RESEARCH

A RETROSPECTIVE ANALYSIS OF THE CAUSES OF SEVERE HYPONATREMIA IN THE PATIENTS AGED OVER 65 ADMITTED TO THE EMERGENCY DEPARTMENT

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Abstract

Introduction: This study aimed to retrospectively analyze the data of patients older than 65 years and diagnosed with severe hyponatremia in the emergency department.

Method: Patients ≥ 65 years and with severe hyponatremia (serum sodium levels ≤ 125 mEq/L) were included in the analyses.

Results: Fifty-five patients were hypovolemic, 22 were normovolemic, and 23 were hypervolemic. 65.5% (n = 36), 59.1% (n = 13) and 60.9% (n = 14) of the groups were females (p > 0.05), and regarding comorbidities, 27.3%, 9.1%, and 4.3% of the groups were diagnosed with a malignancy, respectively (p = 0.031).

Conclusions: Early diagnosis and treatment in the emergency department are critical considering the severity and prognosis of hyponatremia.

Keywords: Emergency Medicine; Geriatrics; Hyponatremia.

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INTRODUCTION

Hyponatremia is a sodium (Na) blood level lower than 135 mEq/L. It is the most common electrolyte disorder. Serum Na level (biochemically) and the development course determine the clinical diagnosis. The serum Na levels between 130–135 mEq/L, 125–129 mEq/L, and < 125 mEq/L are categorized as mild, moderate, and severe hyponatremia. It is acute if it develops in less than 48 hours and chronic if it takes longer (1). Elderly individuals are more prone to hyponatremia because of age-related factors (2). Moreover, medications, comorbidities, and body-fluid disorders may trigger hyponatremia in geriatric patients over 65 years (3).

Volume status, classified as hypovolemic, hypervolemic, or euvolemic, is critical in the etiology of hyponatremia (4). There is a water and an even more significant Na loss in hypovolemic hyponatremia, whereas both water and Na are elevated in hypervolemic hyponatremia (5, 6). Despite the increased body water, euvolemic hyponatremia has normal Na levels and no hypervolemia (7). Although euvolemic hyponatremia is most frequently seen with inappropriate ADH secretion, it may also occur due to hypothyroidism and drugs. Patients with hyponatremia should be evaluated according to their volume status and treated according to the underlying cause. Considering that the severity of hyponatremia increases with age (8), immediate evaluation and treatment after admission are essential. Severe hyponatremia increases in-hospital mortality in elderly individuals (9).

Based on this background, this study aimed to retrospectively analyze the data of patients older than 65 years and diagnosed with severe hyponatremia in the emergency department.

METHOD

Study design

Patients older than 65 and admitted to the emergency department of the Health, Practice, and Research Hospital between 01.07.2020 and 30.09.2020 with severe hyponatremia (Na level≤125 mEq/L) were included in the study. The records, including demographic characteristics, comorbidities, medications, symptoms, serum biochemical markers, hyponatremia volume status, and outcomes, were retrospectively analyzed. Patients younger than 65 years, incomplete data, and admitted due to trauma were excluded. The local ethics committee approved the study protocol (01.07.2020, 2020-09).

Laboratory

The creatinine, albumin, and glucose were analyzed using the colorimetric method in the Roche Cobas 6000 device e501 module. The creatinine measurement determined each patient's glomerular filtration rate (GFR) with the CKD-EPI formula. Potassium analyses were done with the Roche Cobas 6000 device and the indirect ion-selective electrode (ISE) method in the e501 module. The c-reactive protein (CRP) analyses were conducted using a turbidimetric method on the Cobas 6000 device e501 module. All these tests were performed in the biochemistry laboratory of the hospital.

Statistical Analysis

The data were analyzed using SPSS 20.0. Descriptive statistics were presented using frequency, percent, mean, standard deviation, median, minimum, and maximum values. The Kolmogorov–Smirnov test and the Shapiro–Wilk test evaluated normal distribution. The categorical and continuous variables were compared using the chi-square test and one-way ANOVA or Kruskal–Wallis tests based on the normal distribution, respectively. The Dunn–Bonferroni adjustment was applied for pairwise comparisons, and $p < 0.05$ indicated statistical significance.

RESULTS

Fifty-five patients were hypovolemic, 22 were normovolemic, and 23 were hypervolemic. Women constituted 65.5% (n = 36) Of the hypovolemic

group, 59.1% (n = 13) of the hypovolemic group and 60.9% (n = 14) of the hypervolemic group (p = 0.853). The mean (±SD) ages were 76.8 ± 9.1, 79.9 ± 8.9, and 77.1 ± 8.9 years, respectively (p = 0.357). Proportions of patients living in nursery were 45.5% (n = 25), 18.2% (n = 4), and 34.8% (n = 8), respectively (p = 0.079).

Comparisons of comorbidities, including hypertension, diabetes mellitus, coronary artery disease (CAD), congestive heart failure (CHF), cerebrovascular disease (CVD), atrial fibrillation (AF), peripheral artery disease (PAD), hypopituitarism, hypoalbuminemia, chronic renal failure (CRF), hypothyroidism, Alzheimer's disease, dementia, bipolar disorder, or malignancy, revealed no significant difference (p > 0.05). However, the hypovolemic group had significantly higher malignancy rates (27.3% vs. 9.1% in the normovolemic group, and 4.3% in the hypervolemic group; p = 0.031), and the hypervolemic group had significantly higher congestive heart failure rates (34.8% vs. 9.1% in the hypovolemic group, and 13.6% in the normovolemic group; p = 0.030) (Table 1).

The median GFR was higher (p = 0.031), and the median creatinine was lower in the hypovolemic group than in the hypervolemic group (p = 0. 012),

Table 1. Distribution of chronic diseases by groups

	Hypovolemic	Normovolemic	Hypervolemic	
	(n=55) n (%)	(n=22) n (%)	(n=23) n (%)	p
Hypertension	39 (70,9)	17 (77,3)	18 (78,3)	0,736
Diabetes Mellitus	15 (27,3)	5 (22,7)	12 (52,2)	0,057
CAD	7 (12,7)	3 (13,6)	7 (30,4)	0,191
CHF	5 (9,1)	3 (13,6)	8 (34,8)	***0,030***
CVD	6 (10,9)	2 (9,1)	2 (8,7)	1,000
AF	6 (10,9)	3 (13,6)	6 (26,1)	0,234
PAD	1 (1,8)	-	1 (4,3)	0,700
Hypopituitarism	2 (3,6)	-	-	1,000
Hypoalbuminemia	17 (30,9)	4 (18,2)	3 (13,0)	0,186
CRF	6 (10,9)	2 (9,1)	5 (21,7)	0,356
Hypothyroidis	2 (3,6)	-	2 (8,7)	0,324
Alzheimer	5 (9,1)	-	2 (8,7)	0,441
Dementia	1 (1,8)	2 (9,1)	-	0,166
Bipolarity	1 (1,8)	-	1 (4,3)	0,700
Malignity	15 (27,3)	2 (9,1)	1 (4,3)	***0,031***

%: Column Percentage, p: Chi-Square Test

and the median CRP was higher in the hypovolemic group than in the normovolemic group (p = 0.021). The glucose (p = 0.710), potassium (p = 0.188), and albumin (p = 0.060) were similar between the groups (Table 2).

The proportion of patients taking insulin (p = 0.045), clopidogrel (p = 0.009), and diuretic (p = 0.004) was significantly higher in the hypervolemic group (Table 3). Regarding outcomes, hospitalization was higher in the normovolemic group (p = 0.001), discharge was higher in the hypovolemic group (p = 0.008), and mortality was higher in the hypovolemic group (p = 0.009) (Table 4). And for comorbidities, patients aged 85 years and over had significantly more HT (p = 0.016), and CHF (p = 0.019) (Table 5).

DISCUSSION

Hyponatremia is classified as hypovolemic, normovolemic, and hypervolemic according to volume status (10). Studies revealed that hypovolemic hyponatremia is more common (11). Hyponatremia is the most common electrolyte disorder in patients with malignancy, with a prevalence of 4–47% (12). Therefore, target treatment is of great importance. Biological treatment methods used in cancer patients increase the hyponatremia risk (13). At the same time, hyponatremia is negatively correlated with the prognosis in cancer patients. In our study, hypovolemic hyponatremia was frequently observed in patients with malignancies. In geriatric patients, inadequate oral intake following drug use in treatment and subsequent nausea and vomiting may cause this. Although the Na and water increase in hypervolemic hyponatremia, water increase is more prominent (14). This condition is seen in cases of cirrhosis, nephrotic syndrome, acute and chronic kidney failure, and congestive heart failure. In our study, the most common cause of hypervolemic hyponatremia was congestive heart failure, in accordance with the literature.

The glomerular filtration rate (GFR) is a renal mechanism that regulates sodium in the body, and

Table 2. Comparison of laboratory values by groups

	Hypovolemic		Normovolemic		Hypervolemic		
	mean±sd	median (min-max)	mean±sd	median (min-max)	mean±sd	median (min-max)	p
CRP	5.54 ± 7.62	1.27 (0.305 - 9.14)	3.21 ± 6.32	0.260 (0.100 -1.89)	2.81 ± 3.86	0.820 (0.740 - 2.99)	***0,026***
Albumin	3.58 ± 1.08	3.53 (2.90 - 4.01)	3.92 ± 0.769	4.01 (3.54 - 4.29)	3.64 ± 0.342	3.60 (3.43 - 3.89)	0,060
Creatinine	1.14 ± 0.853	0.940 (0.670 - 1.21)	1.91 ± 1.34	0.955 (0.850 -1.27)	1.91 ± 1.34	1.29 (0.955 - 2.55)	***0,012***
K	4.03 ± 0.786	3.87 (3.53 - 4.51)	4.28 ± 0.700	4.32 (3.66 - 4.79)	4.44 ± 1.36	4.20 (3.40 - 5.32)	0,188*
Glucose	141 ± 51.1	129 (108 - 174)	132 ± 56.0	126 (104 - 160)	162 ± 97.7	155 (107 - 178)	0,710
GFR	69.9 ± 31.5	67.5 (50.3 - 90.0)	69.5 ± 22.6	76.4 (55.8 - 90.0)	51.2 ± 29.9	41.3 (24.8 - 79.5)	***0,029***

mean±sd: mean±standard deviation, p: Kruskal Wallis Test, p*: One-way ANOVA Test

Table 3. Comparison of drug groups between groups

	Hypovolemic	Normovolemic	Hypervolemic	
	(n=55) n (%)	(n=22) n (%)	(n=23) n (%)	p
Ca channel blocker	10 (18.2)	2 (9.1)	4 (17.4)	0,710
β blocker	16 (29.1)	5 (22.7)	8 (34.8)	0,672
ACE	20 (36.4)	9 (40.9)	10 (43.5)	0,824
RAAS	15 (27.3)	7 (31.8)	9 (39.1)	0,584
PPI	13 (23.6)	5 (22.7)	7 (30.4)	0,788
Antipsychotic	3 (5.5)	-	-	0,415
Insulin	5 (9.1)	-	5 (21.7)	***0,045***
OAD	9 (16.4)	5 (22.7)	7 (30.4)	0,362
Antidepressant	19 (34.5)	6 (27.3)	3 (13.0)	0,155
ASA	7 (12.7)	5 (22.7)	7 (30.4)	0,165
Clopidogrel	4 (7.3)	3 (13.6)	8 (34.8)	**0,009**
Diuretics	9 (16.4)	5 (22.7)	12 (52.2)	**0,004**

%: Column Percentage, p: Chi-Square Test

it determines the amount of Na filtered. In the geriatric patient group, there was a decrease in GFR. Thus, fluid absorption from the proximal tubule increases, and the amount of water reaching the distal tubule decreases. In this case, the kidney removes less water. As seen in the development of hyponatremia, urine concentrating capacity decreases with age, and as a result, hypovolemia was observed in geriatric patients. In our study, the median GFR was higher in the hypovolemic hyponatremia group compared to the hypervolemic hyponatremia group. This result correlates with the literature about geriatric patients. In the case of hypervolemic hyponatremia, extracellular water volume increased. Heart failure is observed in nephrotic syndrome, cirrhosis, and acute and chronic renal failure (15). Creatinine helps the anamnesis and physical examination of patients with hyponatremia. In our study, the median creatinine, an indicator of renal function, was higher in the geriatric patient group than in the hypovolemic hyponatremia group. Koçyigit and Aydin analyzed the factors associated with hyponatremia in the elderly, and found that the CRP level was higher in patients with hyponatremia compared to patients with normonatremia (16). Similarly, in our study, the median CRP was found to be higher in the hypovolemic hyponatremia group compared to the normovolemic hyponatremia group.

Drugs are one of the most common causes of hyponatremia in geriatric patients. The use of multiple drugs increases the susceptibility to hyponatremia in this age group (17). Many studies have shown that the risk of hyponatremia increases in patients who use drugs, such as diuretics, with varying physiology and multiple comorbidities depending

Table 4. Comparison of prognoses between groups

	Hypovolemic	Normovolemic	Hypervolemic	
	(n=55) n (%)	(n=22) n (%)	(n=23) n (%)	p
Mortality	10 (18,2)	-	-	***0,009***
Service	43 (78,2)	9 (40,9)	20 (87,0)	***0,001***
Intensive Care	7 (12,7)	-	-	0,061
Discharge	41 (74,5)	22 (100)	21 (91,3)	***0,008***
Referral	3 (5,5)	-	2 (8,7)	0,405

%: Column percentage, p: Chi-square Test

Table 5. Distribution of chronic diseases by groups

	65-74	75-84	85+	
	(n=43) n (%)	(n=34) n (%)	(n=23) n (%)	p
Hypertension	31 (72,1)	21 (61,8)	22 (95,7)	***0,016***
Diabetes Mellitus	16 (37,2)	7 (20,6)	9 (39,1)	0,211
CAD	9 (20,9)	5 (14,7)	3 (13,0)	0,653
CHF	4 (9,3)	4 (11,8)	8 (34,8)	***0,019***
CVD	2 (4,7)	7 (20,6)	1 (4,3)	0,060
AF	6 (14)	14,7 (34)	4 (17,4)	0,931
PAD	1 (2,3)	-	1(4,3)	0,705
Hypopituitarism	2 (4,7)	-	-	0,505
Hypoalbuminemia	9 (20,9)	8(23,5)	7 (30,4)	0,688
CRF	8 (18,6)	3 (8,8)	2 (8,7)	0,470
Hypothyroidis	3 (7,0)	1 (2,9)	-	0,549
Alzheimer	2 (4,7)	3 (8,8)	2 (8,7)	0,685
Dementia	1 (2,3)	1 (2,9)	1 (4,3)	1,000
Bipolarity	1 (2,3)	1 (2,9)	-	1,000
Malignity	11 (25,6)	3 (8,8)	4 (17,4)	0,164

%: Column percentage, p: Chi-square Test

on their age (18). Singh et al. stated that the risk of hyponatremia increased in the geriatric age group using diuretics compared to the adult age group. In addition, in the univariate analysis performed in this study, hyponatremia was found to be higher in geriatric patients with hypervolemic conditions who used diuretics (19). In our study, the incidence of hyponatremia was found to be significantly different in geriatric patients in the hypervolemic group who used diuretics. In addition, insulin and clopidogrel, which are drugs used for underlying diseases, were significant in terms of hyponatremia in geriatric patients with hypervolemia.

Al Mawed et al. found that mortality related to hyponatremia was significantly higher in the geriatric age group compared to the younger age groups (20). Hyponatremia has been directly or indirectly associated with an increased risk of death. Studies conducted concurrently indicated that hyponatremia alone did not cause mortality, but it may play a role in underlying diseases (21). Akin et al. found a greater incidence of mortality in the normovolemic group than in the hypervolemic and hypovolemic groups (22). However, in our study, it was observed that hypovolemic hyponatremia caused more mortality in the geriatric patient group, and hypovolemic hyponatremia was found to be significant in terms of discharge. Since high mortality is known, we can attribute this situation to good clinical follow-up and treatment. This situation plays an important role in the practices of geriatric patients.

Another remarkable point in our study was that admission to internal medicine services was significant in the normovolemic hyponatremia group. It is known that normovolemic hyponatremia is often related to inappropriately increased antidiuretic hormone release. Hypothyroidism, physical or emotional stress, and medications are among the causes. In a recent study, the in-hospital mortality related to hyponatremia, but not due to inappropriate ADH release, was 10% higher. In the case of inappropriate ADH release, mortality was reduced, so it had a protective effect (23).

In our study, we divided the patients into three age groups: 65–74 years old, 75–84, and 85 years old and older. We found that hypertension and heart failure were significant in the formation of severe hyponatremia in terms of underlying diseases, but the use of **β**-blocker medication in the 65–74 age group was more significant. In their study, Uyar et al. found hypertension to be the most important accompanying systemic disease in elderly patients (average of 75.28 years), followed by hyponatremia and then heart failure in the third rank (9). In another study, proton pump inhibitors, loop diuretics, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers were among the drugs associated with hyponatremia in the patient group with an average age of 85 years and over (23).

This study also has some limitations. First, the data presented are from a single center, and the number of patients is relatively low when the burden of the condition is considered. Moreover, analyzing whether the hyponatremia resulted from existing comorbidities or the medications was not possible. Nevertheless, the study provided valuable data for the clinical practices in the emergency department.

In conclusion, even patients over the age of 65 who were diagnosed with severe hyponatremia in the emergency department are analyzed by volume status or detailed anamnesis, appropriate treatment after physical examination plays an important role. Another point is that differential diagnosis is the cornerstone of hyponatremia management in the emergency department. However, hyponatremia is a common electrolyte disorder in the geriatric age group and is a severe health problem. Considering the severity and prognosis of hyponatremia, we should know that early diagnosis and treatment in the emergency department can decrease mortality and morbidity.

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