

# Association of Hypochloremia with Mortality among Patients Requiring Continuous Renal Replacement Therapy

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#### **BACKGROUND**

- Chloride is the most abundant anion in the extracellular fluid that plays a critical role in regulating plasma osmolarity, acid-base balance and electroneutrality in the human body [1].
- Hypochloremia and hyperchloremia have been associated with increased risk of mortality in study populations such as peritoneal dialysis patients, hospitalized patients, critically ill patients, and cardiac intensive care unit patients.
- However, there is a lack of literature on whether dyschloremia is associated with mortality after initiation of Continuous renal replacement therapy (CRRT) in patients with AKI.

# **OBJECTIVES**

 Hence, this study aimed to assess the associations of serum chloride before and during CRRT on mortality among critically ill patients with AKI requiring CRRT.

# **METHODS**

- **Design:** Single center, retrospective cohort study.
- Inclusion Criteria: Adult patients admitted to the ICU from December 2006 to November 2015 who received CRRT for AKI for at least 24 hours were included.
- Exclusion Criteria: Patients were excluded if they had history of endstage kidney disease or received any dialysis modalities within 7 days before CRRT initiation, died within 24 hours of CRRT initiation and did not provide research authorization.
- CRRT: Continuous venovenous hemofiltration was the standard CRRT modality performed in our hospital.
- Data Collection: Clinical characteristic, treatment, and laboratory data were abstracted from hospital and ICU electronic databases. The primary predictors were serum albumin measured within ±24 h of CRRT initiation. The normal reference range for serum chloride was 99-108 mmol/L.
- Statistics: We used logistic regression to assess 1) serum chloride before CRRT, and 2) mean serum chloride during CRRT as predictors for 90-day mortality after CRRT initiation.

#### **RESULTS**

- Out of 1758 ICU patients who underwent CRRT during the study period, 1282 eligible patients were included in the analysis.
- The mean age was 61±15 years, 59% (n=759) were male, and 88% (n=1,112) were Caucasian.
- 73% and 67% received mechanical ventilation, and vasopressors, respectively, at CRRT initiation.
- The median duration of CRRT was 6 (IQR 4–10) days.
- The mean serum chloride before CRRT was 103±7 mmol/L. Before CRRT, serum chloride levels of ≤98, 99-108 and ≥109 mmol/L were noted in 25% (n=324), 50% (n=644), and 25% (n=314) of patients, respectively.
- During CRRT, the mean serum chloride was 106±4 mmol/L. During CRRT, serum chloride levels of ≤98, 99-108, ≥109 mmol/L were noted in 4% (n=54), 70% (n=892), and 26% (n=336) of patients, respectively.

# **FIGURE 1:** Restricted cubic spline of the association between serum chloride before CRRT and 90-day mortality

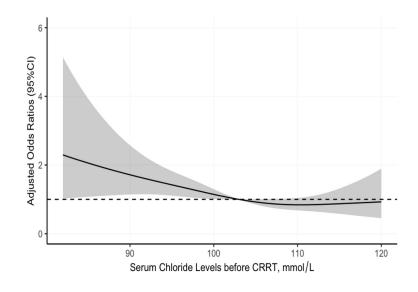
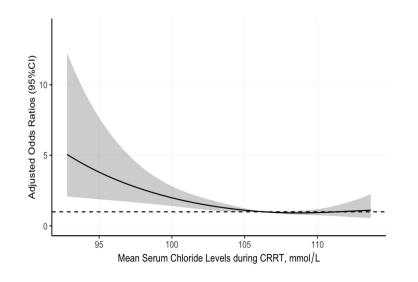


FIGURE 2: Restricted cubic spline of the association between serum chloride during CRRT and 90-day mortality



#### **DISCUSSION**

- In a large cohort of critically ill patients requiring CRRT, hypochloremia (serum chloride ≤98 mmol/L) and hyperchloremia (serum chloride ≥109 mEq/L) were found in 50% of the patient population before CRRT initiation.
- In addition, between low serum chloride (≤98 mmol/L) before and during CRRT was associated with 90-day mortality after adjusting for potential confounders in multivariate analyses.
- In contrast, serum chloride ≥109 mmol/L was not associated with mortality before and during CRRT.
- Several studies have demonstrated that hypochloremia is significantly associated with increased risk of in-hospital and 90day mortality among patients in cardiac ICU, post operative patients with sepsis and cirrhosis in the ICU and increased risk of AKI.
- There have been conflicting reports in the literature on whether hyperchloremia is associated with an increased risk of inhospital mortality.

# CONCLUSIONS

 Hypochloremia, but not hyperchloremia, was associated with increased 90-day mortality before initiation of CRRT and during CRRT.

# REFERENCES

- Kim HJ, Oh TK, Song I-A, Lee JH. Association between fluctuations in serum chloride levels and 30day mortality among critically ill patients: a retrospective analysis. BMC Anesthesiol. 2019;19(1):79.
- 2. Shao M, Li G, Sarvottam K, Wang S, Thongprayoon C, Dong Y, et al. Dyschloremia Is a Risk Factor for the Development of Acute Kidney Injury in Critically III Patients. PLOS ONE. 2016;11(8):e0160322.
- 3. Zhou L, Wang X, Zhan X, Feng X, Wang N, Peng F, et al. Serum Chloride and Mortality in patients on continuous ambulatory peritoneal dialysis: A multicenter retrospective study. EClinicalMedicine. 2021;41:101133.
- 4. McCallum L, Jeemon P, Hastie CE, Patel RK, Williamson C, Redzuan AM, et al. Serum chloride is an independent predictor of mortality in hypertensive patients. Hypertension. 2013;62(5):836-43.
- 5. Breen TJ, Brueske B, Sidhu MS, Kashani KB, Anavekar NS, Barsness GW, et al. Abnormal serum chloride is associated with increased mortality among unselected cardiac intensive care unit patients. PLOS ONE. 2021;16(4):e0250292.
- 6. Kimura S, Matsumoto S, Muto N, Yamanoi T, Higashi T, Nakamura K, et al. Association of serum chloride concentration with outcomes in postoperative critically ill patients: a retrospective observational study. Journal of Intensive Care. 2014;2(1):39.