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Research Article

The Etiology, Presentation, Treatment, and Clinical Outcome of Geriatric Patients Diagnosed with Severe Hyponatremia on Site in the Emergency Department

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Abstract

Introduction: Hyponatremia is a common and serious problem especially for geriatric patients. This study was performed to determine the etiology, presentation, treatment, and clinical outcome of geriatric patients diagnosed with severe hyponatremia.

Methods: 267 (158 severe hyponatremia and 109 mild hyponatremia) geriatric patients were included in the study.

Results: In the severe hyponatremia group, the prevalence was 0.49%, where upon the most common reasons for emergency visit included neurological symptoms (53.2%), weakness (51.9%), and nausea-vomiting (47.5%). The most common reason in the etiology of severe hyponatremia was diuretic use; the most commonly used treatment regime was 3% hypertonic saline. The median time for the correction of Na levels was 96 (24 - 480) hours and 30 (6-360) hours in the severe and mild hyponatremia groups, respectively. 76.6% of the severe and 67% of the mild hyponatremia patients were followed-up in the clinic, whereas 17.1% and 22.9% were followed-up in the intensive care unit, respectively. The median hospitalization period was similar within both groups (6 days). 13% of the geriatric patients with severe hyponatremia and 21.1% of the geriatric patients with mild hyponatremia died. In our study, risk factors associated with severe hyponatremia were female gender, chronic kidney disease, angiotensin receptor blocker and thiazide use. Female gender, hospitalization period, hospitalization and sepsis were identified as risk factors associated with mortality.

Discussion: According to our literature review, this is the first comprehensive study investigating the etiology, presentation, treatment and clinical outcome in geriatric patients diagnosed with severe hyponatremia in the emergency department.

Keywords: *Emergency Department; Severe Hyponatremia; Geriatric Patient; Mortality*

Introduction

Severe hyponatremia is an electrolyte disturbance that has a very high morbidity and mortality rate [1]. Severe hyponatremia is defined as the serum Na concentration being below 120 mEq/L. The presence of acute severe hyponatremia may lead to serious neurological complications that can result in death [2]. Patients may complain of symptoms associated with central nervous system dysfunction due to cerebral edema, which may result from acute severe hyponatremia. Primary symptoms include nausea, vomiting, headache, loss of appetite, lethargy, fatigue, apathy, disorientation, lightheadedness, agitation, muscle cramps, and convulsions [3]. The most common reasons behind hyponatremia in patients visiting the emergency department and who are diagnosed with severe hyponatremia include syndromes of inappropriate antidiuretic hormone secretion (SIADH), hypovolemic hyponatremia associated with diuretic and gastrointestinal system (GIS) loss, and hypervolemic hyponatremia associated with congestive heart failure (CHF) [4]. The drug that most commonly causes severe hyponatremia was found to be thiazides. It was demonstrated that thiazide use increased the severity of hyponatremia [4]. The presence of severe hyponatremia increases the rate of hospitalization and admission to intensive care

unit in patients visiting the emergency department [5]. Short and long-term follow-ups of patients diagnosed with severe hyponatremia show that these patients have increased mortality [6].

The number of elderly people in the world population is growing. Elderly persons are more prone to physiological changes associated with old age, the presence of multiple comorbidities, and severe hyponatremia due to the use of multiple drugs. Severe hyponatremia worsens the progression of diseases found in geriatric patients, and results in morbidity and mortality by causing additional problems, hospitalization, and prolonged hospitalization stays [7]. Therefore, it is necessary to conduct studies in order to investigate the causes of hyponatremia, factors contributing to hyponatremia development, the application symptoms of patients, comorbidities, and drugs used by patients in order to prevent the development of hyponatremia among the elderly population.

For the reasons mentioned above, this study was performed in order to determine the prevalence, etiology, and treatment regimens of geriatric patients diagnosed with severe hyponatremia on site in the emergency department, and to investigate the relationship with mortality.

Materials and Methods

Study population

Those retrospectively included in the study were geriatric patients visiting the emergency department at the Ankara Numune Education and Research Hospital, between March 2016 and March 2017 for any given reason, and who were diagnosed with severe hyponatremia upon examination.

It was found that 82,560 patients visited the emergency department between the aforementioned dates. According to emergency biochemical examinations, 1,853 of these patients had a Na value lower than 135 mEq/L, while 665 patients had had a Na value lower than 120 mEq/L. 267 geriatric patients whose Na value was lower than 120 mEq/L and who had their complete data available were included in the study.

Those excluded from the study include patients under the age of 18, those with a Na value above 120 mEq/L, those who refused either treatment at the emergency department or hospitalization, those who were found to have pseudohyponatremia, isotonic hyponatremia, or hypertonic hyponatremia, those who were pregnant, had a single Na value, and those did not have all of their data available.

Patients aged 65 and above were accepted as being geriatric. Severe hyponatremia was defined as a serum Na value below 120 mEq/L. Lab test findings of the patients at the time of application and during hospitalization were obtained from an electronic information management system using their protocol numbers. Patients' demographic characteristics, additional comorbidities, emergency department-related medical history, vital signs, diagnosis, initial treatment, hospitalized service, treatment administered at the unit of hospitalization, daily follow-up findings, treatment responses, and hospitalization times were entirely obtained from their medical files. Emergency visit symptoms (e.g. nausea, vomiting, diarrhea, dyspnea, fever, neurological symptoms, weakness, muscle cramps), pre-diagnosis at emergency visit (e.g. infection, sepsis, gastrointestinal hemorrhaging, cerebrovascular events, trauma, encephalopathy), place of incidence (e.g. home, nursing home, another hospital), vital signs (e.g. blood pressure, pulse, Glasgow coma score) had been recorded from patient files.

The Clinical Research Ethics Board of Ankara Numune Education and Research Hospital had unanimously decided on the scientific and ethical appropriateness of the study on January 1, 2018 under decision number 1708/2017.

Statistical analysis

The Statistical Package for Social Sciences (SPSS) for Windows 20 (IBM SPSS Inc., Chicago, USA) was used for statistical assessments. The normal distribution of the data was evaluated using the Shapiro Wilk test. Values with normal distribution were presented as mean ± standard deviation, and values without normal distribution were presented as a median (lowest value-highest value). Categorical variables were presented in terms of numbers and percentages. An independent sample t-test (for numeric variables with normal distribution) and Mann Whitney U test (for numeric variables without normal distribution) were used to determine the distribution of numeric

variables between the two groups. The Chi-square and Fisher's exact Chi-square tests were used for the comparison of categorical data. Stepwise multivariable logistic regression analysis was used to determine independent predictors. Diagnostic assessment of independent predictors was performed using a receiver operating characteristic (ROC) curve. In statistical analysis, $p < 0.05$ was considered to be statistically significant.

Results

Table 1 shows the demographic characteristics and laboratory findings of the geriatric patients based on hyponatremia severity. The study population had consisted of 267 geriatric patients with hyponatremia. In terms of demographic characteristics, there was no significant difference between the geriatric patients whose Na value was either < 120 mEq/L and or ≥ 120 mEq/L. In terms of clinical findings, vomiting ($p = 0.001$) and weakness ($p = 0.045$) were more common in the Na < 120 mEq/L group, while fever ($p = 0.004$) was less common. In terms of comorbidities, hypertension ($p < 0.001$), chronic renal failure ($p < 0.001$) and hypothyroidism ($p = 0.003$) was more common in the Na < 120 mEq/L group. In terms of drug use, the Na < 120 mEq/L group had higher thiazide ($p = 0.01$), angiotensin receptor blocker ($p = 0.001$), and proton pump inhibitor ($p < 0.001$) use. In terms of laboratory findings, the albumin level ($p < 0.001$) was found to be higher in the Na < 120 mEq/L group.

Variables	Severe hyponatremia (Na < 120 mEq/L) (n = 158)	Moderate hyponatremia (Na ≥ 120 mEq/L) (n = 109)	P value
Gender, n (%)			
Female	111 (%70.3)	48 (%44)	<0.001
Age (year)	78.4 ± 7.2	79 ± 7.8	0.49
Systolic blood pressure (mmHg)	120 (60-200)	120 (70-200)	0.986
Diastolic blood pressure (mmHg)	70 (40-130)	70 (24-100)	0.665
Pulse (pulse/min)	80 (40-170)	80 (40-140)	0.057
Glasgow coma scale	14 ± 1.8	13.9 ± 2.16	0.981
Location of patient, n (%)			
Home	149 (%94.3)	100 (%91.7)	0.412
Nursing home	2 (%1.3)	4 (%3.7)	0.192
Another hospital	7 (%4.4)	5 (%4.6)	1
Application symptoms, n (%)			
Nausea and vomiting	75 (%47.5)	30 (%27.5)	0.001*
Diarrhea	17 (%10.8)	14 (%12.8)	0.601
Dyspnea	46 (%29.1)	44 (%40.4)	0.055
Fever	11 (%7)	20 (%18.3)	0.004*
Neurological symptom	84 (%53.2)	50 (%45.9)	0.241
Weakness	82 (%51.9)	70 (%64.2)	0.045*
Muscle cramp	4 (%2.5)	6 (%5.5)	0.325
Pre-diagnoses in emergency department, n (%)			
Infection	60 (%38)	42 (%38.5)	0.926
Sepsis	7 (%4.4)	7 (%6.4)	0.473
GIS bleeding	3 (%1.9)	4 (%3.7)	0.448
Acute cerebrovascular event	6 (%3.8)	4 (%3.7)	1
Trauma	8 (%5.1)	5 (%4.6)	0.858
Encephalopathy	4 (%2.5)	3 (%2.8)	1

Comorbidities, n (%)			
Diabetes	55 (%34.8)	37 (%33.9)	0.883
Hypertension	116 (%50.5)	55 (%73.4)	<0.001*
Cerebrovascular event	23 (%14.6)	12 (%11)	0.398
Coronary heart disease	72 (%45.6)	50 (%45.9)	0.961
Demans	16 (%10.1)	6 (%5.5)	0.177
Heart failure	42 (%26.6)	26 (23.9)	0.614
Chronic kidney disease	54 (%34.2)	14 (%12.8)	<0.001*
Hypothryroidism	26 (%16.5)	5 (%4.6)	0.003*
Malignity	26 (%16.5)	27 (%24.8)	0.09
Major surgery in the last 1 month	8 (%5.1)	4 (%3.7)	0.766
Pleural disease	39 (%24.7)	24 (%22)	0.614
Chronic liver disease	4 (%2.5)	8 (%7.3)	0.075
Drug information, n (%)			
Furosemid	35 (%22.2)	19 (%17.4)	0.345
Thiazide	58 (%36.7)	24 (%22)	0.01*
Spironolactone	12 (%7.6)	16 (%14.7)	0.06
Calcium channel blocker	45 (%28.5)	21 (%19.3)	0.08
Beta blocker	65 (%41.1)	40 (%36.7)	0.465
Angiotensin converting enzyme inhibitor	32 (%20.3)	28 (%25.7)	0.295
Angiotensin receptor blocker	48 (%30.4)	15 (%13.8)	0.001*
Proton pump inhibitor	72 (%45.6)	27 (%24.8)	<0.001*
Non-steroid antiinflammatory drug	8 (%5.1)	6 (%5.5)	0.873
Antipsychotics	15 (%9.5)	5 (%4.6)	0.134
Antiepileptic	7 (%4.4)	4 (%3.7)	1
Antidepressant	19 (%12)	8 (%7.3)	0.211
Glomerular filtration rate	52.5 (5-120)	51 (8-109)	0.824
Na (mEq/L)	115 ± 3.7	127.4 ± 4.2	<0.001*
K (mmol/L)	4.25 ± 1.01	4.4 ± 0.89	0.135
Albumin (g/dL)	3.3 ± 0.6	2.7 ± 0.6	<0.001*
Cortisol (µg/dL)	15.3 (2.4-34)	13.2 (2-22)	0.231
Thyroid stimulating hormone (µg/mL)	1.2 (0.007-32)	1.3 (0.002-36)	0.824
Urine Na (mmol/L)	39 (5-160)	61 (9-127)	0.243
Urine osmolality (mosm/kg)	233 (62-644)	252 (163-512)	0.3

Table 1: *Distribution of clinical demographic and laboratory findings according to the severity of hyponatremia in geriatric patients.*

Normally distributed numerical variables were shown as mean ± standard deviation.

Numerical variables that do not show normal distribution were shown with median (min-max).

Categorical variables were shown as number (%).

** p < 0.05 shows statistical significance.*

Table 2 shows the volume status, treatment options, and clinical outcomes of the geriatric patients depending on hyponatremia severity. The time for the correction of Na levels was longer for the Na < 120 mEq/L group compared to the Na ≥ 120 mEq/L group (96 h vs 30h, respectively; p < 0.001). The recurrent hyponatremia count was lower in the Na <120 mEq/L group compared to the Na ≥ 120 mEq/L group (14 vs 18, respectively; p = 0.01). In terms of treatment regimes, 3% saline use (p < 0.001) was more common in the Na < 120 mEq/L group, while isotonic saline use (p < 0.001) was more common in the Na ≥ 120 mEq/L group.

Variables	Severe hyponatremia (Na < 120 mEq/L) (n=158)	Moderate hyponatremia (Na ≥ 120 mEq/L) (n = 109)	P value
Hypovolemic, n (%)	89 (%56.3)	64 (%58.7)	0.698
Vomiting-diarrhea-excessive sweating	30 (%19)	21 (%19.3)	0.995
Losses to the 3rd space	3 (%1.9)	6 (%5.5)	0.166
Diuretic	41 (%25.9)	7 (%6.4)	<0.001*
Mineralocorticoid deficiency	4 (%2.5)	0	0.148
Normovolemic, n (%)	28 (%17.7)	12 (%11)	0.130
Glucocorticoid deficiency	2 (%1.3)	1 (%0.9)	1
Hypothyroidism	2 (%1.3)	0	0.515
Syndrome of inappropriate antidiuretic hormone	17 (%10.8)	8 (%7.3)	0.346
Other	7 (%4.4)	2 (%1.8)	0.317
Hypervolemic, n (%)	41 (%25.9)	33 (%30.3)	0.437
Heart failure	20 (%12.7)	23 (%21.1)	0.065
Chronic liver disease	3 (%1.9)	4 (%3.7)	0.449
Nephrotic syndrome	1 (%0.6)	0	1
Acute renal failure	5 (%3.2)	3 (%2.8)	1
Chronic kidney disease	9 (%5.7)	3 (%2.8)	0.37
Hyponatremia recovery time (h)	96 (24-480)	30 (6-360)	<0.001*
Recurrent hyponatremia, n (%)	14 (%8.9)	18 (%16.5)	0.01*
Treatment regimens, n (%)			
Isotonic saline	48 (%30.4)	59 (%54.1)	<0.001*
%3 saline	52 (%32.9)	11 (%10.1)	<0.001*
Diuretic	27 (%17.1)	28 (%25.7)	0.08
Hemodialysis	10 (%6.3)	5 (%4.6)	0.543
Liquid restriction	18 (%11.4)	6 (%5.5)	0.09
Vasopressin antagonists	3 (%1.9)	0	0.272
Latest situation in emergency department, n (%)			
Hospitalization	121 (%76.6)	73 (%67)	0.083
Intensive care unit	27 (%17.1)	25 (%22.9)	0.235
Transfer to another hospital	4 (%2.5)	3 (%2.8)	1
Emergency discharge	1 (%0.6)	2 (%1.8)	0.569

Death	0	1 (%0.9)	0.408
Clinical outcome, n (%)			
Discharged	114 (%72.2)	80 (%73.4)	0.822
Death	21 (%13.3)	23 (%21.1)	0.09
Transfer to another hospital	7 (%4.4)	5 (%4.6)	1
Discharged at your own request	16 (%10.1)	1 (%0.9)	0.09
Hospitalization time (day)	6 (0-84)	6 (1-47)	0.192
Discharge sodium value (mEq/L)	133 (116-144)	134 (124-141)	0.133
The day of death (day)	14 (1-84)	7 (1-29)	0.061

Table 2: *Volume status, treatment options and clinical outcome according to the severity of hyponatremia in geriatric patients. Numerical variables that do not show normal distribution were shown with median (min-max). Categorical variables were shown as number (%). * p <0.05 shows statistical significance.*

Table 3 shows the distribution of clinical, demographic, and laboratory findings of the geriatric patients based on survival. Female patients had died more frequently than their male counterparts. Those who had died had lower GCS (p = 0.003), fewer complaints of dyspnea (p = 0.045), a lower infection rate (p = 0.015), and lower furosemide (p = 0.014), thiazide (p = 0.022), and proton pump inhibitor (p = 0.026) use compared to those who survived.

Variables	Ex (n = 21)	Survivor (n = 137)	P Value
Gender, n (%)			
Female	10 (%47.6)	101 (%73.7)	0.015*
Systolic blood pressure (mmHg)	120 (94-200)	120 (60-200)	0.615
Diastolic blood pressure (mmHg)	70 (47-100)	70 (40-130)	0.827
Pulse (pulse/min)	80 (70-170)	80 (40-150)	0.329
Glasgow coma scale	12.6±2.9	14.2±1.5	0.003*
Location of patient, n (%)			
Home	19 (%90.5)	130 (%94.9)	0.341
Nursing home	0	2 (%1.5)	1
Another hospital	2 (%9.5)	5 (%3.6)	0.234
Application symptoms, n (%)			
Nausea and vomiting	6 (%28.6)	69 (%50.4)	0.063
Diarrhea	1 (%4.8)	16 (%11.7)	0.474
Dyspnea	10 (%47.6)	36 (%26.3)	0.045*
Fever	3 (%14.3)	8 (%5.8)	0.165
Neurological symptom	12 (%57.1)	72 (%52.6)	0.695
Weakness	10 (%47.6)	72 (%52.6)	0.673
Muscle cramp	0	4 (%2.9)	1
Pre-diagnoses in emergency department, n (%)			
Infection	13 (%61.9)	47 (%34.3)	0.015*
Sepsis	3 (%14.3)	4 (%2.9)	0.05
GIS bleeding	0	3 (%2.2)	1

Acute cerebrovascular event	1 (%4.8)	5 (%3.6)	0.581
Trauma	1 (%4.8)	7 (%5.1)	1
Encephalopathy	0	4 (%2.9)	1
Comorbidities, n (%)			
Diabetes	6 (%28.6)	49 (%35.8)	0.519
Hypertension	16 (%76.2)	100 (%73)	0.757
Cerebrovascular event	5 (%23.8)	18 (%13.1)	0.167
Coronary heart disease	12 (%57.1)	60 (%43.8)	0.253
Demans	3 (%14.3)	13 (%9.5)	0.359
Heart failure	8 (%38.1)	34 (%24.8)	0.200
Chronic kidney disease	7 (%33.3)	47 (%34.3)	0.930
Hypothryroidism	4 (%19)	22 (%16.1)	0.753
Malignity	2 (%9.5)	24 (%17.5)	0.286
Major surgery in the last 1 month	3 (%14.3)	5 (%3.6)	0.07
Pleural disease	8 (%38.1)	31 (%22.6)	0.126
Chronic liver disease	0	4 (%2.9)	1
Drug information, n (%)			
Furosemid	9 (%42.9)	26 (%19)	0.014*
Thiazide	3 (%14.3)	55 (%40.1)	0.022*
Spironolactone	1 (%4.8)	11 (%8)	1
Calcium channel blocker	3 (%14.3)	42 (%30.7)	0.122
Beta blocker	11 (%52.4)	54 (%39.4)	0.261
Angiotensin converting enzyme inhibitor	6 (%28.6)	26 (%19)	0.228
Angiotensin receptor blocker	2 (%9.5)	46 (%33.6)	0.026*
Proton pump inhibitor	9 (%42.9)	63 (%46)	0.789
Non-steroid antiinflammatory drug	2 (%9.5)	6 (%4.4)	0.288
Antipsychotics	1 (%4.8)	14 (%10.2)	0.695
Antiepileptic	1 (%4.8)	6 (%4.4)	1
Antidepressant	2 (%9.5)	17 (%12.4)	1
Glomerular filtration rate	49 (5-120)	53 (6.8-110)	0.296
Na (mEq/L)	116±2.5	114±3.8	0.164
K (mmol/L)	4.48±1	4.22±1	0.174
Albumin (g/dL)	3.13±0.69	3.3±0.59	0.164
Cortisol (µg/dL)	16.1 (5.5-27)	15.3 (2.4-34)	0.790
Thyroid stimulating hormone (µg/mL)	1.85 (0.09-26)	1.17 (0.07-32)	0.358
Urine Na (mmol/L)	46 (5-114)	39 (6-160)	0.992
Urine osmolality (mosm/kg)	287 (147-394)	231 (62-644)	0.713

Table 3: *The distribution of clinical demographic and laboratory findings according to survival in geriatric patients.*

Normally distributed numerical variables were shown as mean ± standard deviation.

Numerical variables that do not show normal distribution were shown with median (min-max).

Categorical variables were shown as number (%).

** p <0.05 shows statistical significance.*

Table 4 shows the volume status, treatment options, and clinical outcomes of the geriatric patients depending upon survival rates. Among those who survived, their recurrent hyponatremia rate (p = 0.015), the number of those who had received hemodialysis (p = 0.029), and the number those who were hospitalized in a regular unit (p < 0.001) was higher. Among those who had died, the number of those hospitalized in the intensive care unit (p < 0.001) as well as the length of their stay in hospital (p = 0.001) was higher.

Variables	Ex (n = 21)	Survivor (n = 137)	P Value
Hypovolemic, n (%)	8 (%38.1)	81 (%59.1)	0.07
Vomiting-diarrhea-excessive sweating	1 (%4.8)	29 (%21.2)	0.130
Losses to the 3rd space	1 (%4.8)	2 (%1.5)	0.350
Diuretic	2 (%9.5)	39 (%28.5)	0.065
Mineralocorticoid deficiency	1 (%4.8)	3 (%2.2)	0.438
Normovolemic, n (%)	3 (%14.3)	8 (%5.8)	0.165
Glucocorticoid deficiency	5 (%23.8)	23 (%16.8)	0.538
Hypothyroidism	1 (%4.8)	1 (%0.7)	0.249
Syndrome of inappropriate antidiuretic hormone	1 (%4.8)	1 (%0.7)	0.249
Other	2 (%9.5)	15 (%10.9)	1
Hypervolemic, n (%)	1 (%4.8)	6 (%4.4)	1
Heart failure	8 (%38.1)	33 (%24.1)	0.173
Chronic liver disease	5 (%23.8)	15 (%10.9)	0.149
Nephrotic syndrome	0	3 (%2.2)	1
Acute renal failure	0	1 (%0.7)	1
Chronic kidney disease	2 (%9.5)	3 (%2.2)	0.132
Hyponatremia recovery time (h)	144 (48-336)	96 (24-480)	0.446
Recurrent hyponatremia, n (%)	5 (%23.8)	9 (%6.6)	0.015*
Treatment regimens, n (%)			
Isotonic saline	3 (%14.3)	45 (%32.8)	0.085
%3 saline	7 (%33.3)	45 (%32.8)	0.965
Diuretic	5 (%23.8)	22 (%16.1)	0.362
Hemodialysis	4 (%19)	6 (%4.4)	0.029*
Liquid restriction	1 (%4.8)	17 (%12.4)	0.471
Vasopressin antagonists	1 (%4.8)	2 (%1.5)	0.350
Latest situation in emergency department, n (%)			
Hospitalization	3 (%14.3)	118 (%86.1)	<0.001*
Intensive care unit	17 (%81)	10 (%7.3)	<0.001*
Hospitalization time (day)	14 (1-84)	6 (0-37)	0.001*

Table 4: *Volume status, treatment options and clinical outcome according to the survival in geriatric patients. Numerical variables that do not show normal distribution were shown with median (min-max). Categorical variables were shown as number (%). * p < 0.05 shows statistical significance.*

Table 5 shows risk factors associated with severe hyponatremia and mortality in detail. The forward stepwise logistic regression model, which included possible risk factors found to be statistically significant and associated with severe hyponatremia in geriatric patients, showed that gender (OR = 2.633; p < 0.001), chronic kidney disease (OR = 0.297; p < 0.001), thiazide use (OR = 0.858; p = 0.04)

and angiotensin receptor blocker use (OR = 0.585; p = 0.023) were predictors of severe hyponatremia. The risk for severe hyponatremia was found to be 2.633 times higher among women. The presence of chronic kidney disease, angiotensin receptor blocker use, and thiazide use was found to affect hyponatremia; however, it was not possible to reach a statistically conclusive result given that the OR value was smaller than 1. Also, the Nagelkerke's R value showed that the variables used in the regression model explained hyponatremia in geriatric patients at a rate of 38%.

Variables	OR	%95 C.I.	P
Severe Hyponatremia			
Female gender	2.633	1.515-4.575	<0.001
Thiazide	0.858	0.402-1.831	0.04
Chronic kidney disease	0.297	0.149-0.594	<0.001
Angiotensin receptor blocker use	0.585	0.256-1.335	0.023
Nagelkerke R = 0.384			
Mortality			
Female gender	5.154	1.105-24.039	0.037*
Hospitalization time	1.125	1.037-1.1222	0.005*
Intensive care unit	0.029	0.007-0.115	<0.001*
Sepsis	0.135	0.025-0.715	0.019*
Nagelkerke R=0.850			

Table 5: *Risk factors associated with severe hyponatremia and mortality.*

** p < 0.05 shows statistical significance.*

Abbreviations: OR: Odd ratio, CI: Confidence intervale

The forward stepwise logistic regression model, which included possible risk factors found to be associated with mortality, showed that gender (OR = 5.154; p = 0.037), hospitalization time (OR = 1.125; p = 0.005), admission to the intensive care unit (OR = 0.029; p < 0.001), and sepsis (OR = 0.135; p = 0.019) were predictors of mortality. The mortality risk was found to be 5.154 higher among men, whereupon prolonged hospital stay had increased mortality rate by 1.125 times. Being transferred to the intensive care unit from the emergency department and sepsis was found to affect hyponatremia; however, it was not possible to reach a statistically conclusive result since the OR value was smaller than 1. Moreover, the Nagelkerke's R value showed that the variables used in the regression model explained mortality at a rate of 85%.

Discussion

In this study, we investigated the prevalence, presentation, etiology, treatment methods, and clinical outcomes of severe hyponatremia in geriatric patients.

The prevalence of geriatric patients with severe hyponatremia was found to be 0.49%. To the best of our knowledge, there is no study in the literature investigating the severe hyponatremia prevalence in geriatric patients visiting the emergency department. Olsson., *et al.* [8] had investigated patients visiting the emergency department who were diagnosed on-site with severe hyponatremia and found the prevalence of severe hyponatremia to be 0.08%. In a similar study, Winzeler., *et al*. [4] found the prevalence of severe hyponatremia to be 0.6%.

In our study, the most common reasons for emergency visit included weakness (56.9%), neurological symptoms (50.2%), and nausea-vomiting (39.3%). The most common reasons for emergency visit among patients who had died, on the other hand, were findings of dyspnea and infection. Similar to our findings, Durmuş., *et al*. [9] had found that the most common complaints at the time of emergency visit among patients with severe hyponatremia included shortness of breath, nausea, vomiting, a loss of appetite, weakness, and mental

fog. The authors suggested that the dyspnea complaint might have developed due to the underlying CHF, pleural diseases, and pneumonia. In the literature, the rate of neurological symptoms and cerebrovascular event was found to be higher among patients with hyponatremia. Olsson., *et al*. [8] had found that neurological symptoms were more common among patients with severe hyponatremia. The rate of severe hyponatremia is considerable among patients who visit the emergency department due to trauma. Such trauma patients were present in our study, as well. Previous studies had shown that hyponatremia was associated with falling, fracture, and osteoporosis [10-14]. Kuo., *et al.* found that more geriatric patients with hyponatremia visited the emergency department due to trauma in comparison to those without hyponatremia. The authors had also found that presence of hyponatremia increased the risk of trauma by 2.5 times in geriatric patients presenting to the emergency department with trauma [15]. In another study, it was reported that a serum Na drop of 5 mEq/L was correlated with a 32% increased risk of fall [16]. In yet another study, hyponatremia was found to be an independent risk factor for falls and fractures in geriatric patients [17].

Previous studies showed that old age might cause susceptibility to hyponatremia [18,19]. Holland-Bill., *et al.* [20] reported that the prevalence of hyponatremia increased with advancing age. In another study, the mean age of emergency department patients diagnosed with hyponatremia was found to be 73 years, which was higher compared to patients without hyponatremia [19]. In parallel with the literature, the mean age of the patients was 69.6 ± 14.3 years, whereas the mean age of the patients with hyponatremia was 78.6 ± 7.4 years in our study. Studies in the literature reported that women were more likely to develop hyponatremia compared to men [18]; however, there is no certain evidence for reason behind the susceptibility of females to hyponatremia [21]. Similar to the literature findings, 70.3% of the patients with severe hyponatremia in our study were female. A comparison of geriatric patients with severe hyponatremia depending on survival revealed that severe hyponatremia was found to be 5.15 times more mortal in men in spite of its rarer prevalence among men compared to women. Being female was found to increase the risk of severe hyponatremia by 2.6 times. In parallel with our results, Rao., *et al.* found the mortality rate to be 9.09% for female and 33.3% for male in patients with severe hyponatremia and reported that the mortality rate was significantly higher among males [22].

In terms of accompanying comorbidities, we determined that chronic kidney disease and hypothyroidism were more common among geriatric patients with hyponatremia. Chronic kidney disease and hypothyroidism increased the risk of severe hyponatremia by 0.297 times. In another study, the rate of liver cirrhosis was found to be higher among emergency department patients with hyponatremia compared to those without hyponatremia [4]. In our study, there was no significant correlation between the hyponatremia severity and rate of liver cirrhosis. In another study, the authors had found no significant relation between hyponatremia severity and diabetes mellitus, hypertension, malignancy, chronic kidney disease, pleural disease, liver cirrhosis, cardiac arrhythmia; while there was a significant relation between coronary artery disease, CHF, neurological diseases, and hypothyroidism. In this study, a comparison between mild hyponatremia and severe hyponatremia had revealed that liver cirrhosis and CHF were more common among patients with mild hyponatremia [23]. In one study, it was found that the prevalence of a serum Na concentration less than 135, 130, and 120 meq/L in patients with cirrhosis, whereas ascites was 49.4%, 21.6%, and 1.2%, respectively [24]. In another study, it was found that the prevalence of a serum Na concentration of 130-134 mEq/L, 125 - 129 mEq/L, and less than 125 mEq/L in patients with CHF was 52.9%, 11%, and 5.7%, respectively [25]. As suggested by these studies, the prevalence of mild hyponatremia is high in patients with liver cirrhosis and CHF.

Studies in the literature showed that drug use and number of drugs used were risk factors for severe hyponatremia development [19,26]. Huwyler., *et al.* [19] found that patients with severe hyponatremia had higher rate of usage of thiazide and potassium-sparing diuretics. In our study, a comparison between the geriatric patients based on hyponatremia severity had showed that thiazide, angiotensin receptor blocker, and proton pump inhibitor use was more common among patients with severe hyponatremia. It was found that thiazide use increased severe hyponatremia risk by 0.858 times, while angiotensin receptor blocker use had increased severe hyponatremia by 0.585 times. Rodenburg., *et al.* [27] investigated thiazide-associated hyponatremia and found that thiazide used increased hyponatremia development by 5 times. In other studies, the researchers showed that the risk of thiazide-associated hyponatremia development was higher among elderly patients and patients with a low body mass index [28-31]. Decreased ability to balance water and Na due to age, more common electrolyte changes during intravascular volume changes, reduced kidney function due to age, and decreased water and drug excretion were suggested as being the reasons behind thiazide-induced hyponatremia in elderly patients [32].

In a study with geriatric patients [33], syndrome of inappropriate antidiuretic hormone secretion (SIADH) was found to be the reason behind hyponatremia among half of the patients. Winzeler., *et al*. [4] found SIADH to be the most common reason behind hyponatremia with 61.2%. SIADH was followed by hypovolemic hyponatremia (gastrointestinal loss and third space loss), hypervolemic hyponatremia (liver, heart, and kidney failure), and primary polydipsia. In terms of hyponatremia severity, the authors found that hypervolemic hyponatremia and hypovolemic hyponatremia were more common in those with Na > 120 mEq/L, while SIADH was more common in those with Na < 120 mEq/L. In our study, a comparison between the geriatric patients based on hyponatremia severity had showed that diuretics use was significantly more common as the reason behind hyponatremia among those with severe hyponatremia. Contrary to the aforementioned study, in our study, SIADH was more common among those without severe hyponatremia.

In terms of treatment regime, a comparison between the geriatric patients based on hyponatremia severity showed that isotonic saline use was more common within the mild hyponatremia group, while 3% saline use was more common within the severe hyponatremia group. A comparison between the geriatric patients with severe hyponatremia based on survival showed that the rate of hemodialysis was higher among those who died. Similar to our results, Olsson., *et al.* [8] had found that the most common regime used in treatment of hyponatremia was isotonic saline. Winzeler., *et al.* [4] found that 3% saline treatment was more commonly administered to patients with Na < 120 mEq/L.

In our study, a comparison between the geriatric patients based on severity of hyponatremia revealed that the median time for the correction of Na levels in the severe hyponatremia group was 96 hours, which was longer than those with mild hyponatremia. Recurrent hyponatremia was more common among the geriatric patients with mild hyponatremia. Abouem., *et al.* [34] found that the median time for the correction of Na levels was 96 hours in patients with a Na value less than 130, which is consistent with our study. An assessment of the patients based on survival revealed no correlation between hyponatremia recurrence and time for the correction of Na levels. Winzeler., *et al.* [4] compared patients with and without severe hyponatremia and found no significant difference in terms of hyponatremia recurrence.

In terms of the patients' emergency department outcomes, we found that 76.6% of the patients with severe hyponatremia were transferred to a normal department, and 17.1% were admitted to the intensive care unit. An assessment of the geriatric patients with severe hyponatremia based on survival showed that 81% of the deceased patients had been admitted to the intensive care unit, and admission to the intensive care unit was an independent risk factor for mortality. A study in the literature [35] reported that mechanical ventilation and admission to the intensive care unit were more common in patients with hyponatremia. In another study [4], 36.7% of patients with hyponatremia were admitted to the intensive care unit. Olsson., *et al.* [8] found that 80% of patients with severe hyponatremia were admitted to the high dependency unit and intensive care unit. As suggested by these studies, the rate of admission to the intensive care unit varies depending on the study population and the center where the study is conducted. However, studies show that presence of severe hyponatremia leads to an increased rate of admission to the intensive care unit.

In our study, it was found that 96.6% of the patients diagnosed with hyponatremia in the emergency department were hospitalized. In terms of the hospitalization duration of the geriatric patients based on hyponatremia severity, it was found that the median hospitalization time was 6 (0 - 84) days in the severe hyponatremia group, and that the hospitalization time did not significantly increase depending on hyponatremia severity. An assessment of the geriatric patients based on survival demonstrated that the median hospitalization time was 6 (0 - 37) days for those who had survived, and 14 (1 - 84) days for those who had died. The hospitalization time was found to be significantly longer among the patients who died compared to those who survived. Also, prolonged hospitalization time was found to increase mortality by 1.12 times. Gosch., *et al.* [26] found that the hospitalization time of patients with hyponatremia was longer. Olsson., *et al.* [8] found that the median hospitalization time was 7 days for patients with severe hyponatremia, which was longer compared to those with mild hyponatremia.

The mortality rate varies depending on the study population and the center where the study is conducted. Ellis., *et al.* [36] found a mortality rate of 29% among patients with severe hyponatremia (Na < 120 mEq/L). Anderson., *et al*. [37] found a mortality rate of 8.7% among patients with a Na value less than 130 mEq/L. In our study, the mortality rate of geriatric patients with severe hyponatremia was found to be 13.2%. Consistent with our study, Kayar., *et al*. [23] found a mortality rate of 17.6% among patients with hyponatremia.

Mortality among male patients was found to increase by 5.15 times, prolonged hospitalization by 1.125 times, admission to intensive care unit by 0.029 times, and sepsis by 0.135 times.

Limitation of the Study

The first limitation of our study was its retrospective and single-center design; the second limitation was the inability to assess the volume status of the patients due to the retrospective design of the study; the third limitation was the inability to calculate the actual prevalence given that the patients were admitted directly to the intensive care unit without visiting the emergency department; the fourth limitation was our inability to reach all examinations related with hyponatremia's etiology; the fifth limitation was the inability to assess the patients in terms of acute and chronic hyponatremia; and finally, the sixth limitation was the inability to assess the complications associated with hyponatremia.

Conclusion

Severe hyponatremia is a serious and urgent clinical issue that causes morbidity and mortality in geriatric patients. Geriatric patients are more susceptible to hyponatremia than other patient populations due to existing comorbidities, drug use, and physiological changes due to aging. For this reason, health professionals need to be aware of hyponatremia and check serum Na values of all geriatric patients visiting the emergency department due to the non-specific nature of hyponatremia symptoms. If hyponatremia is detected, the first step should be to perform etiological examinations and accordingly start treatment immediately.

Declarations of Conflict of Interest

None.

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