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The Magnitude, Associated Factors and Outcome of Dysnatremia and Dyskalemia in the Icus of Three Tertiary Hospitals in Ethiopia

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Abstract **Background:** Electrolyte disturbance is common in critically ill patients and it is independently associated with increased short-term and long-term morbidity and mortality. The main objective of this study was to assess the prevalence, associated factors and outcome of dysnatrmia and dyskalemia in the ICUs of BLH, St peter's and Yekatit 12 hospitals. **Methods:** This was a prospective, hospital-based cohort study of critically ill patients admitted to the ICUs of BLH, St peter's and Yekatit12 hospital between May 1, 2021 and August 31, 2021. A structured questionnaire was used to collect information on sociodemographic characteristics, clinical profile at admission, and outcomes at discharge.To identify determinants of dysnatremia and dyskalemia, bivariable and multivariable binary logistic regression analyses were done. Statistical significance was considered at the level of significance of 5%, and adjusted odds ratio (AOR) with 95% confidence interval (CI) was used to present the estimates of the strength of the association. **Result:** A total of 159 patients included in the study. The majority (64.2%) of study participants are from St. Peter. More than one-third (38.4%) of them were in the age group of 31-50 years. The frequency of hyponatremia was 49.68% while Hypernatremia has been found in 25.48% of ICU admitted patients. The magnitude of hypo and hyperkalemia is found out to be 39.49% and 24.2% respectively. A total of 70.06% of patients were dysnatremic while 61.15% were dyskalemic.The odds of hyponatremia increase 4.53 times with admission diagnosis of endocrine than non-endocrine admissions [AOR=4.53; 95% CI: 1.64 - 12.53], Similarly the odds of hyponatremia increased 3.95 times with those taking beta blockers [AOR= 3.95; 95% CI: 1.43 - 10.97].hypernatremia increased 3.17 times in those who took sedatives as compared to those who didn't [AOR=3.17; 95% CI: 1.28- 7.86] and in those with diagnosis of AKI in their hospital stay.a single unit increase on the mean chloride increased the odds of hypernatremia by1.16 times [AOR=1.16; 95% CI: 1.08- 1.24].Those with admission diagnosis of COVID 19 were 75% less risk of developing hypokalemia than those with non-covid admissions [AOR=0.25; 95% CI: 0.11- 0.61].Those with use of beta blockers were 95% less risk of developing hyperkalemia as compared to those who don't use betablockers [AOR=0.05; 95% CI: 0.01-0.48]. one unit increase in the mean urea increases the risk of hyperkalemia by 1.02 times [AOR=1.02; 95% CI: 1.01- 1.03]. Hypernatremia increased the risk of death 2.73 times among patients in the ICU than those with no hypernatremia. [AOR=2.73; 95% CI: 1.28- 5.85]. similarly, those patients in the ICU with hyperkalemia were 2.43 times more at risk to die than those with no hyperkalemia. [AOR=2.43; 95% CI: 1.13- 5.25]. **Conclusion:** This study demonstrated that dysnatrmia and dyskalemia are frequent findings in the critically ill. There are different determinant factors for the development of dysnatremia and dyskalemia in the ICU. Critically ill patients with hypernatremia and hyperkalemia had a higher incidence of thirty-day ICU mortality.

Keywords: *dysnatremia, dyskalemia, thirty-day ICU mortality*

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1. Introduction

Electrolytes are minerals and compounds which are electrically charged that help our body do much of its work. They are involved in many essential processes in our body such as metabolic and homeostatic functions which including enzymatic and biochemical reactions, maintenance of cell membrane structure and function, neurotransmission, nerve signal conduction,cardiovascular function, muscle contraction, bone composition and fluid and acid regulation. [1]

Electrolyte disturbances are common in critically ill patients. critical patients in ICU are more susceptible to electrolyte abnormalities than the non-critically ill patients. The estimated incidence of electrolyte disturbance in an ICU patient is 25%. [2] There are multiple factors may be involved in electrolyte abnormalities in critically ill patients in ICU, including altered absorption and distribution, inadequate or excess administration, alteration in excretion through gl or renal loss, hormonal alteration as well as changes in fluid status and shifts. other factors include administration of drugs such as diuretics, sodium bicarbonate, glucose solution, sympathomimetics, insulin and dobutamine [1,3]

Dysnatremia is a common a clinical problem in patients admitted to the intensive care unit. Most cases of dysnatremia are acquired after the patient is admitted to the ICU. A study conducted recently involving over 151,000 adult patients from 77 ICUs over a period of 10 years has shown that many cases of dysnatremia are acquired in the ICU, and that the severity of dysnatremia is associated with poor outcome in a graded fashion. Another study on the ICU patients with dysnatremias corroborated these findings, reporting that ICU-acquired hyponatremia and ICU-acquired hypernatremia were associated with increased mortality. [4]

Hyponatremia is a common electrolyte disturbance occurring in critically ill patients. It is also the most common electrolyte abnormality in hospitalized patient. it is defined as a serum sodium concentration less than 135 mmol/L. Mild hyponatremia is defined as serum sodium between 130-134.moderate hyponatremia is when plasma sodium is between 125 and 130 while severe or profound hyponatremia is when plasma sodium level is less than 125. low plasma sodium represents a relative fluid excess together with impaired ability of the kidney to excrete water free electrolyte. Hyponatremia can be classified based on the volume status, osmolality and urinary sodium in to into hypertonic, isotonic and hypotonic types. Hypotonic hyponatremia can be further classified as hypervolemic, euvolemic and hypovolemic. A few studies have revealed that ICU-acquired hyponatremia is not uncommon and has been observed to affect critically ill patients at a rate of 1 in 9 or higher and it is associated with increased mortality. [5,6,7]

Clinical manifestations related to hyponatremia are predominantly the expression of CNS dysfunction. This includes headache, nausea, emesis, abdominal cramp, mild neurologic impairment, gait impairment, restlessness, lethargic, confusion, seizure and coma. The pattern of symptoms correlates with the level of hyponatremia and whether the disorder has developed rapidly or not. [8]

hypernatremia is a water metabolism disorder and usually defined as a plasma sodium concentration above 140meq/L. The main mechanism is a net loss of body water relative to sodium and can occur with or without a loss or even gain in body sodium content. in non-critical general- medical-surgical patients the prevalence of hypernatremia has been estimated at up to 1%. There is a higher prevalence in critically ill patients which is 10-26%. Hypernatremia can be present at ICU admission, but it develops during the ICU stay in about three-quarters of cases. The main causes of hypernatremia in critically ill patents are: renal water loss, inability to express thirst and inadequate fluid management by ICU physicians. [9,10]

Hypernatremia can be life threatening and the clinical consequence include but not limited to cardiac dysfunction, neurologic consequences, and insulin resistance in addition to impaired gluconeogenesis. Slowly developing hypernatremia is better tolerated as brain can adapt to hyperosmolality by solute gain and prevent significant volume loss. [11] Several studies suggest an association between hypernatremia and hospital mortality .The overall mortality is in adult patient with hypernatremia is approximately 40-70%, although the mortality rate directly attributed to hypernatremia itself is likely lower. However, most of the studies were retrospective single-center studies in small numbers of patients or focused exclusively on hypernatremia at ICU admission [1,9]

Potassium disorders are common in intensive care unit. Hypokalemia is defined as serum potassium level less than 3.5 mEq per L and considered severe if below 2.5 meq/L or if a patient is symptomatic. It occurs in up to 21% of hospitalized patients and 2% to 3% of outpatients. The main mechanisms by which hypokalemia develop in ICU are intracellular shifts of potassium, increased losses of potassium, or, less commonly, decreased ingestion or administration of potassium. Metabolic alkalosis, drugs like □ adrenergic agonists (e.g., albuterol), insulin, theophylline, and caffeine cause hypokalemia by intracellular shift of potassium. Common causes of hypokalemia due to potassium losses include potassium-wasting diuretics (loop and thiazide), sodium polystyrene sulfonate, corticosteroids (especially mineralocorticoids such as fludrocortisone), aminoglycosides, amphotericin B, magnesium depletion, renal replacement therapies (e.g., hemodialysis, continuous renal replacement therapy [CRRT]), and GI losses (e.g., diarrhea, nasogastric suctioning) [1,12]

Hypokalemia is often asymptomatic, especially when it is mild (serum potassium between 2.5 and 3.5meq/L). but severe hypokalemia(serum potassium less than 2.5 meq/L) is associated with profound signs. [13] The sign and symptoms are primarily neuromuscular, including paralysis, weakness, nausea, vomiting, constipation, respiratory muscle weakness, and rhabdomyolysis. the most feared complication are cardiac arrhythmias, especially in patients with hypertension, myocardial infarction/ischemia or heart failure. [4]

Hyperkalemia is a potentially life-threatening electrolyte abnormality. Although there is no single agreed upon definition for hyperkalemia, most literatures define hyperkalemia as a plasma level > 5.5 mmol/L and severe hyperkalemia as > 6.5 mmol/L. [14] since acute renal failure is common in ICU, hyperkalemia is common in these settings. Other causes of hyperkalemia include drugs

like ACEI, NSAIDs, succinylcholine, -adrenergic blockers and digoxin overdose. hypoaldosteronism and metabolic acidosis are other causes. Signs and symptoms of hyperkalemia include muscle twitching, cramping, weakness ascending paralysis, ECG changes (e.g., tall peaked T-waves, prolonged PR-interval, widened QRS complex, shortened QT-interval) and arrhythmias (e.g., bradyarrhythmias, ventricular fibrillation, asystole) [1,14,15]

As mentioned above fluid and electrolyte balance is vital in maintaining homeostasis in the body, it has important role in protecting cellular function, tissue perfusion and acid-base balance. Electrolyte imbalances are common findings in many diseases. Fluid and electrolyte balance must also be maintained for the management of many clinical conditions. electrolyte disturbance is very prevalent in expired ICU patients which is compatible with the findings of some other studies. Even though mortality of ICU patients is linked, in greater part, to organ dysfunction, the severity of serum sodium and potassium disturbances remains a significant predictor of mortality. Thus, early identifying and correcting electrolyte disturbances in ICU patients is important. [19,20]

As we go through works of literature, there are various studies done on magnitude of individual electrolyte abnormalities and the determinant factors. In one observational, prospective study of a series of ICU patients during a 12-month period, the frequency of hyponatremia on ICU admission was 34.3% of all ICU admissions and euvolemic hyponatremia was the most common (50.6%) type of hyponatremia. In this study, SIADH is the most common cause of hyponatremia. [5]

Whether dysnatremias play a role as independent factors to predict mortality in surgical critically ill patients was studied in Brazil. it was a 2-year retrospective study which included 1599 patients. in this study both hyponatremia and hypernatremia had an influence on mortality in the ICU. (Relative risk [RR]=1.91 [95% CI=1.13–3.17]) and (RR=5.45 [95% CI=3.65–8.1]) respectively. This association was greater in patients with hypernatremia mortality in the ICU. When the independent variables that could be associated with mortality are evaluated using multivariate analysis and outcome of patients and its correlation with dysnatremia, It was observed that the need for vasopressors, blood transfusions, dialysis-requiring acute kidney injury (AKI), mechanical ventilation, and cases of severe sepsis and septic shock were independent factors associated with mortality. [21]

Another retrospective cohort study based on the prospective registry of all critically ill patients admitted to the medical ICU from south Korea conducted from January 1, 2015 to December 31, 2018. They found out that 16.2% of critically ill medical patients who had normal sodium concentration at the time of ICU admission developed new-onset hyponatremia within the first 48 h after admission. in this study hematologic malignancy and initial potassium were independently associated with the development of ICU-acquired hyponatremia. In addition, net volume balance was the only management profile significantly associated with ICU-acquired hyponatremia [6]

OUTCOMEREA is a retrospective observational study on a prospectively collected multicenter database done in France to assess the epidemiological characteristics and prognostic impact of ICU acquired hypernatremia. In this study 11.1% experienced mild and 4.2% moderate to severe ICU acquired hypernatremia yielding an overall frequency of 15.3%. The time from ICU admission to ICU acquired hypernatremia was 5 days (3–8) for mild cases and 6 days (3–10) for moderate to severe cases. Independent factors associated with male gender; greater disease severity at ICU admission; and septic shock, acute respiratory failure or coma at ICU admission. Before adjustment, hospital mortality was 15.2% in patients without IAH, 29.5% in patients with mild and 46.2% in patients with moderate to severe ICU acquired hypernatremia. [10]

A retrospective study from Netherland, in two large cohort of ICU patients, found a shift in the incidence of dysnatremias. The incidence of hyponatremia decreased over the study period, whereas the incidence of hypernatremia is increased. The shift was explained by the increased use of diuretics and hydrocortisone. [22] In another observational study of postoperative patients, In the subgroup of patients who presented to the ICU with normal sodium values, 13% developed dysnatremia during the ICU stay. The data also show significantly higher rates of congestive heart failure and liver failure in all dysnatremic patient groups, a higher incidence of diabetes and renal failure in patients with hyponatremia, and a higher incidence of hypertension among patients with hypernatremia. In this observational study of postoperative patients, dysnatremia is common and is associated with increased risk of mortality in postoperative patients requiring intensive care. They found that fluctuations in serum sodium were associated with an increase in 28-day mortality, even in those patients with normal serum sodium measurements during the course of the ICU stay. [23]

A two-year retrospective study from Turkey analyzing the ICU records of 440 patients, Hypokalemia was found in 40% of patients. Hypokalemia was observed for the first time on 2.3 +/-1.3th days of patients' ICU stay. Hypothermia, polyuria, vomiting and diarrhea found to be related with increased incidence of hypokalemia. Additionally, the application of dialysis, administration of insulin, diuretics and beta-adrenergic agents was found significantly correlated with higher incidence of hypokalemia. Blood transfusion was also found to be highly correlated with hypokalemia. [13] A cross-sectional study was carried out at cardiac surgical intensive care unit in Rawalpindi, Pakistan, from July – Nov 2013. Hypokalemia (K<3.5 mmol//l) developed in 33% patients and hyperkalemia (K>5 mmol//l) developed in 18% patients. in this study 33% of Hyperkalemic patients had from renal impairment while 50% had hypertension [7]

A prospective cohort study from Thailand involving critically ill patients admitted to the medical ICU from May 2012 to February 2013 showed abnormal mean serum potassium levels were associated with significantly higher ICU mortality (24.3% vs. 39.5%, p=0.04).

Patients with abnormal potassium levels had longer ICU and hospital lengths of stay than patients with normal potassium levels; however, the difference in these

parameters between the two groups was not statistically significant. even though the incidence of overall arrhythmia was not significantly different between patients with normal and abnormal potassium levels, a significantly higher incidence of malignant arrhythmia (i.e., ventricular tachycardia and ventricular fibrillation) was found among patients with abnormal potassium levels (p=0.02) [24].

2. Methods and Materials

An institution based prospective cohort study was conducted in among critically ill patients admitted to the ICUs of Black lion specialized hospital, St peter's and Yekatit 12 hospitals from May 1, 2021, to August31, 2021. All adult patients (>18 years old) who were admitted to the ICUs of those mentioned hospitals during the time period are included in the study. Only Patients who stayed for more that 24hrs in the ICU were included in the study. Patients had at least 2 determinations of electrolyte during ICU stay and the interval between the 1st and the last one should be at least 24hrs. For patients who experienced multiple sodium or potassium disturbance events, each event was analyzed separately. Events and outcomes developed within 1 month after ICU admission were analyzed. This allowed having more electrolyte determinations. Standardized case report format (CRF) prepared to collect enrolled patient's data. Baseline characteristics at the time of admission, including age, sex, marital status, place of residency were recorded. Admission diagnosis was recorded for all patient and Serum electrolytes and organ function tests were followed during the stay. Medications known to affect sodium and potassium concentration and intravenous fluids were recorded. Use of blood products agents, the presence of diabetes and the diagnosis of AKI during hospital stay were assessed. Thirty-day outcome was assessed for all patients admitted to the ICU in the time period.

3. Sample Size Determination

Sample size for the patients will be calculated with the following formula: assuming 95% CI

$$n = \frac{Z^2 x(p)(1-p)}{d^2} = \frac{1.96^2 x 0.104(1-0.104)}{0.05^2} = 144$$

Z α/2 = is standard normal variant (at 5% type 1 Error (P <0.05) it is 1.96

d = margin of error was taken as 0.05.

q =1-p: the probability of non-occurrence of the event of interest.

p = expected proportion of the population with the event outcome.

The calculated sample size is 144 and a 10% loss was added with resulting total size of 159 patients.

4. Operational Definitions

√ **Intensive care unit (ICU)** may be defined as a service for patients who havepotentially recoverable conditions, who can benefit from more detailedobservation and invasive treatment than can be provided safely in an ordinaryward or high dependency area. It is usually reserved for patients with threatenedor established organ failure, often arising as a result or complication of an acuteillness or trauma, or as a predictable phase in a planned treatment program.Intensive care represents the highest level of continuing patient care andtreatment.

√ **Hyponatremia** is defined as a sodium level of less than 135 mEq/L
- Mild: 130-134 mEq/L
- Moderate: 125-129 mEq/L
- Severe: <125 mEq/L

√ **Hypernatremia** is defined as a sodium level of greater than 145 mEq/L
- Mild: 146-149 mEq/L
- Moderate: 150-169 mEq/L
- Severe: >170 mEq/L

√ **Sodium disorders (dysnatremia)** is considered as either hypo/hyperkalemia

√ **Hypokalemia** is defined as a potassium level of less than 3.5 mEq/L
- Mild: 3-3.4 mEq/L
- Moderate: 2.5-2.9 mEq/L
- Severe: < 2.5 mEq/L

√ **Hyperkalemia** is defined as a potassium level of greater than 5.5 mEq/L
- Mild: 5.5-6.5 mEq/L
- Moderate: 6.5-7.5 mEq/L
- Severe: >7.5mEq/L

√ **Potassium disorders (dyskalemia**) is considered as either of hypo/hyperkalemia

5. Statical Analysis

Data was checked for completeness, edited, coded and entered Epi data version 3.1 and exported to SPSS version 24.0 statistical software for cleaning and analysis. Frequencies and proportion are used to describe study subjects and socio-demographic characteristics. Continuous variables are expressed as means ± standard deviation. Differences between group means were tested using two-tailed Student's t-test. Proportions is reported as percentages and compared between groups with Chi-square. Tables are used to present results. A p value of less 0.05 is considered statistically significant.

6. Results

Socio-demographic characteristics

The majority (64.2%) of study participants are from St. Peter and more than one-third (38.4%) of them were in the age group of 31-50 years. Most (74.8%) of them were urban residents at the time of data collection. More specifically most of them were residents of Addis Ababa. Socio-demographic characteristics of the study participants are shown in Table 1.

Table 1. Socio-demographic characteristics

Variables		Frequency (%)	Value percent
Hospital (n=159)			
	St. Peter	102 (64.2)	64.2
	Black lion	41 (25.8)	25.8
	Yekatit 12	16 (10.1)	10.1
Age in year (n=154)			
	18-30	37 (23.3)	23.3
	31-50	61 (38.4)	38.4
	51-90	56 (35.2)	35.2
Sex (n=159)			
	Male	102 (64.2)	64.2
	Female	57 (35.8)	35.8
Residence (n=149)			
	urban	119 (74.8)	74.8
	rural	18 (11.3)	11.3
	semi urban	12 (7.5)	7.5
Region (n=148)			
	Addis Ababa	113 (71.1)	71.1
	Oromia	29 (18.2)	18.2
	Amhara	2 (1.3)	1.3
	SNNPR	4 (2.5)	2.5

Table 2. Admission diagnosis

Variables (n=159)	Frequency	Percent
Respiratory		
Yes	103	64.8
No	56	35.2
CVS		
Yes	65	40.9
No	94	59.1
GIT		
Yes	21	13.2
No	138	86.8
Hematology		
Yes	6	3.8
No	153	96.2
Renal		
Yes	25	15.7
No	134	84.3
Neurology		
Yes	51	32.1
No	108	67.9
Endocrine		
Yes	30	18.9
No	129	81.1
COVID19		
Yes	69	43.4
No	90	56.6
Surgical		
Yes	26	16.4
No	133	83.6
Infectious		
Yes	10	6.3
No	149	93.7

Admission diagnosis

The study participants were admitted by different diagnosis. About 65% and 41% of participants were admitted for respiratory and CVS problem, respectively. About one-third (32.1%) of participants were admitted in neurology and 43.4% were admitted in COVID-19. Only 3.8% and 6.3% were admitted for hematology and infection, respectively. Admission diagnosis are shown in Table 2.

Table 3. Medications and fluids

Medications

Variables (n=159)	Frequency	Percent
Diuretics		
Furosemide		
Yes	55	34.6
No	104	65.4
Thiazide		
Yes	10	6.3
No	149	93.7
Spironolactone		
Yes	10	6.3
No	149	93.7
Vasoactive		
Epinephrine		
No	134	84.3
Yes	25	15.7
Norepinephrine		
Yes	9	5.7
No	150	94.3
Dopamine		
Yes	7	4.4
No	152	95.6
Medications		
Beta-blocker		
Yes	27	17
No	132	83
ACEI		
Yes	14	8.8
No	145	91.2
Antibiotics		
Yes	142	89.3
No	17	10.7
Corticosteroids		
Yes	110	69.2
No	49	30.8
Sedatives		
Yes	56	35.2
No	103	64.8
Proton pump inhibitors		
Yes	136	85.5
No	23	14.5
Antiplatelet and anticoagulants		
Aspirin		
Yes	12	7.5
No	147	92.5
Heparin		
Yes	112	70.4
No	47	29.6
Warfarin		
Yes	7	4.4
No	152	95.6
NOACs		
Yes	10	6.3
No	149	93.7

Medications

Diuretics were administered for 47.2% of the study participants. High percentage (34.6%) of diuretics was accounted by furosemide. Vasoactive medications were administered for 25.8% of participants. Antibiotics and corticosteroids were administered for 89.3% and 69.2% of the study participants, respectively. Regarding antiplatelet & anticoagulants, heparin was administered for 70.4% of the study participants. Among fluids 70,1% of patients were given Normal saline while 28.2 and 7.7% of patients took Ringer's lactate and D5W respectively. Medications administered to the study participants on their hospital stay are shown on Table 3.

IV fluids

Variables	Frequency	Percent	Value percent
Normal saline			
Yes	110	69.2	70.1
No	47	29.6	29.9
D5W			
Yes	12	7.5	7.7
No	144	90.6	92.3
Ringer's lactate			
Yes	44	27.7	28.2
No	112	70.4	71.8

Clinical parameters

Almost 32% of the study participants were diagnosed with AKI during their hospital stay. Renal replacement therapy was done for 3.8% of the study participants. Blood product was transfused to 11.3%. Of the total study participants, 14.5% were diabetic. Clinical parameters of the participant in their ICU stay are shown in Table 4.

Table 4. Clinical parameters

Variables	Frequency	Percent
Diagnosis of AKI during stay		
Yes	51	32.1
No	108	67.9
Renal replacement therapy		
Yes	6	3.8
No	153	96.2
Blood product transfusion		
Yes	18	11.3
No	141	88.7
Is the patient diabetic		
Yes	23	14.5
No	136	85.5

Prevalence of dysnatremia and dyskalemia

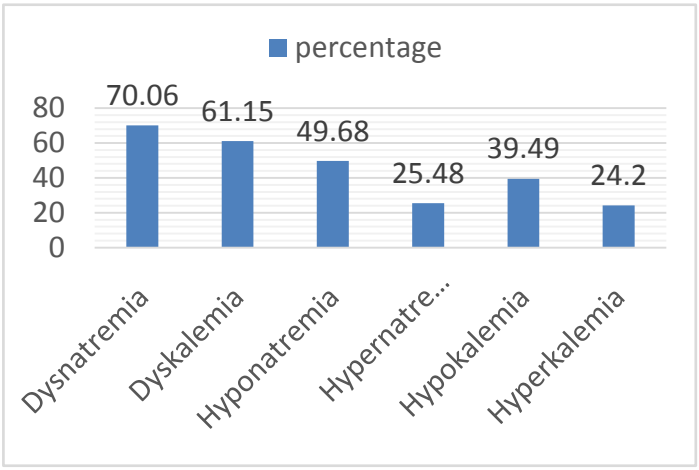

Figure 1. the prevalence of dysnatremia and dyskalemia

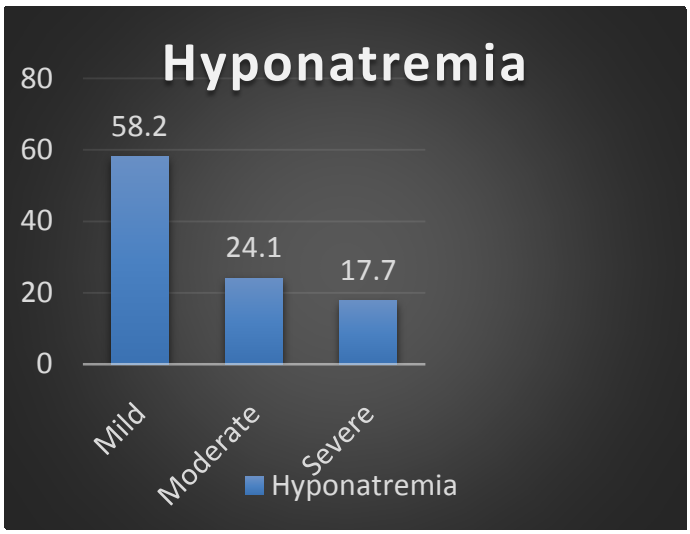

Figure 2. Hyponatremia based on severity

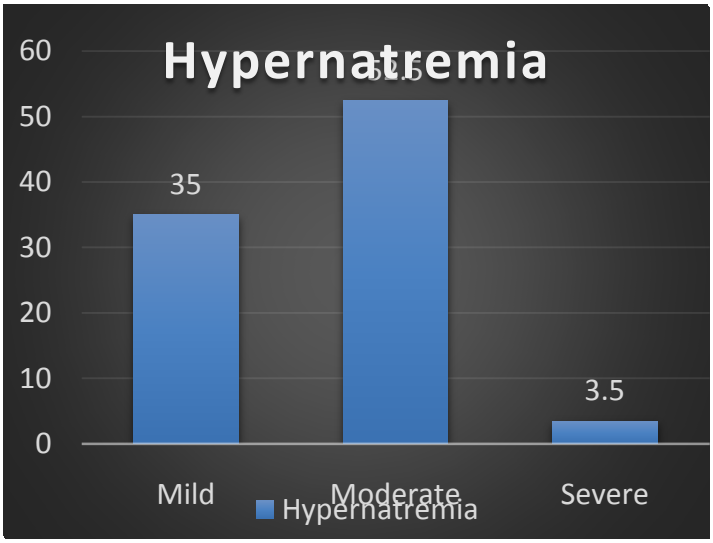

Figure 3. hypernatremia based on severity

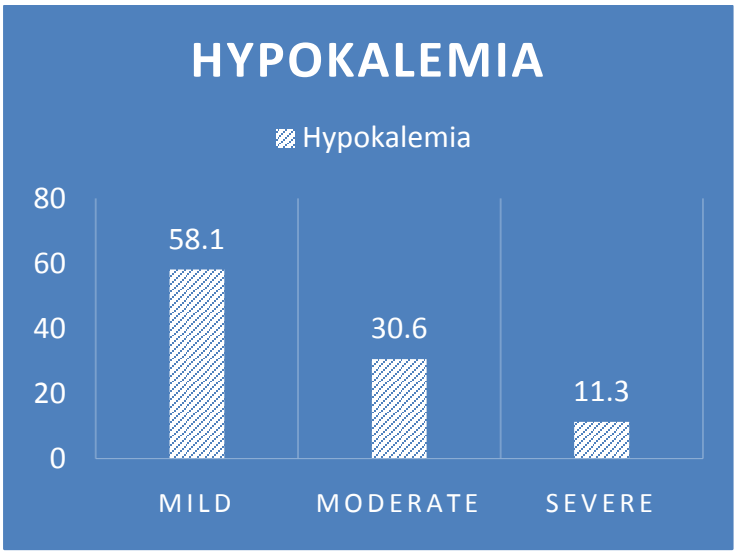

Figure 4. hypokalemia based on severity

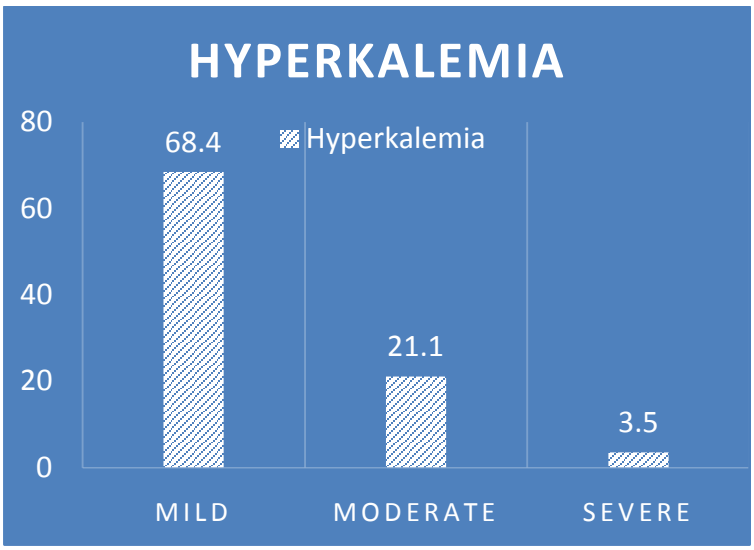

Figure 5. hyperkalemia based on severity

Table 5. Bivariable and Multivariable Logistic Regression analysis results of factors associated with hyponatremia

Explanatory variables		Hyponatremia		COR 95%CI	AOR 95% CI
		Yes	No		
Admission diagnosis of Neurology	Yes	20 (39.2)	31 (60.8)	0.52(0.27,1.04)	0.77(0.34,1.74)
	No	59 (55.1)	48 (44.9)	1	1
Admission diagnosis of Endocrine	Yes	22 (75.9)	7 (24.1)	3.97(1.58,9.95) *	4.53(1.64,12.53)*
	No	57 (44.2)	72 (55.8)	1	1
Admission diagnosis of Surgical	Yes	8 (30.8)	18 (69.2)	0.38(0.16,0.94) *	1.1(0.36,3.32)
	No	71 (53.8)	61 (46.2)	1	1
Mean chloride		85.29±44.2	74.6±48.47	0.94(0.89,0.98) *	0.96(0.91,0.99)*
Beta blocker	Yes	20 (74.1)	7 (25.9)	3.49(1.38,8.81) *	3.95(1.43,10.97) *
	No	59 (45)	72 (55)	1	1
Corticosteroids	Yes	61 (56)	48 (44)	2.05(1.02,4.12) *	1.63(0.72,3.68)
	No	18 (38.3)	29 (61.7)	1	1
Is the patient diabetic	Yes	15 (68.2)	7 (31.8)	2.41(0.93,6.29)	0.34(0.04,3.37)
	No	64 (47.1)	72 (52.9)	1	1
D5W	Yes	3 (25)	9 (75)	0.3(0.08,1.16)	0.86(0.03.1.2)
	No	75 (52.4)	68 (47.6)	1	1

Table 6. Bivariable and Multivariable Logistic Regression analysis results of factors associated with hypernatremia

Explanatory variables		Hypernatremia		COR 95%CI	AOR 95% CI
		Yes	No		
Admission diagnosis of Surgical	Yes	12 (46.2)	14 (53.8)	3.18(1.33,7.65) *	0.86(0.23,3.2)
	No	28 (21.2)	104 (78.8)	1	1
Mean chloride		110.44±11.44	99.35±10.59	1.18(1.09,1.26) *	1.16(1.08,1.24) *
Norepinephrine	Yes	5 (55.6)	4 (44.4)	4.19(1.07,16.48) *	1.39(0.25,7.63)
	No	34 (23)	114 (77)	1	1
Sedatives	Yes	23 (41.1)	33 (58.9)	3.4(1.62,7.17) *	3.17(1.28,7.86) *
	No	17 (17)	83 (83)	1	1
Diagnosis of AKI during stay	Yes	21 (41.2)	30 (58.8)	3.24(1.54,6.84) *	3.13(1.25,7.85) *
	No	19 (17.8)	88 (82.2)	1	1
Blood product transfusion	Yes	9 (50)	9 (50)	3.52(1.29,9.62) *	1.75(0.41,7.43)
	No	31 (22.1)	109 (77.9)	1	1
Normal saline	Yes	33 (30.3)	76 (69.7)	2.48(1.01,6.11) *	2.01(0.53,6.21)
	No	7 (14.9)	40 (85.1)	1	1
D5W	Yes	8 (66.7)	4 (33.3)	7.23(2.04,25.58) *	3.25(1.98,4.21)
	No	31 (21.7)	112 (78.3)	1	1
Ringer's lactate	Yes	15 (34.1)	29 (65.9)	1.86(0.87,4.05)	1.32(2.1,3.2)
	No	24 (21.6)	87 (78.4)	1	1

Factors affecting hyponatremia

In this study based on p value of bivariable analysis and the potential to confound the association factors with hyponatremia 7 variables were identified as candidate variables for multivariable analysis. These are admission diagnosis of neurology, admission diagnosis of surgery, admission diagnosis of endocrine, mean chloride, use of Beta-blocker, use of corticosteroids, patient being diabetic. the result however identified, admission diagnosis of endocrine, mean chloride, use of Beta-blocker as independent variables affecting hyponatremia.

The odds of hyponatremia increase 4.53 times with admission diagnosis of endocrine than non-endocrine admissions [AOR=4.53; 95% CI: 1.64 - 12.53], Similarly the odds of hyponatremia increased 3.95 times with those taking beta blockers than those who don't take beta blockers. [AOR= 3.95; 95% CI: 1.43 - 10.97]. Whereas when there is 1 unit increase in the mean chloride the odds of hyponatremia decrease by 4% [AOR=0.96; 95% CI: 0.91- 0.99]. Patients with hyponatremia are less likely to be given D5W.

Factors affecting hypernatremia

Based on p value of bivariable analysis and the potential to confound the association factors with hypernatremia 6 variables were identified as candidate variables for multivariable analysis these are, admission diagnosis of surgery, mean chloride, use of norepinephrine, use of sedatives, Diagnosis of AKI during stay, blood product transfusion the result however identified, mean chloride, use of sedatives, diagnosis of AKI during stays as independent variables affecting hypernatremia.

The odds of hypernatremia increased 3.17 times in those who took sedatives as compared to those who didn't [AOR=3.17; 95% CI: 1.28- 7.86]. likewise, those with diagnosis of AKI during their hospital stay increased the odds of hypernatremia by 3.13 times than those with no diagnosis of AKI during their hospital stay [AOR=3.13; 95% CI: 1.25- 7.85]. And a single unit increase on the mean chloride increased the odds of hypernatremia by1.16 times [AOR=1.16; 95% CI: 1.08- 1.24]. NS administration

is also associated with hypernatremia and patients are more likely to take D5W if they are hypernatremia.

Factors affecting hypokalemia

Based on p value of bivariable analysis and the potential to confound the association factors with hypokalemia 11 variables were identified as candidate variables for multivariable analysis these are, age, rural residency, admission diagnosis of respiratory, Mean chloride, admission diagnosis of GIT, use of sedatives, admission diagnosis of Neurology, admission diagnosis of COVID 19, use of spironolactone, use of corticosteroids, use of heparin and being diabetic patient, the result however identified admission diagnosis of covid 19 as independent variables affecting hypokalemia.

Those with admission diagnosis of COVID 19 were 75% less risk of developing hypokalemia than those with non-covid admissions [AOR=0.25; 95% CI: 0.11- 0.61].

Factor associated with hyperkalemia

Based on p value of bivariable analysis and the potential to confound the association factors with hyperkalemia 13 variables were identified as candidate variables for multivariable analysis these are, age, admission diagnosis of respiratory, Mean urea, admission diagnosis of Neurology, admission diagnosis of COVID 19,admission diagnosis of surgery, admission diagnosis of endocrine, use of furosemide, use of Epinephrine, use of Betablockers, use of corticosteroids, use of heparin, Diagnosis of AKI during hospital stay the result however identified 6 variables which are admission diagnosis of respiratory, admission diagnosis of neurology, mean urea, use of epinephrine, use of betablockers, and use of corticosteroids as independent variables affecting hyperkalemia.

Those with admission diagnosis of respiratory were 81% less risk to develop hyperkalemia as compared to those with non-respiratory case admission. [AOR=0.19; 95% CI: 0.04- 0.96]. Similarly, those who were admitted with admission diagnosis of neurology were 94% less risk of developing hyperkalemia [AOR=0.06; 95% CI: 0.01- 0.39]. Whereas, one unit increase in the mean urea increases the risk of hyperkalemia by 1.02 times [AOR=1.02; 95% CI: 1.01- 1.03]. Similarly, epinephrine usage increased the odds of hyperkalemia by 3.9 times than non-usage [AOR=3.9; 95% CI: 1.17- 13.04].

Those with use of beta blockers were 95% less risk of developing hyperkalemia as compared to those who don't use betablockers [AOR=0.05; 95% CI: 0.01- 0.48]. However, those who use corticosteroids were 11.98 times more risk to develop hyperkalemia than those who don't use corticosteroids. [AOR=11.98; 95% CI: 1.52- 94.79].

Factors predicting patient's thirty days outcome in the ICU

Two variables Hyperkalemia and Hypernatremia were found to be independent determinants of patient's outcome in the ICU.

Hypernatremia increased the risk of death 2.73 times among patients in the ICU than those with no hypernatremia. [AOR=2.73; 95% CI: 1.28- 5.85]. similarly, those patients in the ICU with hyperkalemia were 2.43 times more at risk to die than those with no hyperkalemia. [AOR=2.43; 95% CI: 1.13- 5.25].

Table 7. Bivariable and Multivariable Logistic Regression analysis results of factors associated with hypokalemia

Explanatory variables		Hypokalemia		COR 95%CI	AOR 95% CI
		Yes	No		
Age		43.34±17.47	49.28±18.45	0.98(0.96,1)	0.99(0.97,1.02)
Living area	Urban	44 (37.3)	74 (62.7)	1	1
	Rural	11 (61.1)	7 (38.9)	2.64(0.95,7.32)	1.09(0.32,3.72)
	Semi urban	3 (25)	9 (75)	0.56(0.14,2.18)	0.25(0.05,1.14)
Respiratory	Yes	31 (30.4)	71 (69.6)	0.35(0.18,0.69) *	2.17(0.65,7.29)
	No	31 (55.4)	25 (44.6)	1	1
GIT	Yes	12 (57.1)	9 (42.9)	2.32(0.91,5.89)	0.74 (0.21,2.57)
	No	50 (36.5)	87 (63.5)	1	1
Neurology	Yes	31 (60.8)	20 (39.2)	3.8(1.89,7.65) *	2.25(0.92,5.49)
	No	31 (29)	76 (71)	1	1
Covid 19	Yes	13 (19.1)	55 (80.9)	0.19(0.09,0.41) *	0.25(0.11,0.61) *
	No	49 (54.4)	41 (45.6)	1	1
Mean chloride		105.45±11.3	100.14±11.73	1.06(1.01,1.1) *	1.04(0.99,1.09)
Spironolactone	Yes	7 (70)	3 (30)	3.95(0.98,15.88)	5.3(0.85,33.18)
	No	55 (37.2)	93 (62.8)	1	1
Corticosteroids	Yes	32 (29.4)	77 (70.6)	0.24(0.11,0.49) *	0.47(0.16,1.36)
	No	30 (63.8)	17 (36.2)	1	1
Heparin	Yes	38 (34.2)	73 (65.8)	0.46(0.23,0.92) *	0.75(0.24,2.3)
	No	24 (53.3)	21 (46.7)	1	1
Is the patient diabetic	Yes	3 (13.6)	19 (86.4)	0.21(0.06,0.73) *	0.51(0.12,2.21)
	No	59 (43.4)	77 (56.6)		1
Normal saline	Yes	51 (46.8)	58 (53.2)	2.88(1.33,6.23) *	2.11(0.21,2.32)
	No	11 (23.4)	36 (76.6)	1	1
Ringer's lactate	Yes	26 (59.1)	18 (40.9)	3.01(1.46,6.19) *	4.12(0.32,2.23)
	No	36 (32.4)	75 (67.6)	1	1

* Statistically significant at P-value ≤0.05

Table 8. Bivariable and Multivariable Logistic Regression analysis results of factors associated with hyperkalemia

Explanatory variables		Hyperkalemia		COR 95%CI	AOR 95% CI
		Yes	No		
Age		52.54±19.37	45.12±17.58	1.02(1.01,1.04) *	1.01(0.98,1.04)
Respiratory	Yes	29 (28.4)	73 (71.6)	2.08(0.9,4.78)	0.19(0.04,0.96) *
	No	9 (16.1)	47 (83.9)	1	1
Neurology	Yes	4 (7.8)	47 (92.2)	0.18(0.06,0.55) *	0.06(0.01,0.39) *
	No	34 (31.8)	73 (68.2)	1	1
Endocrine	Yes	11 (37.9)	18 (62.1)	2.31(0.98,5.47)	2.26(0.77,6.59)
	No	27 (20.9)	102 (79.1)	1	1
Covid	Yes	25 (36.8)	43 (63.2)	3.44(1.59,7.42) *	1.95(0.43,8.84)
	No	13 (14.4)	77 (85.6)	1	1
Surgical	Yes	2 (7.7)	24 (92.3)	0.22(0.05,0.99) *	0.37(0.05,2.56)
	No	36 (27.3)	96 (72.7)	1	1
Mean Urea		82.31±69.74	53.98±45.37	1.01(1.002,1.016) *	1.02(1.01,1.03) *
Frusemide	Yes	21 (38.2)	34 (61.8)	3.13(1.47,6.63) *	0.71(0.24,2.1)
	No	17 (16.5)	86 (83.5)	1	1
Epinephrine	Yes	11 (44)	14 (56)	3.06(1.25,7.48) *	3.9(1.17,13.04) *
	No	27 (20.5)	105 (79.5)	1	1
Beta blocker	Yes	3 (11.1)	24 (88.9)	0.34(0.09,1.21)	0.05(0.01,0.48) *
	No	35 (26.7)	96 (73.3)	1	1
Corticosteroids	Yes	33 (30.3)	76 (69.7)	3.65(1.32,10.05) *	11.98(1.52,94.79) *
	No	5 (10.6)	42 (89.4)	1	1
Heparin	Yes	32 (28.8)	79 (71.2)	3.24(1.17,8.95) *	4.17(0.82,21.27)
	No	5 (11.1)	40 (88.9)	1	1
Diagnosis of AKI during stay	Yes	19 (37.3)	32 (62.7)	2.75(1.29,5.84) *	1.46(0.39,5.44)
	No	19 (17.8)	88 (82.2)	1	1

* Statistically significant at P-value ≤0.05

Table 9. Factors predicting 30 days outcomes in the ICU

		Outcome		**COR 95%CI**	**AOR 95% CI**
		Discharged	Dead		
Hypernatremia	Yes	14(35)	26(65)	2.67(1.27,5.63) *	2.73(1.28,5.85) *
	No	69(59)	48(41)	1	1
Hyponatremia	Yes	41(52.6)	37(47.4)	1.02(0.55,1.92)	1.5(0.74,3.04)
	No	42(53.2)	37(46.8)	1	1
Hyperkalemia	Yes	14(36.8)	24(63.2)	2.37(1.11,5.02)*	2.43(1.13,5.25) *
	No	69(58)	50(42)	1	1
Hypokalemia	Yes	34(54.8)	28(45.2)	0.88(0.46,1.67)	1.29(0.11,15.28)
	No	49(51.6)	46(48.4)	1	1
Dysnatremia	Yes	53(63.9)	57(36.1)	1.89(0.94,3.83)	0.68(0.09,4.69)
	No	30(63.8)	17(36.2)	1	1
Dyskalemia	Yes	47(49)	49(51)	1.5(0.79,2.9)	0.91(0.43,1.96)
	No	36(59)	25(41)	1	1

* Statistically significant at P-value ≤0.05

Table 10. 30 days outcomes based on admission diagnosis

Admission diagnosis		Outcome	
		Discharged	Died
Admission diagnosis of Respiratory		48(47.1)	54(52.9)
Admission diagnosis of CVS		33(51.6)	31(48.4)
Admission diagnosis of GIT		9(45.0)	11(55)
Admission diagnosis of Hematology		2(33.3)	4(66.7)
Admission diagnosis of Renal		12(48)	13(52)
Admission diagnosis of Neurology		33(64.7)	18(35.3)
Admission diagnosis of Endocrine		13(43.3)	17(56.7)

Admission diagnosis		Outcome	
		Discharged	Died
Admission diagnosis of Rheumatology		0	0
Admission diagnosis of COVID 19		35(51.5)	33(48.5)
Admission diagnosis of Surgical		15(57.7)	11(42.3)
Admission diagnosis of Infectious		5(50)	5(50)

Thirty-day Outcomes based on admission diagnosis

More than half of the patients with admission diagnosis of respiratory have an outcome of death 54(52.9%). Similarly, more death was recorded among those admitted with a diagnosis of endocrine 17(56.7%). Whereas, nearly two third of patients with admission diagnosis of neurology had an outcome of discharge from ICU.

7. Discussion

This study tried to assess the magnitude, associated factors and thirty days outcome of dysnatremia and dyskalemia in patients admitted to the intensive care units of BLH, St peter's and Yekatit 12 hospital. The majority (64.2%) of study participants are from St. Peter while patients from BLH and Yekatit 12 account for 28.8% and 10.1% respectively. There is a slight male predominant gender distribution with a male to female ratio of 1.8:1. More than one-third (38.4%) of them were in the age group of 31-50 years. Most (74.8%) of them were urban residents at the time of data collection. More specifically most of them were residents of Addis Ababa.

The study participants were admitted by different diagnosis. About 65% and 41% of participants were admitted for respiratory and CVS problem, respectively. About one-third (32.1%) of participants were admitted in neurology and 43.4% were admitted in COVID-19. Only 3.8% and 6.3% were admitted for hematology and infection, respectively.

Among medications, diuretics were administered for 47.2% of the study participants. High percentage (34.6%) of diuretics was accounted by furosemide. Vasoactive medications were administered for 25.8% of participants. Regarding antiplatelet & anticoagulants, heparin was administered for 70.4% of the study participants. Normal saline was administered for 70.1% of patients while ringer's lactate and D5W was given to 28.2% and 7.7% of patients.

Almost 32% of the study participants were diagnosed with AKI during their hospital stay. Renal replacement therapy was done for 3.8% of the study participants. Blood product was transfused to 11.3%. Of the total study participants, 14.5% were diabetic.

The findings of the study reveal that the frequency of hyponatremia was 49.68% while the Hypernatremia has been found in 25.48% of ICU admitted patients. The magnitude of hypo and hyperkalemia is found out to be 39.49% and 24.2% respectively. A total of 70.06% of patients were dysnatremic while 61.15% were dyskalemic. This study showed a higher prevalence of dysnatremia and dyskalemia compared to other studies, one possible reason is that most studies assess electrolyte imbalances which occurred after admission to the ICU and dyskalemia or dysnatremia prior to admission is an exclusion criterion for most studies.

In this study there was a significant association between having an endocrine diagnosis at admission and hyponatremia. Similarly, the odds of hyponatremia increased 3.95 times with those taking beta blockers than those who don't take beta blockers. Whereas when there is 1 unit increase in the mean chloride the odds of hyponatremia decrease by 4%. This is in contrast to South Korean study which showed hematologic malignancy and net volume balance which showed independent association with hyponatremia.

Overall, the odds of hypernatremia increased 3.17 times in those who took sedatives as compared to those who didn't. likewise, those with diagnosis of AKI during their hospital stay increased the odds of hypernatremia by 3.13 times than those with no diagnosis of AKI during their hospital stay. One possible reason for this association can be the development of hypernatremia in patients recovering from AKI. There was also an association between the administration of normal saline and development of hypernatremia which is consistent with other studies. There was an association between hypernatremia and the administration of D5W.This finding is probably the result of treatment with D5W in patient who are already hypernatremia single unit increase on the mean chloride increased the odds of hypernatremia by1.16 times.

A two-year retrospective study from Turkey analyzing the ICU records of 440 patients, Hypokalemia was found in 40% of patients. The application of dialysis, administration of insulin, diuretics and beta-adrenergic agents was found significantly correlated with higher incidence of hypokalemia. Blood transfusion was also found to be highly correlated with hypokalemia. In our study, those with admission diagnosis of COVID 19 were 75% less risk of developing hypokalemia than those with non-covid admissions.

In this study Those with use of beta blockers were 95% less risk of developing hyperkalemia as compared to those who don't use betablockers. However, those who use corticosteroids were 11.98 times more risk to develop hyperkalemia than those who don't use corticosteroids. Those patients admitted with diagnosis of respiratory and neurologic conditions had 81% and 94% lower risk of developing hyperkalemia.

The study showed Hyperkalemia and Hypernatremia to be independent determinants of patient's thirty days outcome in the ICU. Hypernatremia increased the risk of death 2.73 times among patients in the ICU than those with no hypernatremia. Similarly, those patients in the ICU with hyperkalemia were 2.43 times more at risk to die than those with no hyperkalemia. These findings are

consistent with several studies which suggested increase in ICU mortality with hypernatremia and hyperkalemia. In contrast to several other studies, this study didn't show significant association between hyponatremia and hypokalemia and mortality in the ICU.

Limitation of the study

The major limitation of this study is the small sample size which made it difficult to do a more reliable subgroup analysis. This was because of the low number of admissions and turnover in the ICUs. Another limitation is the difference in the ICU setups among the respective hospitals and the blood samples were processed in different laboratory setting which might have impact on the results.

Some of the patient who received some of the medications and IV fluids after they already developed the electrolyte abnormalities or as a treatment for the specific electrolyte disturbance so it might be difficult to establish a clear correlation and it might create a chicken egg dilemma. This was observed in the case of hypernatremia in which patients took D5W as a treatment for hypernatremia.

The other limitation of the study is that study only assessed the thirty-day mortality.

Abbreviations

ACEI- Angiotensin converting enzyme inhibitors
AKI- Acute kidney injury
BLH- Black lion hospital
CNS- Central nervous system
CRRT- Continues renal replacement therapy
DM- Diabetes mellites
HF- Heart failure
IAH- Intensive care unit acquired hypernatremia
ICU- Intensive care unit
IU/l- international unit per liter
Meq/l- Milliequivalent per liter
NOACs- Novel oral anticoagulants
NSAID- non-steroidal anti-inflammatory drug
qSOFA- Quick sequential organ failure assessment score

Declarations

Author Contributions: conceptualization, Methodology, Investigation, Analysis, and Writing of the manuscript- Atiklet Zerihun Zewdie, Addisu Melkie Ejigu, Henok Baharu Wedajeneh

Methodology, Data curation, Drafting, Interpretation, and Supervision and edition of the manuscript- Ayanaw Guade Mamo, Muluken Alemayehu Workiye, Eyosias Lemma, Ermias Fikru Yesuf, Eyerusalem Yalew Talema

All authors revised the manuscript and have approved the final version of the manuscript.

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Ethical Clearance

Institutional Review Board Statement: The study was conducted by the Declaration of Helsinki and approved by the Institutional Review Board of Addis Ababa University, College of Health Sciences, Yekatit 12 hospital and St peter's hospital.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The authors confirm that the data supporting the findings of this study are available within the article.

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