original article

Prevalence of hyponatremia among medically hospitalized patients and associated outcomes: a retrospective cohort study

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BACKGROUND: Hyponatremia is a common electrolyte disturbance among hospitalized patients and is linked to increased mortality as well as poor outcomes.

OBJECTIVES: Study the prevalence of hyponatremia among medically admitted patients and the outcomes associated with hyponatremia.

DESIGN: Retrospective cohort

SETTING: Medical ward at tertiary hospital setting

PATIENTS AND METHODS: The study included adult (≥18 years) hospitalized patients in general medical wards. Three readings of serum sodium level were taken (initial sodium level, nadir during admission, and before discharge).

SAMPLE SIZE AND BASIS: The sample size of 350 was determined based on a presumed 35% incidence of hyponatremia among hospitalized patients, with a 5% error margin.

MAIN OUTCOME MEASURES: The prevalence of hyponatremia among medically hospitalized patients and association with health outcomes including length of hospital stay, inpatient mortality, 90-days readmission and 1-year mortality.

RESULTS: In this study, 736 patients met the inclusion criteria. Of these, 377 (51.2%) had hyponatremia on admission, increasing to 562 (76.35%) during hospitalization. Mild hyponatremia was observed in 49.6% (n=365), moderate in 13.6% (n=100), and severe in 13.2% (n=97). Severe hyponatremia patients were significantly older (P<.01), predominantly female (P=.014), and had lower serum magnesium and albumin levels (P<.01). Hypertension, ischemic heart disease, heart failure, and diabetes were more prevalent in severe hyponatremia cases (P<.01, P<.01, P=.045, P<.01, respectively). Hospital stays were significantly shorter for patients with normal sodium levels (P<.01). Patients with severe hyponatremia had a shorter time for first hospital readmission (HR=0.80, P<.01 [95% CI; 0.69-0.94]).

CONCLUSION: Hyponatremia was prevalent among medically hospitalized patients and more common among old patients, women, and patients with comorbidities. Hyponatremia was associated with increased length of stay in hospital and increased risk of 90-day readmission.

LIMITATIONS: Single-centre design and retrospective nature.

CONFLICT OF INTEREST: None.

Serum osmolarity must be maintained tightly as body cells are highly sensitive to minor changes in the osmolarity, leading to shrinkage or swelling and, ultimately, dysfunction. This is mainly achieved by maintaining sodium levels in the extracellular fluid, with the target being sodium, the major cation controlling serum osmolarity.[1] Hyponatremia is a frequently seen electrolyte abnormality in clinical practice with a 5-35% prevalence. The variation in the prevalence of hyponatremia in clinical practice is due to many factors, including the cut-off value used to define hyponatremia, frequency of testing of serum sodium level, and the health care setting.[2-4] In general, hyponatremia is defined by a serum sodium level of <135 mmol/L and further classified into mild (130-135 mmol/L), moderate (125-129 mmol/L), severe (<125 mmol/L).[5,6] Hyponatremia can be a chronic condition and asymptomatic; in contrast, it can also be symptomatic and life-threatening.[6] Hyponatremia is further classified based on the patient's volume status at the initial presentation; this includes hypervolemic, euvolemic, and hypovolemic hyponatremia.[5]

The pathophysiology of developing hyponatremia is attributed mainly to water excess or sodium loss.[3] Thus, hyponatremia can present with several conditions resulting in one of the two mechanisms or both, including chronic kidney disease (CKD), heart failure, liver cirrhosis, malignancies, gastrointestinal loss, syndrome of inappropriate antidiuretic hormone (ADH) secretion (SIADH) secondary to pulmonary or neurological conditions, medications or endocrine disorders.[5]

The brain is the main affected organ in hyponatremia, and the severity of brain swelling determines the clinical symptoms.[7] Acute hyponatremia occurs rapidly within 48 hours, allowing little time for the brain to adapt. Chronic hyponatremia develops gradually over more than 48 hours, giving the brain time to adapt fully. Severe hyponatremia can lead to hyponatremic encephalopathy, characterized by seizures, coma, and potentially fatal brain herniation.[7] Certain types of acute hyponatremia, such as water intoxication and postoperative hyponatremia, represent a higher risk for hyponatremic encephalopathy.[3] Moderate symptoms of hyponatremia include lethargy and confusion, while mild symptoms include fatigue, nausea, and headache. Recent evidence suggests that even mild hyponatremias can cause subtle symptoms that require specialized neurological testing for detection.[4] Chronic hyponatremia, even at mild levels, has been associated with increased mortality and morbidity, including gait disturbances, osteoporosis, and increased risk of falls and bone fractures.[3]

Treating severe symptomatic hyponatremia is crucial to prevent cerebral edema, which is achieved by hypertonic saline infusion. Chronic asymptomatic hyponatremia is treated mainly based on the fluid status, either with diuretics or isotonic saline infusion, with the aim of sodium raising not more than six mmol/L, and the underlying cause of hyponatremia should be investigated and treated.[3,8]

Hyponatremia is linked with various adverse health outcomes. These include an increased risk of falls and fractures, cognitive impairment, impaired quality of life, prolonged hospital stays, increased healthcare costs, and greater utilization of medical resources.[4,9,10] however, studies assessing the impact of hyponatremia in patients admitted to medical wards are sparse.[10]

This study aimed to explore the prevalence and health outcomes associated with hyponatremia among medically hospitalized patients.

METHODS

Study Design, Setting, and Population

This was a retrospective cohort study conducted at Sultan Qaboos University Hospital (SQUH) from December 29, 2020, to September 12, 2021, involving hospitalized adult patients (18 years) under the care of the General Internal Medicine Unit. SQUH is an academic tertiary hospital with 600 beds and provides multispecialty care for inpatients from all areas of Oman.[11] All adult Omani patients (≥18 years) admitted to the general medical wards were included in the study from December 29, 2020, to September 12, 2021. Three values of serum sodium were recorded: serum sodium on admission, the nadir serum sodium during hospital stay, and serum sodium upon discharge. Exclusion criteria included patients younger than 18 years old, patients with sodium level >145 upon admission, patients with fewer than two readings of sodium during admission, patients admitted directly to the high dependency unit (HDU) or intensive care unit (ICU), as well as adult patients admitted under subspecialties other than the General Internal Medicine Unit.

Data collection

Data were extracted from the patient's electronic health records, capturing relevant demographic information such as age and gender, along with their medical history, including hypertension, diabetes mellitus (DM), chronic kidney disease (CKD), heart failure (HF), ischemic heart disease (IHD), and chronic liver disease. The medications known to potentially cause hyponatremia, such as diuretics, antidepressants, antipsychotics, and antiepileptic medications, were documented. Sodium levels at admission and discharge and the nadir value recorded during hospitalization were recorded. Additionally, biochemical data were collected, including electrolyte levels such as calcium, potassium, phosphate, magnesium, and albumin. The patient's volume status at presentation was also recorded, and information regarding the treatment of hyponatremia was documented. The ICD-10 (the 10th revision of the International Statistical Classification of Diseases and Related Health Problems) categorized the primary diagnosis.[12]

The Indirect Ion Selective Electrode (ISE) method was used to measure sodium levels, a common practice in automated clinical labs. However, this method can be influenced by the electrolyte exclusion effect, potentially resulting in pseudohyponatremia influenced by hyperproteinemia.[13]

Based on the serum total sodium concentration, a normal sodium level was defined as serum sodium >135 mmol/L–145 mmol/L, while hyponatremia was defined as a sodium level <135 mmol/L, with subclassification into mild (130–135 mmol/L), moderate (125–129 mmol/L), and severe (<125 mmol/L). The prevalence of hyponatremia was calculated based on admission sodium readings and the nadir of sodium during admission. We utilized nadir serum sodium readings to assess hospitalization outcomes according to the severity of hyponatremia.

The research received approval from the Medical and Research Ethics Committee at the College of Medicine and Health Sciences, SQU, Muscat, Oman (MREC #2866; SQU-EC/ 087/2022; dated August 28th, 2022). This study adheres to the ethical guidelines and principles set forth in the Declaration of Helsinki/ Due to this study's retrospective design, the Medical and Research Ethics Committee waived the necessity for consent.

The sample size was calculated based on the presumed incidence of hyponatremia. The previously estimated incidence of hyponatremia was 35% among hospitalized patients.[14] It was estimated that a sample size of 350 patients is needed to assess the prevalence of hyponatremia among medically hospitalized patients (95% confidence, 5% margin of error).

Statistical analysis

Analysis was performed using the nadir sodium level during admission. Frequencies and percentages were used to present categorical variables. The mean and standard deviation (SD) were used to describe the continuously normally distributed variables, while the median and interquartile ranges (IQRs) were used to describe continuously abnormally distributed variables. Univariate analysis was performed using the Kruskal Wallis test or the ANOVA test along with the Bonferroni tests depending on the normality of the variables when compared with different hyponatremia and normal sodium groups. The Chi-Square test examined the relationships between categorical variables and different hyponatremia and normal sodium groups. Fisher's exact test was applied when the cells had an anticipated frequency of fewer than five. Kaplan-Meier survival estimates, and log-rank tests were performed to illustrate the time to the studied clinical outcomes among the patients with hyponatremia of different levels. Finally, after initiating hyponatremia treatments during admission, the Wilcoxon Signed Rank Sum test was used to identify the effect on sodium level (on admission versus discharge). The two-tailed significance level was established at $P<.05$. STATA version 17.0 was used for statistical analysis (StataCorp, 1985-2021, Stata Statistical Software, College Station, TX, USA).

RESULTS

A total of 898 patients were screened during admission. Among them, 34 patients were excluded due to a high sodium level (>145) on admission, and 128 patients were excluded as they had only one sodium reading during admission. Analysis was performed on 736 patients who met the inclusion criteria. 377 patients (51.2%, [95% CI: 0.476-0.548]) had hyponatremia on the day of admission, and using nadir serum sodium, there were total of 562 patients (76.35%, [95% CI:0.731-0.793]) who had hyponatremia during hospitalization.

Among the included patients, 49.6% (n=365/736) had mild hyponatremia, 13.6% (n=100/736) had moderate hyponatremia, and 13.2% (n=97/736) had severe hyponatremia. The clinical and biochemical characteristics of the groups stratified according to the severity of hyponatremia (mild, moderate, and severe) and normal sodium are presented **Table 1**.

More women were present in the severe hyponatremia group compared to other groups (P=.014). Also, patients in the severe hyponatremia group were older compared to other groups ($P<.01$). The serum magnesium level was significantly lower in the severe hyponatremia group compared to other groups ($P<.01$). Also, albumin level was significantly associated with the difference among the sodium groups, and we identified that patients with moderate and mild hyponatremia had statistically significant lower albumin levels compared to patients with normal sodium levels, P=.01 and P=.043, respectively, using Bonferroni test. Serum magnesium concentration was significantly lower in

Table 1. Clinical and biochemical characteristics and medications profile of admitted patients stratified according to hyponatremia (nadir) severity and normal sodium (n=736).

Characteristics	Total n=736 (100)	Severe hyponatremia <125 mmol/L n=97 (13.2)	Moderate hyponatremia 125–129 mmol/L n=100 (13.6)	Mild hyponatremia 130-135 mmol/L n=365 (49.6)	Normal level 136–145 mmol/L n=174 (23.6)	*P* value
Female	335 (45.5)	55 (56.7)	35 (35.0)	160 (43.8)	85 (48.9)	**.014**
Age (years)	65 (44-74)	72 (61-80)	64 (51-74)	59 (42-71)	61 (41-74)	**<.01**
Biochemical profile						
Calcium (mmol/L)	2.23 (2.14-2.32)	2.23 (2.13-2.32)	2.21 (2.12-2.28)	2.26 (2.14-2.33)	2.23 (2.14-2.31)	.212
Potassium (mmol/L)	3.7 (3.3-4.1)	3.8 (3.2-4.3)	3.7 (3.25-4.05)	3.7 (3.3-4.1)	3.7 (3.4-4.0)	.844
Magnesium (mmol/L)	0.77 (0.69-0.86)	0.71 (0.63-0.81)	0.76 (0.69-0.82)	0.78 (0.7-0.87)	0.81 (0.71-0.88)	**<.01**
Phosphate (mmol/L)	0.96 (0.74-1.18)	0.95 (0.77-1.27)	0.95 (0.71-1.13)	0.95 (0.7-1.18)	0.99 (0.77-1.19)	.856
Albumin (mmol/L)	31.6 (7.98)	32.4 (8.13)	30.0 (7.57)	31.1 (7.78)	33.1 (8.34)	**<.01**
Comorbidities						
Hypertension	412 (56.0)	73 (75.3)	63 (63.0)	189 (51.8)	87 (50.0)	**<.01**
Ischemic heart disease	155 (21.1)	34 (35.1)	26 (26.0)	66 (18.1)	29 (16.7)	**<.01**
Heart failure	106 (14.4)	22 (22.7)	17 (17.0)	43 (11.8)	24 (13.8)	**.045**
Diabetes mellitus	355 (48.2)	62 (63.9)	56 (56.0)	174 (47.7)	63 (36.2)	**<.01**
Chronic liver disease	39 (5.3)	4 (4.1)	6 (6.0)	21 (5.8)	8 (4.6)	.877
Chronic kidney disease	136 (18.5)	22 (22.7)	21 (21.0)	68 (18.6)	25 (14.4)	.319
Medications						
Diuretics	309 (42.0)	47 (48.5)	52 (52.0)	139 (38.1)	71 (40.8)	**.043**
Anti-psychotics	36 (4.9)	5 (5.2)	2 (2.0)	18 (4.9)	11 (6.3)	.454
Anti-depressants	25 (3.4)	4 (4.1)	4 (4.0)	8 (2.2)	9 (2.2)	.256
Antihypertensives	454 (61.7)	76 (78.4)	69 (69.0)	213 (58.4)	96 (55.2)	**<.01**
Anti-epileptics	63 (8.6)	10 (10.3)	6 (6.0)	28 (7.7)	19 (10.9)	.420

Data are number (percentage) unless specified otherwise. Age, and other continuous variables are median (25th-75th percentile) except albumin (mean, SD).

Table 2. Volume status assessment of admitted patients with hyponatremia stratified according to their severity (mild, moderate, and severe) (n=562).

Volume status assessment	Total n=562 (100)	Severe hyponatremia <125 mmol/L, n=97 (13.2)	Moderate hyponatremia 125-129 mmol/L, n=100 (13.6)	Mild hyponatremia 130-135 mmol/L, n=365 (49.6)	*P* value
Hypovolemic	128 (22.8)	32 (33.0)	18 (18.0)	71 (21.4)	**.024**
Euvolemic	47 (8.4)	13 (13.4)	4 (4.0)	30 (8.4)	.058
Overloaded	70 (12.5)	18 (18.6)	17 (17.0)	35 (9.6)	**.019**
Not assessed	317 (56.4)	34 (35.1)	61 (61.0)	317 (56.4)	**<.01**

Data are number (percentage).

the severe hyponatremia group compared to other groups (*P*<.01) (**Table 1**). Hypertension, ischemic heart disease, heart failure, and diabetes mellitus were more present among the severe hyponatremia group compared to normal sodium level, *P*<.01, *P*<.01, *P*=.045, *P*<.01, respectively. Also, the use of diuretics was more common among the moderate hyponatremia group in comparison with other groups (*P*=.04). In contrast, the use of antihypertensives was more common among the severe hyponatremia groups compared to other groups (*P*<.01) (**Table 1**).

The volume status assessment of admitted patients with hyponatremia is presented in **Table 2**. Among the 562 patients with hyponatremia, 128 (22.8%) patients were hypovolemic, 70 (12.5%) were overloaded, and only 47(8.4%) were euvolemic, whereas 317 (56.4%) were not assessed. The clinical assessment, whether hypovolemic or overloaded, was more apparent with severe hyponatremia than other levels of hyponatremia, *P*=.024 and *P*=.019, respectively.

Table 3 demonstrates the type of treatment provided for patients with hyponatremia during admission. There were 363 patients (64.6%) were treated with normal saline (0.9%) and 31 patients (5.5%) treated by free water restriction.

Also, we found that the treatment provided during admission was associated with significant improvement in sodium level by the discharge when compared with sodium level by the admission (median (IQR); 133 (130-135) vs 136 (133-139), *P*<.01).

As shown in **Table 4**, patients with normal sodium have significantly shorter lengths of hospital stay compared to other groups (*P*<.01). Also, admission to HDU/ICU was less common among severe hyponatremia groups compared to other groups (*P*=.013). 90-day readmission was less frequent among patients with normal sodium levels compared to other groups, but the difference was not statistically significant (*P*=.066). Also, there was no statistically significant difference in 1-year mortality across the groups.

Figure 1 illustrates the time to 90-day readmission analysis among patients readmitted within 90 days and compared with different sodium levels (total n=736). Patients in the severe hyponatremia group had a short duration to the first readmission with 90 days compared to other groups (HR)=0.80, *P*<.01 [95% CI; 0.69-0.94].

DISCUSSION

This study presents the prevalence of hyponatremia in patients admitted to a medical ward. It included a rela-

Table 3. Type of treatments provided for patients with hyponatremia (sodium ≤135 mmol/L) during admission (n=562).

Treatment of hyponatremia	Total (n=562)
No treatment	110 (19.6)
Free Water restriction	31 (5.5)
Normal Saline (0.9%)	363 (64.6)
Hypertonic saline (3.0%)	2 (0.4)
Free Water restriction + Normal Saline (0.9%)	21 (4.2)
Normal Saline (0.9%) + Hypertonic saline (3.0%)	20 (3.7)
Free Water restriction + Hypertonic saline (3.0%)	1 (0.2)
Free Water restriction + Normal Saline (0.9%) + Hypertonic saline (3.0%)	14 (2.5)

Data are number (percentage).

Table 4. Clinical outcomes of admitted patients stratified according to severity of hyponatremia (mild, moderate, and severe) and normal sodium (n=736).

Clinical outcomes	Total (n=736)	Severe hyponatremia <125 mmol/L n=97 (13.18%)	Moderate hyponatremia 125–129 mmol/L n=100 (13.59%)	Mild hyponatremia 130-135 mmol/L n=365 (49.59%)	Normal level 136–145 mmol/L n=174 (23.64)	P value
Length of stay (days)	6.7 (3.5-12.9)	6.8 (3.3-12.5)	7.5 (4.5-17.7)	7.0 (3.9-13.5)	5.0 (2.5 -8.3)	**<.01**
Admission to HDU/ICU	316 (43.0)	27 (27.8)	46 (46.0)	168 (46.0)	75 (43.1)	**.013**
Cardiorespiratory resuscitation	92 (12.5)	12 (12.4)	10 (10.0)	45 (12.3)	25 (14.4)	.768
Inpatient mortality	113 (15.4)	13 (13.4)	16 (16.0)	59 (16.2)	25 (14.4)	.889
90-day readmission	155 (21.1)	28 (28.9)	25 (25.0)	74 (20.3)	28 (16.1)	.066
1-year mortality	84 (11.4)	16 (16.5)	13 (13.0)	33 (9.0)	22 (12.6)	.170

Data are number (percentage) except length of stay.

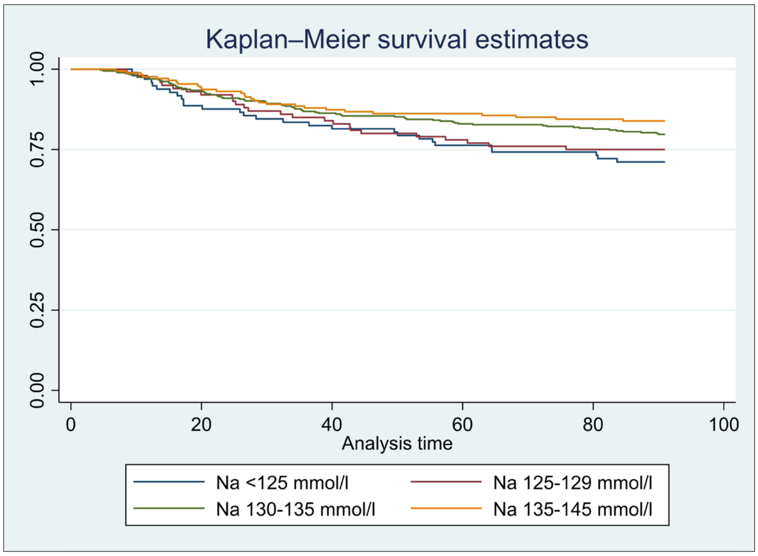

Figure 1. Analysis of time to 90-days readmission among the patients with different levels of sodium (n=736) [HR: 0.80, *P*<.01 [95% CI; 0.69-0.94].

tively large sample size and assessed factors associated with hyponatremia. The study also followed patients for one year to determine health outcomes associated with hyponatremia. The prevalence of hyponatremia was high among medically hospitalized patients. Also, hyponatremia was associated with increased length of hospital stay.

Previous studies reported that the prevalence of hyponatremia among medically hospitalized patients ranged between 30-42%.[10,14-16] However, the prevalence in our cohort was 51.2% upon admission and went up to 76.4% during hospitalization, which is higher than the previously reported prevalence. This difference could be attributed to several factors, including population age, medical background of the patients included in the study, frequency of measuring sodium, the use of medications, and their side effects. The study identified old age as a risk factor associated with severe hyponatremia, which is consistent with previous studies' findings.[17] Hyponatremia is more common in older individuals due to age-related factors such as decreased glomerular filtration rate, reduced prostaglandin production, and decreased total body water content.[18] Elderly individuals may also have a higher sensitivity to osmotic stimuli. Hyponatremia in the elderly often occurs due to increased water intake, medication use, underlying diseases, and low-salt diets. Reduced protein intake osmolytes deficient diet can further contribute to the development of hyponatremia in this population.[18,19]

Our study revealed a significant association between women and hyponatremia. This was also observed in multiple studies that confirmed the prevalence of hyponatremia is higher in women compared to men, including a large population-based study in the USA, which identified that hyponatremia was more common among women.[17,20,21] This association between women and hyponatremia was attributed to medication side effects; this difference could be secondary to differences in body sensitivity to medications. In our study, antidepressant prescription was more common in women compared to men (4.5% vs. 2.5%), which might contribute to the difference in hyponatremia between genders. In addition, men tend to have a higher proportion of lean mass, while women typically have a greater fat mass than men, and hence less water content.[22]

Serum magnesium concentration was significantly lower in severe hyponatremia groups; this could be explained by common factors causing both electrolyte derangement, including the use of diuretics, and malnutrition.[23-25] In addition, hypomagnesemia is associated with poor health outcomes among hospitalized patients.[26] The study revealed that albumin levels were significantly higher in patients with normal sodium levels. Hyponatremia is a common complication observed in patients with hypoalbuminemia, particularly in cirrhotic patients. The albumin level measured at presentation is a risk factor for hyponatremia, primarily due to the dilutional effect or intravascular volume depletion resulting from ineffective intravascular redistribution caused by splanchnic vasodilatation.[27-29]

This study demonstrated a significant association between hyponatremia and chronic medical conditions such as hypertension, diabetes mellitus, ischemic heart disease, and heart failure. Previous studies have indicated that hyponatremia serves as a poor prognostic indicator in several chronic conditions.[17,30] The prevalence of these chronic condition especially hypertension (56.0%) and diabetes mellitus were high (48.2%) which might contribute to high prevalence of hyponatremia in our cohort.

In patients with chronic heart failure, hyponatremia is attributed to many factors, including the activation of antidiuretic hormone (ADH), the renin-angiotensin-aldosterone system (RAAS), and also diuretics used to treat fluid overload play a major role.[31] Hyponatremia upon admission is considered a poor prognostic factor for patients with heart failure, with increased in-hospital mortality rates. However, treatment of hyponatremia in patients with chronic heart failure may improve this outcome.[32]

Diabetes mellitus can induce hyponatremia in several ways. Glucose acts as an osmolar molecule, which, when elevated in the blood, results in fluid shifting to the intravascular compartment, ultimately leading to hyponatremia. Additionally, hyperglycaemia can also result in hyponatremia due to its diuretic effects, causing hypovolemic hyponatremia.[33] Another factor contributing to hyponatremia in diabetic patients is the medications used to treat diabetes or complications of uncontrolled diabetes, such as neuropathies.[33,34]

Hyponatremia is a well-known complication of liver disease, which can manifest as dilutional or hypovolemic hyponatremia due to the net effect of water shifting to the extracellular compartment.[35] The morbidity and mortality rates are increased in cirrhotic patients with hyponatremia, significantly impacting the patient's prognosis both before and after liver transplantation.[36] However, we have not identified any association between hyponatremia and chronic liver disease in our cohort due to the small number of included patients with chronic liver disease.

Drugs play a major role in the development of hyponatremia, primarily by affecting sodium and water homeostasis. Several classes of medication have been implicated in hyponatremia,[36] but the main groups are drugs acting on the cardiovascular and nervous systems, as well as psychotropic and anti-cancer treatments.[37,38] This study included only the most frequently prescribed drugs for patients admitted to medical wards. Hyponatremia is a known side effect of diuretic therapy,[39] as confirmed by the significant association between diuretics and hyponatremia in the study.

Other antihypertensive medications were commonly prescribed in our cohort, and more than 60% of patients received at least one antihypertensive medication, which probably contributed to the high prevalence of hyponatremia in our cohort. A cohort study published in 2020 illustrated the association between the initiation of antihypertensive treatment, specifically calcium channel blockers (CCB), beta-blockers (BB), angiotensin-converting enzyme (ACE) inhibitors, and hyponatremia requiring hospitalization. However, ongoing long-term treatment with the same medications was found to be a risk factor for hospitalization secondary to hyponatremia.[39] Our study revealed a significant association between antihypertensive treatment and hyponatremia. A recent study published in 2021 addressed the association of hyponatremia with thiazide diuretics mainly compared to other categories of diuretics, with the highest incidence within the first month of initiation, followed by gradually reduced sodium values with the inability to have complete normalization.[40] Conversely, inconclusive, and conflicting data exist regarding non-thiazide diuretics and their association with hyponatremia. A recent study published in 2021 showed that loop diuretics are inversely related to hyponatremia, while potassium-sparing diuretics were associated with hyponatremia.[41]

Antidepressants and antipsychotic medications are also known to be associated with hyponatremia, mainly secondary to the Syndrome of Inappropriate ADH Secretion (SIADH), resulting in water retention.[37] Newly initiated SSRIs are strongly associated with hyponatremia requiring hospitalization; in comparison, this association is less prominent with tricyclic antidepressants.[42] On the other hand, antipsychotics also have an association with hyponatremia. They are associated with severe hyponatremia, causing hospitalization, mainly the first generation of antipsychotic medications.[43]

Categorizing hyponatremia based on volume status is crucial as it determines the treatment. A recent study published in 2023 revealed that hypovolemic hyponatremia was the most common, followed by euvolemic, then hypervolemic, and this was impactful in mortality as hypervolemic hyponatremia was significantly linked to higher rates of mortality.[5] Another recent study published in 2023 showed that symptomatic hyponatremia with more severe symptoms was observed in higher rates with hypervolemic hyponatremia.[44] Regarding the treatment of hyponatremia, correcting sodium levels by 4-6 mEq/L within 6 hours in severe cases is achieved through hypertonic saline boluses. A goal of raising sodium levels by six mEq/L over 24 hours is recommended, at most 10-12 mEq/L in any 24 hours, to avoid osmotic demyelination.[45,46] This can be accomplished through various methods. The method of correcting hyponatremia differs based on volume status and correcting the underlying disease. A systematic review was conducted to study the guidelines for managing hyponatremia, illustrating that the degree of raising sodium levels shouldn't exceed 8-12 mEq/L/24 hrs. Additionally, it concluded that severely symptomatic or acute onset hyponatremia in less than 48 hours should be treated with hypertonic saline. However, different guidelines differed in the initial dose and rate of infusion.[47] Our study illustrated that most patients with hyponatremia were mainly treated with normal saline (64.21%), with only 4.97% treated with water restriction. It is important to highlight that around 19.48% of patients didn't receive hyponatremia treatment, with the majority having mild to moderate hyponatremia and a minority having severe hyponatremia. The choice of treatment is decided based on hyponatremia severity and volume status. Symptomatic hyponatremia is treated with hypertonic saline, whereas hypovolemic hyponatremia is treated with normal saline. However, hypervolemic hyponatremia is mainly treated with water restriction, but other medications, such as loop diuretics and SGLT2 inhibitors, are also utilized.[8,48] Additionally, the underlying cause of hyponatremia should be treated. Tolvaptan, a V2-receptor antagonist, prevents water retention by acting on the renal system, contributing to treating euvolemic and hypervolemic hyponatremia.[49]

In this study, patients with normal sodium levels had significantly shorter hospital stays than those with hyponatremia. This finding is consistent with observations from multiple studies.[10,50] For instance, one study indicated that patients with hyponatremia experienced prolonged hospital stays, although it did not specify the severity of hyponatremia.[51] Additionally, a cross-sectional study conducted on patients admitted with pneumonia revealed a significant association between hyponatremia at presentation and the length of hospital stay.[52,53] Prolonged hospital stays were also noted in patients presenting with severe hyponatremia, which were associated with higher mortality rates and worse prognosis. This observed association between hyponatremia and poor outcomes across various domains could be explained by the crucial role of sodium levels in maintaining normal circulation and possibly due to the effect of serum osmolarity on different body cells, including neurons.[50,53-55] However, this study revealed that patients with severe hyponatremia had a lower rate of requirement for transfer to HDU/ICU , which contradicts findings from previous studies associating hyponatremia with a more increased need for high-acuity care.[55] One possible explanation is that in our cohort, more patients with severe hyponatremia had their intensive care deemed futile for various reasons. This is supported by the lack of differences in other indicators of poor health outcomes, including cardiopulmonary arrest and inpatient mortality.

The 90-day readmission rate was lower in patients with normal sodium levels than those with hyponatremia. However, the difference was not statistically significant (P=.066), nevertheless, survival analysis showed that the time for the first hospitalization was significantly shorter in patients with severe hyponatremia compared to patients with normal sodium levels. A study conducted in Turkey illustrated the increased rate of readmission within one year and all-cause mortality in patients with hyponatremia in general.[56] A meta-analysis of multiple studies confirmed the increased hospital readmission rates in patients with hyponatremia, with variable durations from discharge to readmission.[52] Similarly, the readmission rate within 30 days was higher among patients hospitalized but not receiving hyponatremia treatment.[57] In fact, several studies have shown that hyponatremia is associated with prolonged hospitalization duration and increased mortality rates regardless of severity, ultimately increasing healthcare costs.[7,52] An observational study evaluated the association of hyponatremia in patients with congestive heart failure and their outcomes. It demonstrated that lower sodium values were associated with longer hospital stays, increased mortality rates, and circulatory dysfunction.[58]

Several studies have shown that both hyponatremia and hypernatremia are significant predictors of increased inpatient mortality. However, our study did not demonstrate differences in inpatient mortality nor 1-year mortality, possibly due to the small sample size.[50,59]

This study has several strengths, including a reasonably large sample size and a focus on patients admitted to general medical wards. Additionally, the study collects comprehensive data regarding the potential causes of hyponatremia, treatment, and associated health outcomes. Limitations of the study include its single-center design and retrospective nature.

In conclusion, hyponatremia was prevalent among adult patients admitted to general medical wards Patients of old age and female gender and patients with hypertension, ischemic heart disease, heart failure, and diabetes mellitus had a higher incidence of severe hyponatremia. Prolonged hospital stays and 90-day re-admission risk were higher in patients with hyponatremia.

Author contributions

Conceptualization; A.A., design/methods; A.A., I.Y., and S.K., bibliographic research; I.Y., data curation; I.Y, A.F. and R.J., investigation; A.A., and I.Y., data analysis; J.M. writing—original draft preparation, I.Y., and J.M.; writing—review and editing, A.A. and J.M.

Institutional review board statement

The research received approval from the Medical and Research Ethics Committee at the College of Medicine and Health Sciences, SQU, Muscat, Oman (MREC #2866; SQU-EC/ 087/2022; dated August 28th, 2022). This study adheres to the ethical guidelines and principles set forth in the Declaration of Helsinki.

Informed consent statement

Due to this study's retrospective design, the Medical and Research Ethics Committee waived the necessity for consent.

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