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HYPONATREMIA, THE SEVERITY INDICATOR IN ICU PATIENTS AT FRPMC ALLIED HOSPITALS

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Abstract

Objective: *To measure the frequency of hyponatremia in critically ill patients and correlate it to severity of critical illness.*

Study design: *Quasi-experimental study*

Place and duration of study*: Medicine department of Fazaia Ruth Pfau Medical College*
PAF Base Faisal

Methodology: *After approval from the ethical Institutional Review Board (IRB), we studied a sample of 280 patients admitted to intensive care unit of hospital. The patients were randomized into two groups based on the development of hyponatremia and they were followed for adverse outcomes. The primary outcome was the severity of disease quantified through quick-Sequential Organ Failure Assessment (SOFA) and we correlated it to hyponatremia.*

Results: *The primary outcome was the severity of critical illness quantified by SOFA score. The group-H patients had high severity of illness indicated by Q-SOFA. Forty-one (29.3%) patients had Q-SOFA score ≥2 in group-H and only 8 (5.7%) patients in group-N had score greater than equal to 2 with p value of <0.001. The severity of illness was low in 132(94.3%) patients, moderate in 6 (4.3%) patients and high in 2 (1.4%) patients in group-N and it was low in 99 (70.7%) patients, moderate in 29 (20.7%) patients and high in 12 (8.6%) patients with p value of <0.001*

Conclusion: *We concluded that hyponatremia is not merely a laboratory anomaly but a clinically relevant indicator of disease severity in critically ill patients*

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INTRODUCTION

Dysnatremia, a sodium imbalance in the body, may be linked to a higher death rate in critically ill patients. Research indicates that variations in the serum sodium level at the time of admission to the intensive care unit (ICU) could have a negative impact on the patient's outcome.[1]. Total body water and exchangeable sodium and potassium determine plasma sodium levels. Patients whose sodium content is initially normal upon ICU admission may develop ICU-acquired dysnatremia. Since hypernatremia typically develops after admission rather than at the time of admission in critically ill patients, research on ICU-acquired dysnatremia has historically concentrated on hypernatremia and ICU-acquired hyponatremia has frequently been overlooked.[2] More than one-sixth to one-fourth of patients develop hyponatremia on intensive care unit (ICU) and it adds complexity to treatment of critically ill patients.[3] Hyponatremia is now a significant indicator of the severity and prognosis of major illnesses like cirrhosis and heart failure. Hyponatremia in cancer patients is a sign of poor prognosis.[4]

Hyponatremia, therefore, cannot be considered only a biochemical bystander in critically ill patients. It is an underrated electrolyte imbalance in setting of intensive care, and it should be identified early and treated appropriately. Critically ill patients with sepsis, syndrome of in appropriate ADH secretion, pneumonia, volume depletion, CCF, use of diuretics and SSRIs, emergency surgery, renal failure, hypercortisolism and low thyroid hormones can develop hyponatremia.[5] It has been recommended to be a strong predictive marker of poor outcome and in-hospital mortality for COVID-19 patients and it was treated to improve outcomes.[6] So, the role of hyponatremia in determining disease severity in critically ill patients needs to be determined.

To highlight hyponatremia in setting of intensive care unit and measure it correlation with severity if critical illness. Our study will help the medical specialists and intensivists in understanding the importance of hyponatremia so that it can be corrected timely for the benefit of patients as it is an under rated electrolyte imbalance.

Methodology:

After seeking permission from the ethical committee of hospital, with **IERB number: 0070/2025** The study was conducted at the Medicine department of FRPMC Hospital, Karachi. WHO sample size calculator was used to calculate sample size keeping level of significance 5%, power of test 80 percent, the mortality with mild hyponatremia to be 8%[7] and mortality with severe hyponatremia to be 10%[7]. The sample size was estimated to be 138. The sample was collected with the help of non-probability consecutive sampling technique. **Inclusion criteria**: Patients admitted to medical intensive care unit (ICU) with ages greater than 18 years who had normal serum sodium levels at time of admission and developed hyponatremia afterwards in intensive care. **Exclusion criteria:** Patients with hypernatremia, patients on mannitol infusion, patients who had history of Addison's disease or hyper aldosteronism.

After detailed clinical history and examination the randomization of patients was done on basis of serum sodium levels among the patients admitted in medical intensive care unit (ICU). One-fifty normonatremic and 140 hyponatremic patients were recruited in study and 140 normo-natremic patients were recruited by non-probability consecutive sampling. The groups were named: Group-N and Group-H. Group-N included normo-natremic patients and group-H included hyponatremic patients. The patient's laboratory work and vital signs were recorded for calculation of quick-sequential organ and failure assessment (Q-SOFA) score. The hyponatremia[8] was divided into three categories: Severe hyponatremia (Serum sodium ≤ 120 m Eq/l), moderate hyponatremia (Serum sodium 120 to 129 m Eq/l) and mild hyponatremia (Serum sodium 130–134 m Eq/l). The patients were followed during the ICU stay for one week after development hyponatremia and sequential organ and failure assessment (SOFA)[9] score was done daily for one week. The median score of all 7 days was recorded. The primary outcome will be the severity of critical illness quantified by SOFA score recorded during stay in medical ICU

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categorized as low (Q-SOFA<2), moderate(Q-SOFA=2), and high(Q-SOFA>2). The sofa score was calculated from 0 to 3, assigning one point for each sign: systolic blood pressure below 100 mmHg, respiratory rate above 22 breaths per minute, and altered mental status. A total score of >2 suggested high disease severity, 2 suggested moderate severity and less than 2 indicated low disease severity. The secondary outcome was mortality and severity of hyponatremia in hyponatremic patients. Only euvolemic patients were included in the study and volume status of patients will be assessed with help of following clinical signs. Pitting edema on feet or sacrum, jugular venous pressure and capillary refill time. Parameters like age, gender, BMI and need of mechanical ventilation, Baseline labs including blood complete picture, liver functions (ALT, ALP and Bilirubin), Kidney functions (Urea, creatinine), serum electrolytes (Na, K, Cl, Ca and Mg), CRP quantitative, Serum Albumin, Prothrombin time, activated partial thromboplastin time, INR, morning cortisol, T4, T3, TSH, CKMB and CK were done daily in all patients as part of ICU protocol.

Data was analyzed using Statistical Package for Social Sciences (SPSS). The quantitative parameter like age was subjected to Shapiro-wilk tests first to check normality. The distribution was found normal; therefore, age was presented as mean and standard deviation. Frequency and percentages were calculated for all qualitative (or discrete) parameters. Chi-square analysis was employed for comparison of frequencies and independent sample T-test was employed for comparison of means and standard deviation. The p value less than 0.05 was considered significant.

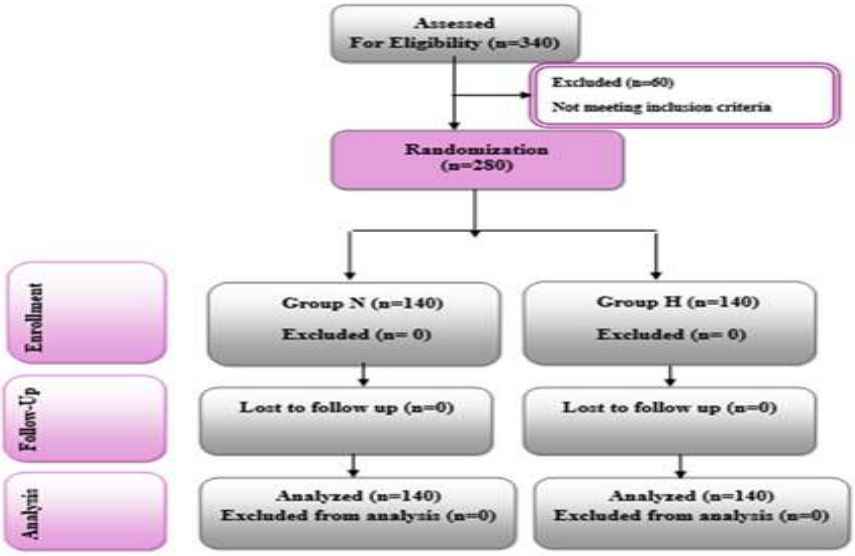

Figure-1: Consort diagram of study flow

Results:

A total of two hundred and eighty patients completed the study protocol. The patients with hyponatremia according to criteria furnished were followed till one week of development of hyponatremia and the patients without hyponatremia were also followed for one week to avoid study bias. The primary outcome will be the severity of critical illness quantified by SOFA score. Demographics were comparable between study groups. There were 140 patients in each group. The mean age of patients in group-N was 63.52 ±1.23years and mean age of group-H patients was 63.3 ± 12.20 years with p value of 0.045. The body mass index and gender distribution were also similar between two groups with no significant statistical difference. There were 67 (47.9%) diabetics and 55 (39.3%) hypertensives in group-N and there were 77 (55.0%) diabetics and 59 (42.1%) hypertensives in group-H with p values of 0.141 and 0.358. The

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distribution of comorbid conditions was also analogous between the groups.

The primary outcome was the severity of critical illness quantified by SOFA score. The group-H patients had high severity of illness indicated by Q-SOFA. Forty-one (29.3%) patients had Q-SOFA score ≥2 in group-H and only 8 (5.7%) patients in group-N had score greater than equal to 2 with p value of <0.001. The severity of illness was low in 132(94.3%) patients, moderate in 6 (4.3%) patients and high in 2 (1.4%) patients in group-N and it was low in 99 (70.7%) patients, moderate in 29 (20.7%) patients and high in 12 (8.6%) patients with p value of <0.001. The frequency of mortality was seen in 9 (6.4) group-N patients and 38 (27.1) group-H patients with p value of less than 0.001. There were 8 (5.7%) patients who required mechanical ventilation in group-N and 41 (29.3%) who required mechanical ventilation in group-H who were followed up in the study with p value <0.001.

Table-I: The comparison of demographic variables of samples under study (n=280)

Parameter		Group-N mean ±SD n=140	Group-H mean ±SD n=140	P value
Age (years)		63.52 ±1.23years	63.3 ± 12.20	0.045
Gender	Male	107 (76.4)	105 (75.0)	0.889
	female	33 (23.6)	35 (25.0)	
Body mass index (BMI) kg/m^2	25-30	113(80.7)	114 (81.4)	0.069
	31-35	22 (15.7)	26 (18.6)	
	>35	5 (3.6)	0(0)	
Diabetes mellitus	Yes	67 (47.9)	77 (55.0)	0.141
	No	73 (52.1)	63 (45.0)	
Hypertension	Yes	55 (39.3)	59 (42.1)	0.358
	No	85 (60.7)	81 (57.9)	

Table-II: The comparison of outcomes between two groups (n=280)

outcome		**Group-N mean ±SD n=140**	**Group-H mean ±SD n=140**	p value
Mechanical ventilation	Yes	8 (5.7)	41 (29.3)	<0.001
	No	132 (94.3)	99 (70.70	
Hyponatremia severity	Mild	0(0)	109 (77.9)	<0.001
	Moderate	0(0)	6 (4.3)	
	Severe	0(0)	25 (17.9)	
Severity of illness	Low	132 (94.3)	99 (70.7)	<0.001
	Moderate	6 (4.3)	29 (20.7)	
	High	2 (1.4)	12 (8.6)	
Q-SOFA* Score	<2	132 (94.3))	99 (70.7)	<0.001
	≥2	8 (5.7)	41 (29.3)	
Mortality	Yes	9 (6.4)	38 (27.1)	<0.001
	No	131 (93.6)	102 (72.9)	

*Quick-sequential organ failure score

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Discussion:

The findings of our study indicated that moderate to severe hyponatremia was notably more frequent among critically ill patients exhibiting moderate to high disease severity. This association was statistically significant when evaluated against patients with comparable demographic profiles. Our results are in concordance with recent evidence that underscores the clinical significance of hyponatremia in critically ill populations. Kumar et al[11] observed that serum sodium levels below 130 mmol/L were independently associated with elevated Sequential Organ Failure Assessment (SOFA) scores. Their data revealed a two-to-three-fold increase in the likelihood of mechanical ventilation among patients with moderate to severe hyponatremia, emphasizing the correlation between hyponatremia and disease burden. Unlike their observational study, we employed a quasi-experimental approach.

Goddard et al[12] reported a case involving a previously healthy 26-year-old male presenting with dyspnea ulcerative lesion. The patient was diagnosed with severe hyponatremia and radiological findings indicated pneumonia. Management included intravenous saline, broad-spectrum antibiotics, and ventilatory support, necessitating ICU admission and intubation. This case underscored the necessity of early recognition and management of hyponatremia to prevent complications and improve prognosis. The severe sodium deficit was a critical marker of illness severity and required urgent treatment. Proper understanding and management of hyponatremia remain essential skills for emergency physicians. In our study, we used the Q-SOFA[12] score as a predictor of severity and mortality, which effectively correlated with disease severity in our study population.

Gustafson et al[13] conducted a retrospective single-center analysis on pneumonia patients and found hyponatremia in twenty-nine percent of general pneumonia and fifty-six percent of COVID-19 cases. Hyponatremic patients had higher mortality (39% versus 16 %) and longer hospital stays (14 versus 16 days), both of which were statistically significant, reaffirming the increased risk in critically ill settings.

Rondon-Berrios et al[14] identified hyponatremia as the most common electrolyte imbalance in critical illness, significantly contributing to morbidity, mortality, and healthcare costs. Their work highlighted its pathophysiology reflecting hypotonicity from excess total body water and its potential to cause cerebral edema. Rapid correction, however, posed neurological risks. We observed that disease severity paralleled the presence of hyponatremia and hyponatremic patients had higher (38%) mortality as compared to normo-natremic patients (9%).

Kinoshita et al[15] reported that 0.7% of ICU patients experienced severe hyponatremia. Their findings linked prompt correction with increased hospital- and ICU-free days and reduced mortality, without significantly elevating neurological risk. The results of their study reinforced that hyponatremia was not to be ignored. According to Workeneh et al[16] hyponatremia is a prevalent yet often misunderstood electrolyte disorder due to its complex water regulation mechanisms. Its prevalence varies with diagnostic thresholds and populations but consistently associated with poorer outcomes. Similarly, Itoh[17] et al conducted a retrospective cohort study and showed that early-onset hyponatremia in critically ill patients predicted worse clinical trajectories. Those developing sodium deficits within 48 hours of ICU admission exhibited greater in-hospital mortality, prolonged ICU stays, and higher rates of acute kidney injury. In our study, we also presented that severe hyponatremia was associated with increased disease severity and mortality.

Ayus et al[18] performed a systematic review and meta-analysis exploring correction rates and outcomes in patients with severe hyponatremia. They found that rapid sodium correction (≥8 m Eq/L/24h) was linked to reduced in-hospital mortality, without increased osmotic demyelination risk. These results support our study's conclusion that hyponatremia is both a marker and modifiable contributor to disease severity when managed appropriately.

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Wang et al[19] noted that in neurocritical patients, sodium imbalances were frequent, and hyponatremia was significantly associated with cerebral edema and poorer Glasgow Outcome Scores (p=0.003). We correlated hyponatremia as an independent factor which correlated to severity in critical illness irrespective of cause.
Limitation of study: The pathophysiological basis of hyponatremia is multifactorial, and our data did not account for all etiological subtypes which and study did not evaluate the effect of correction rate on outcomes

Conclusion: We concluded that hyponatremia is not merely a laboratory anomaly but a clinically relevant indicator of disease severity in critically ill patients

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Authors' contributions:
Author 1 & 2: Drafting of work, design analysis, data acquisition, data interpretation and approval of final version to be published

Author 3 & 4: Data analysis, data acquisition, drafting of work, critical revision, approval of final version to be published

Author 5 & 6: Drafting of work, critical review, approval of final version to be published

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