

# Incidence of Hyponatremia in Geriatric Patients Presenting to the Emergency Department with Headache

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## ABSTRACT

**Objective:** Headache is one of the most common neurological complaints in elderly population. Hyponatremia is a rare condition that can cause headache. The aim of our study was to evaluate the frequency and etiology of hyponatremia in geriatric patients presenting to the emergency department (ED) with atraumatic headache.

**Methods:** This is an observational, retrospective study. Patients aged 65 years and older with serum sodium levels who presented to the ED with headache were included in the study. Demographic data, comorbidities, other admission complaints, medications, and sodium levels were retrospectively reviewed.

**Results:** The study included 429 patients. Hyponatremia was detected in 17.7% (n=76) of the patients and was mostly mild (56.6%). In comparison with normonatremic patients, hyponatremic patients had increased frequency of hypothyroidism and diuretic use, longer hospital stays, higher blood urea nitrogen, and lower serum osmolality, hemoglobin, and albumin levels (p<0.05 for all values).

**Conclusion:** Our results showed the presence of hyponatremia in a significant proportion of patients presenting to the ED with headache. Most cases of hyponatremia were hypovolemic and was caused by diuretic use, dehydration, and inappropriate antidiuretic hormone syndrome. In patients with comorbidities and polypharmacy, hyponatremia should be prioritized as a potential cause of secondary headache and should contribute to the management of patients in emergency settings.

**Keywords:** Geriatric, headache, hyponatremia

## INTRODUCTION

Headache is one of the most common neurological complaints in elderly population (1-3). The assessment and management of headache in geriatric patients can be challenging both diagnostically and therapeutically. New-onset headache in older patients is more likely to be secondary. In one study, 15% of people over 65 years of age with new-onset headache had a serious underlying cause, compared to 1.6% of people under 65 years of age (2). Hyponatremia is one of the conditions that can cause secondary headache, although it is not common (4).

Hyponatremia is the most common electrolyte disturbance in older adults and can increase morbidity and mortality (5). Elderly patients presenting to the emergency department (ED) may present with medical conditions related to hyponatremia or traumatic conditions related to possible neurological

effects (6). Hyponatremia is common in geriatric population, particularly due to physiologic decline, comorbidities, and/or polypharmacy (7-9). In addition, several elderly patients with heart failure or hypertension are on a salt diet, which is associated with decreased serum sodium levels. This may increase their hyponatremia susceptibility. Changes in sodium concentration can cause neurologic symptoms (imbalance, dizziness, headache, cognitive deterioration, confusion), seizures, coma, and even death. Clinical symptoms are generally related to the severity of hyponatremia (1,9,10). While common symptoms include nausea, fatigue, and headache, recent studies have shown that low serum sodium may be related to cognitive health in older adults in the general population and associated with poorer scores on cognitive assessments of attention, memory, and psychomotor function (11,12). Although mild chronic hyponatremia is classically defined as asymptomatic, recent studies have shown that mild

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hyponatremia may be clinically significant in geriatric patients and may be associated with gait disturbances and new-onset neurologic symptoms (5,6). In a study evaluating hyponatremia in geriatric patients, the majority of patients (81%) were symptomatic and most (62%) had more than one symptom (13). Fatigue (50%), headache (40%), and abnormal behavior (39%) were reported as common symptoms (11). Another study from Türkiye reported that nausea/vomiting and changes in consciousness (confusion, etc.) were the most common symptoms, while headache was less common (10). In our clinical practice, we observed a significant rate of hyponatremia in geriatric patients presenting to the ED with atraumatic headache. In this study, we aimed to evaluate the presence and etiologies of hyponatremia, a cause of secondary headache, in geriatric patients presenting to the ED with atraumatic headache.

## METHODS

### Study Design and Settings

Our study is a retrospective study. The study was conducted in a level three ED with an annual admission rate of 360,000 patients. The study got approval from the University of Health Sciences Türkiye, Ankara Atatürk Sanatorium Training and Research Hospital Scientific Studies Ethics Committee (no: 2024-BÇEK/35, date: 28.02.2024). Patient data was collected from patient charts and electronic medical records.

### Study Population

Patients aged 65 years and older with documented serum sodium levels who presented to the University of Health Sciences Türkiye, Ankara Atatürk Sanatorium Training and Research Hospital with headache between 01.01.2023-31.12.2023 were included in the study. Patients were screened according to ICD-10 (International Statistical Classification of Diseases: R51, G44 and its subcodes). Patients without sodium levels, patients with neurological deficits, patients diagnosed with acute cerebrovascular disease after imaging, patients with a history of head trauma and headache, ICD codes defined as end-stage malignancy, decompensated heart failure, decompensated cirrhosis, and hemodynamically unstable (oxygen saturation <90, systolic blood pressure <90 mmHg,  $PCO_2 > 50$  mmHg, body temperature  $> 37.3$  °C) were excluded. Patients with pseudohyponatremia due to multiple myeloma and other monoclonal gammopathies were excluded from the study. Meanwhile, pseudohyponatremia due to hyperlipidemia could not be evaluated because lipid profiles were not obtained from patients in the ED.

In hyperglycemic patients, the "corrected sodium" level was calculated using the following formula, and patients with a corrected sodium level below 135 mmol/L were considered hyponatremia.

For glucose levels between 100 and 399 mg/dL; Corrected Na = Measured Na +  $1.6 \times [(Glucose - 100) / 100]$  mmol/L

For glucose level  $\geq 400$  mg/dL; Corrected Na = Measured Na +  $2.4 \times [(Glucose - 100) / 100]$  mmol/L.

## Methods

Demographic data, comorbidities (diabetes mellitus, cardiac disease, hypertension, pulmonary disease, hypothyroidism, dementia, malignancy), complaints other than headache on admission, vital signs, laboratory results, medications [proton pump inhibitors (PPIs), selective serotonin reuptake inhibitors (SSRIs), diuretics (loop and/or thiazide diuretics)], and computed tomography (CT) scan were retrospectively reviewed. Discharge, hospitalization status, and length of stay were analyzed. Patients were classified as having either primary (migraine, tension, and cluster) or secondary headaches. The secondary headache etiologies were evaluated (1). Patients with no cause in their records were classified as unknown. In patients with normal glucose levels and hyperglycemia, hyponatremia was considered if the sodium level was less than 135 mmol/L. Patients were classified as severe hyponatremia (<125 mmol/L), moderate hyponatremia (125-129 mmol/L), and mild hyponatremia (130-134 mmol/L) according to plasma sodium concentrations.

### Statistical Analysis

Data analysis was performed with the statistical program IBM SPSS 20.0 (Chicago, IL, USA). Continuous numerical variables are presented as median (interquartile range: 50), and categorical variables are presented as number of cases and (%). The Kolmogorov-Smirnov test was used to determine whether the distribution of discrete and continuous numerical variables was normal. Categorical variables were evaluated using the chi-square test, and continuous variables by Mann-Whitney U test. Although a multivariate regression analysis was planned at baseline to identify risk factors that could predict hyponatremia, a multivariate regression analysis was not performed to create a model with only unadjusted odds ratio (UOR) values because the frequencies of risk factors that were significant in the univariate analyses did not meet the required sample size and the number of patients with significant hyponatremia was low. Results were considered statistically significant at  $p < 0.05$ .

## RESULTS

During the study period, 946 patients were found to have presented to the ED with headache. Five hundred and four patients with missing data (without sodium level) and 13 patients who did not meet the inclusion criteria were excluded from the study, and 429 patients were included. 71.1% of the patients were female, and the median age was 72 (68-78) years. The most common comorbidities were hypertension and diabetes mellitus. Head CT imaging was performed in 19.6% of patients. In addition to headache, the most common complaint was fatigue (15.6%). Tension-type headache was the most common type of headache, and hypertension-induced headache was the most common secondary headache. Hyponatremia was found in 17.7% (n=76) of the patients, and the majority of these hyponatremia cases were mild (56.6%). Additionally, 5.4% of all patients were hospitalized, with 2.3% specifically due to hyponatremia. Patient demographics are presented in Table 1. Possible etiologies of hyponatremia are shown in Table 2. When the hyponatremic patients were

**Table 1. Demographic data of patients (n=429)**

<b>Age</b> > years, median (IQR)	72 (10)
Sex, n (%)	
Female	305 (71.1)
<b>Co-morbidity, n (%)</b>	
Hypertension	255 (59.4)
Diabetes mellitus	173 (40.3)
Cardiac disease	185 (43.1)
Chronic renal failure	44 (10.3)
Hypothyroidism	18 (4.2)
Dementia	33 (7.7)
Chronic obstructive pulmonary disease	110 (17)
<b>Drugs, n (%)</b>	
ACE-I	134 (31.2)
Antidepressant	25 (5.8)
PPI	195 (45.5)
Diuretic	143 (33.3)
<b>Symptoms, n (%)</b>	
Fatigue	67 (15.6)
Dizziness	55 (12.8)
Nasua/vomiting	46 (10.7)
Weakness	30 (7)
Convulsion	1 (0.2)
<b>Vital signs, median (IQR)</b>	
GCS	15 (0)
Pulse	86 (9)
Systolic	129 (14)
Diastolic	86 (8)
Temperature	36.2 (0.1)
<b>Headache type, n (%)</b>	
<b>Primer</b>	
Tension	173 (40.3)
Migraine	42 (9.8)
<b>Secunder</b>	
Hypertension	134 (31.2)
Hyponatremia	33 (7.7)
Cervical spine disorders	6 (1.4)
Drugs	6 (1.4)
Unknown	45 (10.5)
Cranial computed tomography, n (%)	182 (19.6)
Hyponatremia, n (%)	76 (17.7)
<b>Severity of hyponatremia, n (%)</b>	
Mild	43 (56.6)
Moderate	28 (36.8)
Severe	5 (6.6)

**Table 1. Continued**

<b>Laboratory, median (IQR)</b>	
Hemoglobin	13.1 (1.1)
Glucose	108 (6)
Sodium	138 (6)
Corrected sodium	138.3 (5.1)
BUN mg/dL	46 (23)
Creatinine mg/dL	1.02 (0.19)
Albumin g/dL	4 (0.4)
Osmolarity	287 (11)
Hospitalization rate, n (%)	23 (5.4)
Hospitalization due to hyponatremia	10 (2.3)
Hospital stay duration, (days) median (IQR)	4 (4)

IQR: interquartile range, ACE-I: angiotensin-converting enzyme inhibitors, PPI: proton pump inhibitor, GCS: Glasgow coma scale, BUN: blood urea nitrogen

**Table 2. Possible causes of hyponatremia according to volume status**

Hypovolemic	48 (63.2%)
• Diuretic use	38 (79.2)
• Decreased oral intake/vomiting	10 (20.8%)
Normovolemic	22 (28.9%)
• SIADH	15 (68.2%)
• Hypothyroidism	7 (31.8%)
Hypervolemic	6 (7.9%)
• Chronic renal disease	4 (75%)
• Hypoalbuminemia	2 (25%)

SIADH: syndrome of inappropriate antidiuretic hormone secretion

evaluated according to volume status, the most common type of hyponatremia was hypovolemic hyponatremia (63.2%), which was most often related to diuretic use. When normonatremic and hyponatremic patients were compared, hyponatremic patients had more frequent hypothyroidism and diuretic use, longer hospital stays, higher blood urea nitrogen, and lower serum osmolarity, hemoglobin, and albumin levels ( $p < 0.05$  for all values, Table 3). A univariate regression analysis was performed to determine the impact of the parameters listed in Table 3 on hyponatremia risk (Table 4). In this regression analysis, hypothyroidism (UOR: 3.154, 1.181-8.423), Diuretic use (UOR: 1.695, 1.022-2.813), and decreased oral intake/vomiting (UOR: 2.554, 1.301-5.014) were found to be predictors of hyponatremia.

## DISCUSSION

In this study, in which we investigated the prevalence and factors influencing hyponatremia in geriatric patients who presented to the ED with headache, we found that the prevalence of hyponatremia was 17.7% and was mostly mild. Most hyponatremia cases were hypovolemic hyponatremia. We found that diuretic use, dehydration, and inappropriate antidiuretic hormone (ADH) syndrome caused hyponatremia and prolonged hospital stay.

**Table 3. Comparisons of patients according to sodium levels**

Characteristic	Hyponatremia patients (n=76)	Normonatremic patients (n=353)	p-value
<b>Sex, n (%)</b>			
Female	58 (76.3)	247 (70)	0.268
Age > years, median (IQR)	73 (12)	71 (10)	0.131
<b>Co-morbidity, n (%)</b>			
Hypertension	48 (63.2)	207 (58.6)	0.467
Diabetes mellitus	35 (46.1)	138 (39.1)	0.262
Cardiac disease	35 (46.1)	150 (42.5)	0.570
Chronic renal failure	6 (7.9)	38 (10.8)	0.454
Hypothyroidism	7 (9.2)	11 (3.1)	0.025
Dementia	10 (13.2)	23 (6.5)	0.049
<b>Drugs, n (%)</b>			
ACE-I	26 (34.2)	108 (30.6)	0.537
Antidepressant	7 (9.2)	18 (5.1)	0.177
PPI	32 (42.1)	163 (46.2)	0.518
Diuretic	33 (43.4)	110 (31.2)	0.040
<b>Symptoms, n (%)</b>			
Fatigue	38 (50)	29 (8.2)	<0.001
Dizziness	6 (7.9)	49 (13.9)	0.157
Nasua/vomiting	15 (19.7)	31 (8.8)	0.005
Weakness	4 (5.3)	25 (7.1)	0.567
Convulsion	1 (1.3)	0 (0)	0.177
<b>Laboratory, median (IQR)</b>			
Hemoglobin	12.8 (2.1)	13.2 (1.3)	0.002
Glucose	108 (34)	108 (36)	0.293
BUN mg/dL	44 (22.5)	47 (22)	0.039
Creatinine mg/dL	1.25 (0.41)	1.25 (0.51)	0.306
Albumin g/dL	3.9 (0.2)	4.05 (0.4)	0.002
Osmolarity	278 (264-280)	289 (9)	<0.001
Hospital stay duration, days, median (IQR)	5 (2.5)	2.5 (3)	0.011

IQR: interquartile range, ACE-I: angiotensin-converting enzyme inhibitors, PPI: proton pump inhibitor, BUN: blood urea nitrogen

**Table 4. Univariate regression analysis to predict the development of hyponatremia**

	Wald	p-value	Unadjusted odds ratio (95% CIs)
Age	1.67	0.196	1.024 (0.998-1.062)
Sex	1.21	0.27	0.723 (0.407-1.286)
Hypertension	0.52	0.467	1.209 (0.725-2.017)
Diabetes mellitus	1.25	0.263	1.33 (0.807-2.191)
Cardiac disease	0.323	0.570	1.155 (0.702-1.901)
Chronic renal failure	0.459	0.456	0.711 (0.289-1.746)
Hypothyroidism	5.25	0.022	3.154 (1.181-8.423)
Dementia	3.73	0.053	2.174 (0.989-4.781)
Hypoalbuminemia	1.46	0.226	0.548 (0.207-1.451)
ACE-I	0.38	0.538	1.18 (0.698-1.994)
Antidepressant	1.84	0.171	1.888 (0.759-4.694)
PPI	0.41	0.518	0.848 (0.514-1.399)
Diuretic	4.17	0.041	1.695 (1.022-2.813)
Decreased oral intake/vomiting	7.426	0.006	2.554 (1.301-5.014)

ACE-I: angiotensin-converting enzyme inhibitor, PPI: proton pump inhibitor, CIs: confidence intervals

Headache prevalence in older adults, ranges from 12% to 50% (1,2). In 17% of people over 65 years of age, frequent headache occurs more than 2 times per month (2). Although headache in older adults is usually caused by a primary headache disorder; aging, comorbidities, medication use, polypharmacy, and altered pharmacokinetics increase the risk of secondary headache (1,2). As with younger individuals, the first step in diagnosing new-onset headache in the elderly is to exclude secondary causes. New-onset geriatric headache and possible secondary headache disorders should be systematically managed, and diagnostic evaluation, ranging from neuroimaging to blood tests, should be performed in appropriate patients.

Sodium disturbances are common in geriatric patients (5-7). Changes in sodium levels can cause seizures, coma, and even death due to mild neurologic symptoms (14). Nausea and weakness are the earliest symptoms; as the severity of hyponatremia increases, headache, drowsiness, confusion, and finally seizures, coma, and respiratory arrest may occur (15). In our study, the most common symptom besides headache was weakness. We observed that altered consciousness and vomiting were more common in hyponatremia patients. Vomiting may have developed secondary to hyponatremia, or vomiting and dehydration may have predisposed to hyponatremia. One patient presented with post-ictal headache who was found to have severe hyponatremia.

Hyponatremia in the elderly is often secondary to multifactorial medications and ADH syndrome (8,16). Inappropriate ADH syndrome is often asymptomatic and idiopathic in the elderly (8). In addition, many classes of medications, such as thiazide diuretics, renin-angiotensin-aldosterone system inhibitors, antidepressants, PPIs, and antipsychotics can increase both volume and sodium loss, leading to inappropriate ADH syndrome and hyponatremia in this age group (8,16,17). The most common type in our study was hypovolemic hyponatremia. Most hypovolemic hyponatremia cases were the result of side effects caused by diuretic use. Although no statistically significant difference was observed in the hyponatremia group, the rate of antidepressant use was higher (9.2%). Hyponatremia due to antidepressant use is mostly hypotonic (dilutional) hyponatremia, and the underlying cause is often elevated plasma ADH levels. Again, most of our patients were taking more than one drug that can cause hyponatremia. Hyponatremia may also develop because of drug interactions. Many non-analgesic drugs, especially nifedipine, nitrates, SSRIs, and PPIs, which are commonly prescribed to elderly patients, may also be associated with headache (1). New-onset headache should be considered an adverse effect of recently started medications (1,18). Patients may develop headache due to hyponatremia as well as due to adverse drug reactions.

One of the causes of hyponatremia is hypothyroidism. The main mechanism of hyponatremia in patients with hypothyroidism is the decrease in free water excretion due to high ADH levels, which has been shown to be mainly due to the decrease in cardiac output caused by hypothyroidism (19). In our study, hypothyroidism was present in 9.2% of patients in the hyponatremic group and was

statistically more frequent in the normonatremic group. In Uyar et al.'s (10) study, hypothyroidism was found at a rate of 7.2% in normovolemic hyponatremia patients, and although the literature on this subject is insufficient, it has been suggested that the frequency of hyponatremia due to hypothyroidism is higher. The presence of hypothyroidism in our study may have predisposed patients to hyponatremia.

Although a multivariate regression analysis was planned at baseline to identify risk factors that could predict hyponatremia, a multivariate regression analysis was not performed to create a model with only unadjusted OR values because the frequencies of risk factors that were significant in univariate analyses did not meet the required sample size. A univariate regression analysis was performed to determine the impact of the parameters on the prediction of hyponatremia and hypothyroidism. Diuretic use and decreased oral intake/vomiting were found to be predictors of hyponatremia. In our study, most patients had mild hyponatremia, and after appropriate management in the ED, these patients were discharged. However, 2.3% of patients were hospitalized due to hyponatremia. We believe that medication adjustments, appropriate fluid and electrolyte replacement, and ordering thyroid function tests, when necessary, could contribute to better patient management in patients with secondary headaches due to hyponatremia in the ED.

### Study Limitations

Due to the retrospective nature of the study, missing hospital records may have affected the study results. Because this was a single-center study, our results cannot be generalized to all centers. Sodium levels measured at the time of presentation to the ED were used, and follow-up was not performed. Pseudohyponatremia due to hyperlipidemia was not evaluated because a lipid profile was not obtained from the ED patients. Although the prevalence of hyponatremia due to hyperlipidemia was low, this condition may have influenced our results.

Regression analysis could not be performed because we did not have a sufficient sample size to perform regression analysis, and data losses that may occur due to the retrospective nature of our study (drugs that may cause hyponatremia, conditions that we did not obtain from patient records, etc.) may cause various biases. Again, due to missing data, it was not possible to differentiate acute hyponatremia from chronic hyponatremia.

### CONCLUSION

Older adults are at higher risk for secondary headache. We demonstrated the presence of hyponatremia in a significant proportion of patients presenting to the ED with headache. We have shown that most hyponatremia is hypovolemic and is caused by diuretic use, dehydration, and inappropriate ADH syndrome. Although primary headaches are more common in the geriatric age group, hyponatremia should be prioritized as a potential cause of secondary headaches in patients with comorbidities and polypharmacy, as it may play a role in the emergency management of these patients.

**Ethics Committee Approval:** This study protocol was approved by Scientific Studies Ethics Committee of University of Health Sciences Türkiye, Ankara Atatürk Sanatorium Training and Research Hospital (no: 2024-BÇEK/35, date: 28.02.2024). The study was conducted in accordance with the Good Clinical Practice and the Declaration of Helsinki ethical standards.

**Informed Consent:** This study was a retrospective study based on anonymous data; patient consent was not obtained.

**Author Contributions:** Concept - E.E., H.Ö.O.; Design - E.E., H.Ö.O., Y.Ç.; Data Collection and/or Processing - H.Ö.O., A.Ş., H.E.Y.; Analysis and/or Interpretation - E.E., H.Ö.O., A.Ş., H.E.Y., Y.Ç.; Literature Search - H.Ö.O., A.Ş., H.E.Y.; Writing - E.E., H.Ö.O., Y.Ç.

**Conflict of Interest:** The authors have no conflict of interest to declare.

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