mechanisms associated with sodium behavior. Lastly, as previously stated, our cohort mainly exhibited mild and moderate forms of AKI. In this sense, a prospective study that includes more patients with more advanced stages of AKI (KDIGO III) may improve the analysis and understanding of plasma sodium variations in these patients.

In clinical practice, our findings offer valuable insights for the early prevention and treatment of hypernatremia in critically ill patients recovering from AKI. For prevention, it is crucial to exercise caution at all stages of AKI, given that 70% of our patients presented with mild to moderate AKI (KDIGO I and II), whereas only 30% had severe forms (KDIGO III). Furthermore, vigilance is warranted even during periods of clinical improvement. Our study reveals that increases in plasma sodium levels and the onset of hypernatremia often coincide with the phase when the patient's creatinine levels, and urine output are normalizing. Therefore, monitoring plasma sodium diligently and identifying trends toward hypernatremia, especially in patients at higher risk, such as those with elevated plasma urea and lower sodium levels during kidney injury, becomes imperative.

Regarding treatment, the approach to a patient becoming hypernatremic involves a comprehensive evaluation of electrolytes, fluid balances, and osmotic loads on the kidneys. This entails promptly reducing the sodium and potassium load being administered and adjusting fluid therapy in accordance with the patient's daily electrolyte-free water clearance. Additionally, in the case of excessive urea generation, it might be useful to reduce the amount of protein intake and to be cautious in detecting situations that might develop hypercatabolism, such as infections, gastrointestinal bleeding, or the use of corticosteroids. Concurrently, monitoring blood glucose levels is essential to prevent the additional osmotic loading from glucose in the urine.

5. Conclusion

During AKI recovery, increased plasma sodium concentrations and a high incidence of hypernatremia were observed. These findings can only partially be attributed to the water and electrolyte balances recorded in this period. However, the most significant increases in plasma sodium can be expected in patients who, at the time of recovery of renal function, have higher plasma urea concentrations and lower sodium levels.

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Authorship and contributions

Angeloni NA served as the primary investigator and project coordinator. Together with Masevicius FD, they were instrumental in designing and planning the study. Outi I, Alvarez MA, Sterman S, and Fernandez Morales J were pivotal as responsible investigators at each of the participating centers, overseeing team coordination, data collection, and ensuring data quality control. The data analysis and interpretation were conducted by Angeloni NA and Masevicius FD. Additionally, Masevicius FD made significant contributions through major revisions and provided expert insights. All authors were actively involved in the critical revision of the manuscript and have given their approval for the final version to be published.

CRediT authorship contribution statement

Natalia Alejandra Angeloni: Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Validation, Writing – original draft, Writing – review & editing. **Irene Outi:** Data curation, Supervision, Validation. **Monica Alejandra Alvarez:** Data curation, Validation, Visualization. **Sofia Sterman:** Data curation, Validation. **Julio Fernandez Morales:** Data curation, Validation. **Fabio Daniel Masevicius:** Investigation, Methodology, Resources, Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The Authors of this study declare that there is no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcrc.2024.154544.

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