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ASSOCIATION OF IN-HOSPITAL DYSNATREMIA WITH CLINICAL OUTCOME AMONG CRITICALLY ILL PATIENTS

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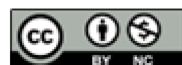

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ABSTRACT

Background: Dysnatremia includes both hyponatremia and hypernatremia, represents a common and significant electrolyte disturbance in critically ill patients. Deranged plasma sodium levels subject cells to hypotonic or hypertonic stress, with clinical manifestations primarily involving neurological symptoms. This study intended to identify whether there is any association between dysnatremia and outcomes in critically ill patients. **Materials and Methods:** A prospective observational study was among 300 hyponatremia and 100 hypernatremia patients who were admitted in the admitted in the intensive care unit ward during the period July 2023 to January 2025 in a tertiary care hospital Serial monitoring of serum sodium level, APACHE and SOFA score was done. Duration of ICU stay and outcome of patient were documented. The association between in-hospital change in sodium concentration and mortality was also assessed. **Result:** The mean of patients with hypo and hypernatremia was 60.2 ± 8.9 years and 55.4 ± 7.2 years respectively. The overall proportion of males and females were 61.3% and 38.8%. Among the hyponatremia group there was correlation between the sodium level and duration of ICU stay but not for the hypernatremia group. The mortality was higher in the hypernatremia group (52.0%) compared to the hyponatremia group (43.3%) but this difference was not significant. **Conclusion:** Serum sodium levels at isolated time points demonstrated limited predictive ability for mortality or ICU length of stay. However, dynamic fluctuations in sodium, alongside worsening APACHE-II and SOFA scores, reflected underlying physiological instability were associated with clinical deterioration. Serum sodium when interpreted alongside comprehensive clinical severity scoring systems, provide valuable insights into patient prognosis.

INTRODUCTION

Dysnatremia is the presence of an unusual (low or high) concentration of sodium in the blood; abnormal serum sodium level (less than 135 mEq/L or more than 145 mEq/L respectively).[1] Disorders of serum sodium concentration are caused by abnormalities in water homeostasis, leading to changes in the relative ratio of sodium to body water. Hyponatremia is defined as plasma sodium concentration less than 135 mEq/L.[1] It is a very common disorder occurring in upto 22% of hospitalized patients.[2] There are 3 types of hyponatremia namely euvolemic, hypovolemic, hypervolemic hyponatremia. Risk factors for developing hyponatremia in critically ill patients are syndrome of inappropriate antidiuretic hormone secretion, pneumonia, severe sepsis, renal failure, heart failure, cirrhosis of liver, sub arachnoid hemorrhage and elective surgery.[3]
Hypernatremia is defined as an increase in plasma sodium concentration more than 145 mEq/L.[1] Mechanism is water deficit and electrolyte excess. Hypernatremia is associated with high mortality rate of 40-60%.[4] Risk factors of hypernatremia are central diabetes insipidus, nephrogenic diabetes insipidus, gastrointestinal water loss, remote renal water loss, mechanical ventilation, severe burn and excessive sodium administration.[5]
Dysnatremia includes both hyponatremia and hypernatremia, represents a common and significant

electrolyte disturbance in critically ill patients. Prevalence of dysnatremia in the intensive care unit (ICU) varies widely, ranging between 6.9% and 17.7%, depending on factors such as the timing of onset (on admission or acquired during the ICU stay), the diagnostic threshold, and the characteristics of patient population.[6] Critically ill patients are at highest risk for developing both hyponatremia and hypernatremia due to the complex interplay of disease processes and medical interventions.

Dysnatremia is associated with poor prognosis in critically ill patients.[7] Hospital ICU patients with hypernatremia have very high rate of mortality of almost 40-60%.[8] Hence prevention, early diagnosis and early treatment will help to reduce the mortality. This study intended to identify whether there is any association between dysnatremia and outcomes in critically ill patients.

MATERIALS AND METHODS

Study design and setting: A prospective observational study was in the Medical Intensive Care Unit (MICU) of Mahatma Gandhi Mission's Medical College Kamothe, Navi Mumbai, Maharashtra between July 2023 to January 2025 with the objective to identify the association of in-hospital dysnatremia with clinical outcome in critically ill patients.

Sample size: Based on the prevalence of hyponatremia i.e 24.25% and hypernatremia i.e. 6.75%from a previous study by Shiburaj et al. [9] the sample size was calculated using the formula n=Z2 PQ/d2 ,where random normal variate Z = 1.96 for 95% of confidence interval, P is the prevalence, Q is 100-P and d is margin of error kept at 5%. The sample size for hyponatremia and hypernatremia was calculated to be 300 and 100 respectively.

Sampling methods: Consecutive sampling of all cases based on inclusion and exclusion criteria during the study period was till the desired sample size was reached.

Study population: Patients who were critically ill and admitted in the MICU during the study period and aged more than 18 years. Inclusion criteria for hyponatremia and hypernatremia weredecrease in sodium less than 135 mEq/L and increase in sodium more than 145 mEq/L after 48 hours of admission respectively. Exclusion criteria were pregnant women, those presenting with hypo or hypernatremia and those not giving consent.

Data collection: A pre-structure questionnaire was used for data collection. All patients admitted in MICU was initially screened for sodium level and later on after 48 hours. APACHE-II score,[10] and SOFA,[11] score was assessed on admission to estimate the mortality risk. Serial monitoring of serum sodium level was done. Duration of ICU stay and outcome of patient were documented. The association between in-hospital change in sodium concentration and mortality was assessed.

Statistical analysis: The data was collected using predesigned pre validated standard research tool. The Cleaned data was stored in MS-Excel for basic analysis such as descriptive statistics mean, standard deviation, frequency and percentage. Statistical analysis was done using SPSS version 26. The Parametric t-test was used for Continues variables and Non-Parametric tests chi-sq test, was used for Categorical data. Pearson correlation (r) was used to assess the correlation between serum sodium level and duration of hospital stay. A p value<0.05 was considered to be statistically significant.

Ethical consideration: The study was done after obtaining Institutional Ethical Committee Clearance dated on 30.06.2023 (DHR-EC/SC/2023/06/39). Informed consent from patients and/or their caretaker was obtained prior to recruitment. Patients confidentially were maintained.

RESULTS

A total of 400 patients were recruited in this study of which 100 had hyponatremia and the remaining 300 had hypernatremia. The mean of patients with hypo and hypernatremia was 60.2 ± 8.9 years and 55.4 ± 7.2 years respectively. The overall proportion of males and females were 61.3% and 38.8% and this proportion was similar among the hypo and hypernatremia group.

Among patients with hyponatremia, the most common diagnosis was pneumonia, accounting for 21% of cases, followed by septic shock (15%) and chronic kidney disease (11%) followed by acute cerebrovascular accident (9%) and heart failure (6%). In hypernatremic patients, pneumonia was the most frequently observed diagnosis, present in 19% of cases, followed by intracranial hemorrhage (16%) and septic shock (11%). Other significant conditions included chronic kidney disease (10%) and acute cerebrovascular accident (7%). [Table 1]

Among hyponatremia patients, the most common comorbidity was hypertension (23.0%), followed by COPD (14.7%), type II diabetes (13.0%), and chronic kidney disease (11.0%). A smaller proportion had ischemic heart disease (8.7%) and seizure disorders (2%). However 27.3% had no comorbidity. In the hypernatremia group, hypertension (33.0%) and type II diabetes (15.0%) were the leading comorbidities, followed by COPD (13.0%) and ischemic heart disease (10 %). Chronic kidney disease was present in 8.0% of patients. Rest 20% had no comorbidity.

Table 1: Distribution as per Diagnosis in hyponatremia and hypernatremia patients

Diagnosis	Hyponatremia Frequency (%)	Hypernatremia Frequency (%)	Total Frequency (%)
Pneumonia	63 (21%)	19 (19%)	82 (20.5%)
Septic shock	45 (15%)	11 (11%)	56 (14%)
Chronic Kidney Disease	33 (11%)	10 (10%)	43 (10.7%)

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Acute CVA	27 (9%)	7 (7%)	34 (8.5%)
Intracerebral Haemorrhage	14 (4.7%)	16 (16%)	30 (7.5%)
Heart Failure	18 (6%)	5 (5%)	23 (5.7%)
AECOPD	12 (4%)	4 (4%)	16 (4%)
Miscellaneous	9 (3%)	6 (6%)	15 (3.7%)
DCLD	9 (3%)	5 (5%)	14 (3.5%)
Acute Coronary Syndrome	11 (3.7%)	2 (2%)	13 (3.3%)
Seizure	10 (3.3%)	3 (3%)	13 (3.3%)
DKA	7 (2.3%)	5 (5%)	12 (3%)
Type II Respiratory Failure	6 (2%)	5 (5%)	11 (2.7%)
Meningitis	8 (2.7%)	2 (2%)	10 (2.5%)
Cardiogenic Shock	6 (2%)	2 (2%)	8 (2%)
Acute Liver Failure	7 (2.3%)	0(0%)	7 (1.7%)
Acute Kidney Injury	5 (1.7%)	2 (2%)	7 (1.7%)
MODS	6 (2%)	1 (1%)	7 (1.7%)
Upper GI Bleed	4 (1.3%)	2 (2%)	6 (1.5%)
Traumatic Brain Injury	3 (1%)	2 (2%)	5 (1.3%)
OPC poisoning	4 (1.3%)	0 (0%)	4 (1%)
Snake bite	2 (0.7%)	2 (2%)	4 (1%)

CVA-Cerebrovascular accident, AECOPD- Acute Exacerbation of Chronic Obstructive Pulmonary Disease, DCLD- Decompensated Chronic Liver Disease, DKA- Diabetic Ketoacidosis, MODS- Multiple Organ Dysfunction Syndrome

In both hyponatremia and hypernatremia there was no significant mean difference on day 2 but significantly increased on change day. There was improvement in this value on the last by with a variation among the patient as seen by a wide standard deviation of 8.2 and 8.4 for hypo and hypernatremia group. [Table 2]

Table 2: Change in mean sodium level at various time point among hyponatremia and hypernatremia

Time point	Mean serum Sodium level (mEq/L)			
	Hyponatremia Group (n=300)	**p-value**	**Hypernatremia Group (n=100)**	**p-value**
Day 1	139.6 ± 3.1	Reference	139.5 ± 3.2	Reference
Day 2	140.0 ± 3.1	0.92	139.5 ± 3.1	0.93
Change day	129.7 ± 2.9	<0.001*	147.9 ± 1.5	<0.001*
Last day	139.4 ± 8.2	<0.001*	144.1 ± 8.4	<0.001*

In the hyponatremia group, there was a significant increase in mean APACHE score on change indicating clinical deterioration during the peak of hyponatremia. By the last day, scores showed a mild decrease to 17.84 ± 8.22 (p = 0.0027), suggesting partial recovery with gradual stabilization on the last day.In hypernatremia patients, there was no significant change in mean APACHE score on Day 2 (p=0.16). From the change day to the last day, the scores remained elevated (p = 0.7028), showing no significant improvement. [Table 3]

Table 3: Change in mean APACHE score at various time point among hyponatremia and hypernatremia

Time point	APACHE score			
	Hyponatremia Group (n=300)	**p-value**	**Hypernatremia Group (n=100)**	**p-value**
Day 1	16.3±7.2	Reference	17.2±8.1	Reference
Day 2	16.1±7.3	0.003*	16.9±8.3	0.165
Change day	18.8±6.8	<0.001*	19.2±7.9	0.016*
Last day	17.8± 8.2	0.002*	19.4±9.3	0.703

In hyponatremia patients, there was statistically significant decline on Day 2 (p = 0.0003), indicating initial clinical improvement. However, SOFA scores increased again by the day when sodium changed (p = 0.002), reflecting transient deterioration associated with worsening hyponatremia. By the last day, the mean SOFA score rose slightly, though the change from sodium changed day was not statistically significant (p = 0.1333). In hypernatremia patients, a slight, non-significant reduction was seen on Day 2 (p = 0.051), suggesting initial stability. However, scores significantly increased by the time of sodium change, indicating clinical deterioration associated with peak hypernatremia. By the last day, SOFA scores further increased, although the change from sodium change day was not statistically significant (p = 0.0783). [Table 4]

Table 4: Change in mean SOFA score at various time point among hyponatremia and hypernatremia

Time point	SOFA score			
	Hyponatremia Group (n=300)	**p-value**	**Hypernatremia Group (n=100)**	**p-value**
Day 1	5.17±2.5	Reference	5.28±2.7	Reference

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Day 2	4.93±2.7	0.003*	5.07±2.8	0.051
Change day	5.52±2.7	<0.002*	6.17±2.7	0.002
Last day	5.77±3.8	0.133	6.60±3.8	0.078

The mortality was higher in the hypernatremia group (52.0%) compared to the hyponatremia group (43.3%) but this difference was not significant (p value =0.164). [Table 5]

Table 5: Association between outcome and category of serum sodium level

Outcome	Total (N=400)	Hyponatremia Group (n=300)	Hypernatremia Group (n=100)	p-value
Death	182 (45.5%)	130 (43.3%)	52 (52.0%)	0.164
Shift to ward	218 (54.5%)	170 (56.7%)	48 (48.0%)	

In hyponatremia patients, serum sodium levels at all time points did not differ significantly between those who died and those who were shifted to the ward. [Table 6] While among the hypernatremia patients, no significant differences were observed in serum sodium levels between those who died and those who were shifted to the ward during the initial days. However, by the last day, the mean sodium in the death group remained elevated at 147.29 ± 10.19 mmol/L compared to 140.60 ± 3.52 mmol/L than those who shifted to the ward which showed statistically significant difference ($p < 0.0001$). [Table 7]

Table 6: Comparing mean sodium level with outcome in patients with hyponatremia

Time point	Mean sodium level		p-value
	Death (n=130)	Shifted to ward (n=170)	
Day 1	139.5 ±3.2	139.8 ± 3.1	0.337
Day 2	140.0 ± 3.1	139.9 ± 3.3	0.844
Change day	129.6 ± 2.8	129.7 ± 3.0	0.873
Last day	138.7 ± 11.9	139.9 ± 3.2	0.245

Table 7: Comparing mean sodium level with outcome in patients with hypernatremia

Time point	Mean sodium level		p-value
	Death (n=52)	Shifted to ward (n=48)	
Day 1	139.6 ± 3.3	139.5± 3.1	0.826
Day 2	139.5 ± 2.9	139.6± 3.2	0.816
Change day	147.8 ± 1.5	147.9±1.4	0.656
Last day	147.3 ± 10.2	140.6± 3.5	<0.000*

In hyponatremia patients, serum sodium levels on most days showed no correlation with ICU length of stay except for the last Day sodium level (r = 0.196, p = 0.0006) suggesting that higher sodium levels by the end of ICU stay may be associated with a longer duration of hospitalization. While for the hypernatremia group there was no correlation at any time point suggesting that the presence of hypernatremia does not affect the duration of hospital stay.

Table 8: Pearson correlation between sodium level and length of stay in ICU in patients with hyponatremia and hypernatremia

Time point	Hyponatremia Group (n=300)		Hypernatremia Group (n=100)	
	r	p-value	r	p-value
Day 1	-0.070	0.227	0.068	0.501
Day 2	0.033	0.563	-0.074	0.463
Change day	-0.010	0.863	0.143	0.154
Last day	0.196	0.000	-0.101	0.315

r- Pearson Correlation

DISCUSSION

In our study, the mean of patients with hypo and hypernatremia was 60.2 ± 8.9 years and 55.4 ± 7.2 years respectively. This finding aligns with that of Yeung Ng et al,[12] who reported a median age of 64 years among over 160,000 ICU patients in Hong Kong with dysnatremia, highlighting that electrolyte disturbances predominantly affect the elderly. Similarly, Lascarrou et al,[13] analyzing post-cardiac arrest patients across four randomized trials, noted a mean age of 63 ± 13 years and highlighted that older patients were more likely to experience early hyponatremia, which correlated with poorer long-term neurological outcomes. These consistent age trends reflect the susceptibility of older populations to sodium imbalances, owing to reduced renal function and higher comorbidity burden.

A male predominance was noted among critically ill patients with dysnatremia, with males constituting 61.3% of the total population while 60% in case of hyponatremia and 65% in case of hypernatremia patients. This pattern is consistently observed in multiple studies across varied ICU settings. Yeung Ng et al,[12] in a large retrospective cohort from Hong Kong, similarly reported that 61.6% of their ICU

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cohort were male, suggesting that sex-based differences in disease prevalence, healthcare utilization, or physiological susceptibility may influence ICU admissions with electrolyte disturbances. Similarly, Uddin et al,[14] found that 61.5% of their critically ill hyponatremic cohort were male, with men more likely to require mechanical ventilation and experience poor outcomes. These findings collectively suggest that males not only comprise a higher proportion of dysnatremic ICU admissions but may also be more vulnerable to severe manifestations or consequences, possibly due to differences in underlying diseases, hormonal regulation of sodium, or delay in health-seeking behavior.

Our study highlighted hypertension (25.7%), COPD (14.5%), diabetes (13.5%), and CKD (9.5%) as the most prevalent comorbidities among total ICU patients. Hyponatremia patients had hypertension (23%), COPD (14.7%), and diabetes (13%) while 27.3% had no comorbid conditions. On the other hand hypernatremia patients had hypertension (33%), COPD (13%), and diabetes (15%) while; 20% had no comorbid conditions. These findings cross with the data from Uddin et al,[14] who reported a high frequency of diabetes mellitus (90.5%), hypertension (75.5%), and CKD (50.5%) in hyponatremic ICU patients, underscoring that metabolic and renal dysfunctions are often intertwined with sodium disturbances.

In our study, among 100 hypernatremia patients, serum sodium levels significantly fluctuated during ICU stay, with significant rise by on change day, and slight drop by Last Day ($p < 0.001$ at both times), indicating dynamic sodium shifts during critical care. Similarly, in 300 hyponatremia patients, a comparable pattern was observed, with normal sodium levels on day 1 and day 2 and drop on change day and improvement by last day ($p < 0.001$ at change day and last day), highlighting the evolving and critical nature of dysnatremia management. These trends suggest the common pattern of transient hyponatremia or fluctuation during the critical phase of illness, potentially due to fluid resuscitation, sepsis, or syndrome of inappropriate antidiuretic hormone secretion (SIADH). In support of this, Cohen et al,[15] demonstrated in a multicenter cohort of patients with aneurysmal subarachnoid hemorrhage that high mean sodium concentrations and greater variability over time were significantly associated with poor six-month neurologic outcomes. They observed that sodium levels often peaked early and declined later, a pattern similarly seen in our study, and highlights that both high initial sodium and wide fluctuations were harmful, regardless of baseline levels.

APACHE scored showed significant variation at various time points in the hyponatremia patients while among the hypernatremia group showed significant fluctuations, with a slight drop by Day 2, a sharp rise at change day, and persistently elevated levels by Last Day ($p < 0.001$ at change day), highlighting evolving severity during ICU stay. Uddin et al,[14] similarly found that hyponatremic patients had significantly higher APACHE-II scores compared to normonatremic individuals ($p = 0.001$), indicating greater illness severity. They also noted that hyponatremic patients more frequently required mechanical ventilation and had poorer outcomes, highlighting the predictive utility of APACHE-II in the context of electrolyte imbalances. The elevated scores during intermediate ICU stay in our cohort could indicate that dysnatremia contributes not only to baseline severity but also complicates the clinical course, especially in the presence of fluctuating sodium levels.

Our study showed a higher mortality rate in patients with hypernatremia (52.0%) compared to hyponatremia (43.3%), though the difference was not statistically significant ($p=0.164$). These findings are echoed by Karalynn Otterness et al,[16] who reported a stronger association of hypernatremia with hospital mortality than hyponatremia across all severity grades. Severe hypernatremia had an especially high adjusted odds ratio for death (55.75), compared to 6.98 for severe hyponatremia. This suggests that while both extremes of sodium imbalance are dangerous, hypernatremia may represent a more critical and less reversible state in ICU patients. Similarly, Hu et al,[17] found that hospital-acquired and persistent hypernatremia had the highest odds ratios (OR) for mortality i.e. >13, while even overcorrection of hyponatremia to hypernatremia yielded an OR as high as 56.9, highlighting the grave prognosis associated with elevated sodium levels.

In our study, serum sodium levels demonstrated minimal correlation with ICU length of stay across most time points in both hypernatremic and hyponatremic patients. In hypernatremic patients, no statistically significant association was observed between sodium levels at any stage and ICU duration. In contrast, among hyponatremic patients, a modest but statistically significant positive correlation was identified between Last Day sodium levels and ICU stay ($r = 0.196$, $p = 0.0006$), suggesting that patients with persistently higher sodium levels toward the end of hospitalization tended to have longer ICU stays. These findings indicate that sodium stabilization dynamics, particularly in hyponatremia, may influence the overall length of critical care and reinforce the importance of careful electrolyte management throughout the ICU course.

Similar conclusions were drawn by Cohen et al,[15] who found that increased variability in sodium concentrations was associated with longer ICU and hospital length of stay among patients with aneurysmal subarachnoid hemorrhage. Their findings emphasized that not only absolute sodium values but also fluctuations contribute to extended critical care needs. Likewise, Jin et al,[18] reported that sodium fluctuation above a threshold of 8.5 mmol/L was independently associated with prolonged ICU stay and increased in-hospital mortality, reinforcing that instability in sodium

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homeostasis is both a marker and mediator of critical illness severity.

CONCLUSION

The present study highlights the importance of dysnatremia as a marker of clinical course and disease severity in ICU patients. While both hyponatremia and hypernatremia were common, serum sodium levels at isolated time points demonstrated limited predictive ability for mortality or ICU length of stay. However, dynamic fluctuations in sodium, alongside worsening APACHE-II and SOFA scores, reflected underlying physiological instability were associated with clinical deterioration. Serum sodium when interpreted alongside comprehensive clinical severity scoring systems, provide valuable insights into patient prognosis. These findings highlights that dysnatremia must be assessed dynamically and as part of an integrated clinical evaluation rather than in isolation, for better risk stratification and management planning in critically ill patients.

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