



## RESEARCH

# The incidence of hyponatremia in hospitalized patients due to hip fracture and its effect on mortality

Kalça kırığı nedeniyle hastaneye başvuran hastalarda yatış sırasındaki hiponatremi insidansı ve mortaliteye etkisi

Kemal Kayaokay<sup>1</sup>, Derya Arslan Yurtlu<sup>2</sup>

<sup>1</sup>Izmir Katip Celebi University, Atatürk Training and Research Hospital, Department of Orthopaedics and Traumatology, <sup>2</sup>Department of Anesthesiology and Reanimation, Izmir, Turkey

### Abstract

**Purpose:** Hyponatremia is associated with high morbidity and mortality in elderly patients. This study aimed to investigate the incidence of hyponatremia and its effects on the duration of hospitalization, in-hospital and 1-year mortality in elderly patients admitted to the hospital due to hip fracture.

**Materials and Methods:** After the approval of the ethics committee, patients over the age 65 and had hip surgery between January-December 2020 were retrospectively analyzed. The age, gender, fracture type, current comorbidities, and American Society of Anesthesiology physical status scores of the patients were recorded. Plasma Na, K, and Ca values in admission to hospital were recorded. Patients with hyponatremia and normonatremia were compared in terms of demographic data, comorbidities, duration of hospitalization, in-hospital, and 1-year mortality rates.

**Results:** Of the total 253 patients, 52(%20.5) had hyponatremia at hospital admission. Demographic data were similar in hyponatremic and normonatremic patients. In hyponatremia group mean Na values were  $131.13 \pm 3.96$  mmol/L and significantly lower than normonatremia group ( $138.73 \pm 2.27$ ). In the hyponatremic group, diabetes mellitus was observed in 23 (44%) patients, and congestive heart failure was observed in 9 (17%) patients, which was higher than the normonatremic group. The preoperative and total duration of hospitalization was  $5.21 \pm 2.68$  and  $9.92 \pm 4.49$  days respectively and higher in patients with hyponatremia. In-hospital and 1-year mortality rates were similar between the groups.

**Conclusion:** The incidence of hyponatremia was found to be 20.5% in patients with hip fractures, and both the preoperative and total hospital stays were prolonged in these patients. Although mortality rates were similar in this study, hyponatremia requires careful follow-up and early

### Öz

**Amaç:** Hiponatremi, kalça kırığı nedeniyle hastaneye yatırılan kırılğan yaşlı hastalarda yüksek morbidite ve mortalite ile ilişkilidir. Bu çalışmada, kalça kırığı nedeniyle hastaneye başvuran yaşlı hastalarda hiponatremi insidansının, hastanede yatış süresi, hastane içi ve 1 yıllık mortalite üzerine etkilerinin araştırılması amaçlandı.

**Gereç ve Yöntem:** Ocak-Aralık 2020 tarihleri arasında Ortopedi Kliniğine kalça kırığı nedeniyle başvuran 65 yaş üstü hastalar retrospektif olarak incelendi. Hastaların yaşı, cinsiyeti, kırık tipi, ek hastalıkları ve ASA fiziksel durumu kaydedildi. Hastaneye yatıştaki plazma Na, K ve Ca değerleri kaydedildi. Hiponatremik ve normonatremik hastalar demografik veriler, komorbiditeler, hastanede kalış süreleri, hastane içi ve 1 yıllık mortalite oranları açısından karşılaştırıldı.

**Bulgular:** Toplam 253 hastanın 52 (%20,5) 'sinde hastaneye yatışta hiponatremi mevcuttu. Hiponatremik ve normonatremik hastalarda demografik veriler benzerdi. Hiponatremi grubunda ortalama Na değerleri  $131,13 \pm 3,96$  mmol/L idi ve normonatremi grubuna göre anlamlı derecede düşüktü ( $138,73 \pm 2,27$ ). Hiponatremik hastalarda diabetes mellitus (n:23, %44) konjestif kalp yetmezliği (n:9, %17) oranları daha yüksekti. Ameliyat öncesi ve toplam hastanede yatış süresi sırasıyla  $5,21 \pm 2,68$  ve  $9,92 \pm 4,49$  gündü ve hiponatremili hastalarda anlamlı olarak daha yüksekti. Hastane içi ve 1 yıllık mortalite oranları gruplar arasında benzerdi.

**Sonuç:** Kalça kırığı olan hastalarda hiponatremi insidansı %20,5 olarak saptandı ve bu hastalarda hem ameliyat öncesi hem de toplam hastanede kalış süresi uzadı. Bu çalışmada mortalite oranları benzer olsa da, hastanede kalış süresinin mortaliteyi arttırdığı bilindiğinden hiponatremi bu hastalarda dikkatli takip ve erken tedavi gerektirmektedir.

Address for Correspondence: Kemal Kayaokay, Izmir Katip Celebi University, Atatürk Training and Research Hospital, Department of Orthopaedics and Traumatology, Izmir, Turkey. Email: kemalkayaokay@gmail.com

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treatment in these patients, since it is known that the length of hospital stay increases mortality.

**Keywords:** hyponatremia, hip fracture, mortality, length of hospital stay

**Anahtar kelimeler:** hiponatremi, kalça kırığı, mortalite, hastanede kalış süresi

## INTRODUCTION

Hyponatremia is the electrolyte disorder defined as serum sodium (Na) concentration below 135 mmol/L and is the most common electrolyte disorder in daily clinical practice<sup>1</sup>. Hyponatremia can be observed more frequently in elderly patients with high frailty who are hospitalized for fractures. The hyponatremia observed in these patients may be caused by existing comorbidities such as hypothyroidism, liver failure, kidney disease and congestive heart failure, the use of multiple medications such as antihypertensives, antiepileptics, antidepressants, hospitalization, perioperative fluid management, and an inflammatory process secondary to surgery<sup>2</sup>. Chronic mild hyponatremia can be asymptomatic and is usually caused by inappropriate antidiuretic hormone release<sup>3,4</sup>. Symptoms of chronic mild hyponatremia may be subtle and it may go undiagnosed. These symptoms include nausea, malaise, headache, lethargy, muscle cramps, disorientation and restlessness which may easily overlooked in a sick geriatric patient. In the recent years more evidence has accumulated about the hyponatremia and gait imbalances, falls and fractures. In severe cases of hyponatremia it may present with seizures, coma an even cardiorespiratory arrest particularly if the onset is rapid. Therefore acute, severe hyponatremia requires emergency evaluation and treatment regardless of its reason.

However, chronic hyponatremia is associated with low bone mineral content and density in almost all regions of the hip, including more pronounced in the femoral trochanteric and femoral neck region<sup>5</sup>. It can also cause osteoporosis, abnormal walking patterns, bone demineralization, cognitive impairment, respiratory failure, non-cardiogenic pulmonary edema, falls and fractures<sup>6-10</sup>.

If hyponatremia is not recognized and treated early in elderly patients, it may become symptomatic depending on the level of hyponatremia. This age group is at a higher risk for complications of hyponatremia, such as brain injury, which is closely related to morbidity and mortality<sup>11</sup>. It has also been shown that chronic hyponatremia is associated with

increased postoperative sepsis rates and chronic prolonged hyponatremia is associated with an increase in long-term mortality<sup>12</sup>. Therefore, it is recommended to investigate the potential etiology of hyponatremia in these patients in the preoperative period, to evaluate their fluid status, and to perform the surgical process in optimal time and conditions by making an appropriate clinical evaluation<sup>13</sup>. This may cause delays in the timing of surgery in patients hospitalized for fractures. On the other hand, hip fracture is a subacute condition in which delays in definitive surgical repair increase postoperative mortality. According to recent guidelines, surgical treatment for hip fracture should be completed within the following a few days after the fracture in order to obtain early recovery, better functional status, and lower mortality rates. The presence of acute or chronic hyponatremia in hip fracture patients may interfere with this goal.

We aimed to detect hyponatremia incidence in hip fracture patients admitted to our institution and hyponatremia treatment effects on the continuation of surgical therapy and postoperative results. We have hypothesized that the presence of hyponatremia increases hospitalization duration and mortality in these hip fracture patients. The primary outcome was in-hospital and out-of-hospital mortality rates of the hyponatremic patients and the secondary outcome was length of hospital stay.

## MATERIALS AND METHODS

### Sample

The study was conducted retrospectively in the Orthopedics and Traumatology Department of Izmir Katip Çelebi University Atatürk Training and Research Hospital. Clinical and laboratory data of patients hospitalized for proximal femur fracture between January 2020 and December 2020 were analyzed. Ethics committee approval was obtained from the Non-Interventional Clinical Trials Ethics Committee of Izmir Katip Çelebi University. (Date: 21.04.2022, Decision no: 0218). Since the study was a retrospective analysis written consent was not required by the ethics committee. The criteria for inclusion in the study were patients over the age of

65 who presented with both extracapsular and intracapsular femoral fractures. The exclusion criteria were patients under the age of 65 who were admitted with a femoral fracture. The data were obtained from the hospital's electronic database. In our hospital, the time and reason of the patient's hospitalization, the time and reason for the operation, the duration of hospitalization, blood and biochemical test results, and additional treatments are available in the electronic data recording system. All femoral fracture surgeries are performed by orthopedic specialist doctors and also specialist doctors of anesthesiology in the Department of Orthopedics and Traumatology. The patients were evaluated by anesthesiologists during the preoperative period, American Society of Anesthesiology (ASA) physical status (PS) scores were determined and recorded<sup>14</sup>. The ASA Physical Status system is a classification consisting of 6 categories that provide a summary and comparison of the preoperative health status of surgical patients. It is also used as a risk-scoring system by anesthesiologists, and as the score increases, postoperative morbidity and mortality rates increase. The necessary suggestions and treatments related to the comorbidities of the patients were arranged by the anesthesiologist in consultation with the relevant clinical units. The characteristics of all patients' surgery and information about what was done in their surgery are recorded in the electronic system.

### Procedure

The patient's age, gender, and fracture type (extracapsular and intracapsular femur fracture) were recorded. The patients' existing comorbidities such as hypertension (HT), diabetes mellitus (DM), congestive heart failure (CHF), chronic renal failure (CRF), and ASA-PS scores were recorded from the electronic database.

The biochemical parameters of the patients during hospitalization were examined. Venous blood samples of all patients were taken at hospital admission, 1 day before and 1 day after surgery. The blood serum was separated in the laboratory and all biochemical analyses were performed on the same day with an AU 5800 brand (Medkim, USA) automatic analyzer. Blood sodium (Na), potassium (K), and calcium (Ca) values were recorded. Patients with blood Na values lower than 135 mmol/L during hospitalization were considered hyponatremic. The

elapsed time between hospitalization and surgery and the total length of hospital stay were recorded in all patients. In-hospital mortality rates of patients after surgery were obtained from hospital records, and 1-year mortality rates were obtained from the national death notification system that physicians can reach for their patients.

### Statistical analysis

Descriptive statistics, including mean, standard deviation, median, minimum, maximum, frequency, and percentage, were employed to summarize the data. The distribution of variables was assessed using the Kolmogorov-Smirnov test. For the comparison of quantitative data, Independent Samples t-test and Mann-Whitney U test were utilized. The Chi-Square test was employed for the comparison of qualitative data. Statistical analyses were performed using SPSS version 28.0.

## RESULTS

Screening the patient's database between January 2020 and December 2020 as "age over 65" and "femur fracture", 253 patients were found and all of them were included in the study. None of these patients were excluded from the study.

Fifty-two of these patients (20.5%) were found to have hyponatremia during hospitalization. The mean age of patients with hyponatremia was  $76.44 \pm 12.48$  and the mean age of patients without hyponatremia was  $76.76 \pm 12.48$ , and there was no significant difference between the groups in the ratio of men and women. There was no statistical difference between the comorbidities of hypertension, chronic renal failure, chronic obstructive pulmonary disease, and ASA physical status scores in the groups. Patients with diabetes mellitus and congestive heart failure were significantly higher in the hyponatremia group ( $p < 0.05$ ). When the fracture types of the patients were examined, extracapsular fractures were detected in 154 patients, and intracapsular hip fractures were detected in 99 patients. A total of 52 patients, including 37 patients with extracapsular fractures and 17 patients with intracapsular fractures, had hyponatremia at the time of hospital admission. There was no significant difference in the incidence of hyponatremia according to fracture types (Table 1).

**Table 1. Demographic data of patients with hyponatremia and normonatremia**

	Hyponatremia (n=52)	Normonatremia (n=201)	P
Age	76,44 ±12.48	76,79±12.48	0.935
Sex (F/M)	39(%75)/13(%25)	124(%62)/77(%38)	0.74
ASA (II/III/IV)	14/33/5	46/127/28	0.646
HT	33(%63)	108(%54)	0.208
DM	23(%44)	52(%26)	<b>0.010*</b>
CRF	8(%15)	22(%11)	0.377
CHF	9(%17)	14(%7)	<b>0.021*</b>
COPD	7(%13)	46(%23)	0.137
Fracture Type (Int/Ext)	17(%33)/35(%67)	82(%41)/119(%60)	0.286

Age is presented as mean±std and the other data is presented as number (n) and percentage (%).

Pierson Chi-Square, Mann-Whitney U analysis, \*P < 0.05

ASA: American Society of Anesthesiology, HT: Hypertension, DM: Diabetes mellitus, CRF: Chronic renal failure, CHF: Congestive heart failure, COPD: Chronic obstructive pulmonary disease, Int: Intracapsular, Ext: Extracapsular

At the time of first hospitalization, the mean Na values in the group with hyponatremia were  $131.13 \pm 3.96$ , while it was  $138.73 \pm 2.27$  in the group without hyponatremia, which was statistically low ( $p < 0.05$ ). K, Ca values measured during hospitalization were similar in the hyponatremia and normonatremia groups. There was no difference in terms of Na, K, and Ca values measured the day before the operation and postoperatively. The duration of preoperative hospitalization and the total length of hospital stay of the patients presenting with hyponatremia were significantly higher than the

group without hyponatremia ( $p < 0.05$ ). There were additional diseases such as HT, DM, CRF, CHD, and COPD that could affect the duration of hospitalization in hyponatremic patients. However, no significant differences were found when considering the duration of hospitalization in hyponatremic patients with and without concomitant additional diseases. (HT,  $p:0.880$ , DM,  $p:0.347$ , CRF,  $p:0.421$ , CHF,  $p:0.643$ , COPD,  $p:0.794$ ). In-hospital mortality and 1-year mortality rates were similar between the groups (Table 2).

**Table 2. Electrolyte values and mortality rates of the patients**

Variables	Hyponatremia (n=52)	Normonatremia (n=201)	P
Pre-Op Na (mmol/L)	$131.13 \pm 3.96$	$138.73 \pm 2.27$	0.000*
Pre-Op K (mmol/L)	$4.15 \pm 0.49$	$4.25 \pm 0.58$	0.235
Pre-Op Ca (mg/dL)	$8.28 \pm 0.64$	$8.21 \pm 0.60$	0.019*
Post-Op Na (mmol/L)	$135.52 \pm 4.19$	$137.30 \pm 3.48$	0.006*
Post-Op K (mmol/L)	$4.21 \pm 0.59$	$4.24 \pm 0.56$	0.726
Post-Op Ca (mg/dL)	$7.94 \pm 0.57$	$7.94 \pm 0.55$	0.991
Pre-Op Hospitalization (day)	$5.21 \pm 2.68$	$4.38 \pm 1.76$	0.039*
Total Hospitalization (day)	$9.92 \pm 4.49$	$7.86 \pm 2.47$	0.002*
In-hospital mortality(n)	5 (% 10)	13 (% 6)	0.431
One-year mortality (n)	18 (%35)	75 (37)	0.719

All data presented as mean±std, number (n) and percentage (%).

Pierson Chi-Square Mann-Whitney U analysis, \*P < 0.05

Pre-Op: Preoperative Post-Op: Postoperative Na: Sodium, Potassium: K, Calcium: Ca

## DISCUSSION

As a result of this study, in which we investigated the relationship between the incidence of hyponatremia,

length of hospital stay, and mortality in patients admitted to our hospital due to femoral fracture, it was determined that the time from patient admission to operation and total hospital stay were statistically significantly longer in the hyponatremic patient group

than in the normonatremia group. In our study, it was determined that there was no statistically significant difference between in-hospital mortality and one-year survival results between hyponatremic and normonatremic patient groups. Studies previously reported in the literature reveal that chronic hyponatremia is an independent factor that increases the incidence of femoral fracture<sup>15,16</sup>. In recent years, more studies have listed hyponatremia among the pathogenic factors of osteoporosis<sup>17,18</sup>.

Although mild and chronic hyponatremia has been found to be associated with decreased bone and mineral density in the hip joint<sup>19</sup>. Although this relationship is evident in the femoral neck, trochanter, and total hip regions, the same density and mineral loss is not observed at the lumbar vertebra level. Therefore, the presence of hyponatremia in the preoperative period in a patient with femoral fracture is important as it may mean possible osteoporosis in the hip region. The presence of preoperative osteoporosis in the hip bones also negatively affects the results of surgery.

In a study conducted by Aqil et al.<sup>20</sup> using the national data system in the United Kingdom, the factors affecting the time of operation for patients with femoral fractures were retrospectively examined. The UK best practice guideline for hip fracture recommends that patients be operated within the first 36 hours. According to this study, hyponatremia was found to be the only factor that delayed patients' admission to surgery within the first 36 hours. However, in the same study, no difference in mortality was found between hyponatremic and normonatremic patients. In the end, the authors suggested that the only valid reason for delaying surgery could be considered contributing to mortality and potentially optimizable causes. Similarly, our data show that hyponatremia increases the time from hospital admission to surgery. In addition, hyponatremia was a factor in prolonging the hospital stay. Similar to this study, it was found that hyponatremia did not cause a difference in in-hospital and one-year mortality rates. However, in their study with a large number of patients, Madsen et al. found that abnormal plasma sodium levels were common in patients with hip fractures, and the rates of hyponatremia and hypernatremia were 19.0% and 1.7%, respectively. They concluded that both hyponatremia and hypernatremia were associated with an increased risk of death within 30 days of admission<sup>21</sup>. In another study by Kalaylana et al.,

19.1% of patients with hip fractures had hyponatremia at admission, 29.5% had hyponatremia in the first 24 hours, and 20% at discharge. In this study, a significant relationship was found between hyponatremia and the time from admission to surgery. They found that patients with hyponatremia waited longer for surgery. In addition, this study was associated with hyponatremia and mobility, and the authors concluded that efforts should be made to identify and correct hyponatremia in hip fracture patients<sup>22</sup>.

In their study, Hagino et al. found hyponatremia in 49 (9.6%) of 512 patients and it was found to be associated with in-hospital mortality<sup>23</sup>. In our study, no increase was found in in-hospital mortality rates. This may be because we analyzed a relatively small patient population. However, when we combined both our current study and other studies in the literature, we concluded that preoperative hyponatremia is associated with mortality in patients with hip fractures.

The limitations of our study include retrospective scanning, missing data in data acquisition processes, a single-center study, and a limited number of patient data for analysis. The strength of our study is that it is a country-specific study that reveals the relationship between hip fractures and the incidence of hyponatremia in our country. This point is important because it has been shown that mortality rates in hip fracture patients produce different results depending on regional characteristics<sup>24</sup>.

As a result, the incidence of hyponatremia in hip fracture patients admitted to our hospital was determined as 20.5% and increased both preoperative and total hospital stays in these patients. However, no difference was found in in-hospital and 1-year mortality rates. In this patient group, the prolongation of hospital stays due to hyponatremia may cause hospital-acquired infections and increased morbidity due to immobilization, as well as increase the cost of care.

In this study, the incidence of hyponatremia in hip fracture patients was found to be 20.5%, and both preoperative and total hospital stay time increased in these patients. Although the mortality rates are similar in hyponatremic and normonatremic patients, hyponatremia requires careful follow-up and early treatment in these patients, as it is known that the length of hospital stay increases mortality. More research is needed on whether preoperative

treatment of hyponatremia should be done at the expense of prolonging hospital stays.

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