

Prevalence of Hyponatremia in Elderly Patients with Hip Fractures: A Two-Year Study

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Significance of the Study

- In this study, the prevalence of hyponatremia was high (19%) in elderly patients ≥ 65 years with hip fractures. Since hyponatremia is associated with significant morbidity and mortality, our findings could help improve health care delivery by highlighting the importance of a constant assessment of serum sodium concentration during hospital stay and of tailoring treatment.

Keywords

Hyponatremia · Hip fracture · Elderly patients

Abstract

Objective: This study investigated the prevalence of hyponatremia in elderly patients (≥ 65 years old) with hip fractures. **Subjects and Methods:** All records containing clinical and laboratory data on the 334 elderly patients admitted to the San Giovanni di Dio e Ruggi d'Aragona Hospital of Salerno, Italy, with hip fractures during 2014 and 2015, were retrieved from the hospital database. Patients were divided into 4 groups, according to their sex and the type of hip fracture. Sodium serum concentrations were retrieved from the medical records. Hyponatremia was defined as the presence of at least 1 episode of hyponatremia during the hospital stay. **Results:** Of 334 elderly patients, hyponatremia was found in 64 (19%). The prevalence of hyponatremia was 18% (28/157) for female patients with extracapsular proximal

femoral fracture, 22% (17/79) for female patients with intracapsular proximal femoral fracture, 20% (12/60) for male patients with extracapsular proximal femoral fracture, and 18% (7/38) for male patients with intracapsular proximal femoral fracture. **Conclusion:** There was a high prevalence of hyponatremia in the elderly patients with hip fractures. Hence, serum sodium concentrations should be regularly assessed to prevent occurrence of hyponatremia.

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Introduction

Hyponatremia is defined as a serum sodium concentration < 135 mmol/L [1], and is the most common electrolyte imbalance encountered in clinical practice. The prevalence of hyponatremia increases in frail patients, such as the elderly, hospitalized, and perioperative patients with fractures [2–5]. Elderly patients with fragility

fractures are particularly susceptible to hyponatremia because of their impaired physiology, multiple comorbidities (such as hypocortisolism, hypothyroidism, hepatic cirrhosis, renal disease, and congestive heart failure), polypharmacy (e.g., antihypertensives, antidepressants, and antiepileptics), hospitalization, perioperative fluid restrictions, and homeostatic stress from the fracture itself and the subsequent surgery [6]. These patients are also at a higher risk of the complications of hyponatremia such as brain injury, the main result of acute symptomatic hyponatremia and associated with significant morbidity and mortality [7, 8]. Severe hyponatremia (i.e., a serum sodium concentration <125 mmol/L), if unrecognized in its first stages and left untreated, has a high rate of mortality; for this reason, an accurate clinical assessment must be made, focusing on fluid status, examining the potential etiology, and conducting the appropriate investigations [9]. In approximately 50% of patients, chronic hyponatremia results from inappropriate antidiuretic hormone secretion [10]. Chronic mild hyponatremia is usually asymptomatic and is traditionally regarded as benign [11]. However, it is associated with a lower bone mineral content and density in nearly all regions of the hip, with more pronounced losses in the trochanteric and femoral neck regions [12]. It can also lead to osteoporosis, abnormal gait patterns, cognitive impairment, bone demineralization, respiratory failure, noncardiogenic pulmonary edema, falls, and fractures [2, 13–16].

Compared to normonatremic individuals, hyponatremic individuals are known to have a longer time from admission to surgery and an increased length of index hospital admission [17]. Hip fractures are a most serious consequence of falls in the elderly, leading to a significant risk of morbidity and mortality [18]. Furthermore, the combination of old age and falls is a common cause of admission to a nursing home [19]. Age is a nonmodifiable risk factor, but falls are preventable [20, 21]. Therefore, the aim of this study was to investigate the prevalence of hyponatremia in elderly patients with hip fractures, focusing on the differences in prevalence between female and male patients with extra- or intracapsular proximal femoral fractures.

Subjects and Methods

All records containing clinical and laboratory information about patients admitted with a hip fracture to the San Giovanni di Dio e Ruggi d’Aragona Hospital of Salerno, Italy, in 2014 and 2015, were retrieved from the hospital database. Inclusion criteria were

Table 1. Number of hyponatremic patients in each group, the prevalence of hyponatremia, and a comparison of prevalence across groups

	Patients with hyponatremia/ group, <i>n</i>	Prevalence of hyponatremia, %
Female ECPFF	28/157	18
Female ICPFF	17/79	22
Male ECPFF	12/60	20
Male ICPFF	7/38	18
Total population	64/334	19
Comparison of prevalence across groups, <i>p</i> value		
Female ECPFF/ICPFF	0.307	
Male ECPFF/ICPFF	0.472	
Males/females	0.471	
ECPFF/ICPFF	0.426	

ECPFF, extracapsular proximal femoral fracture; ICPFF, intracapsular proximal femoral fracture.

an age of ≥65 years and the occurrence of hip fractures (extra- and intracapsular proximal femoral fractures).

Based on the above criteria, a total of 334 patients were identified in the database. They were divided into 4 groups according to sex and type of femoral neck fracture: 157 female patients with extracapsular proximal femoral fracture, 79 female patients with intracapsular proximal femoral fracture, 60 male patients with extracapsular proximal femoral fracture, and 38 male patients with intracapsular proximal femoral fracture. This division was made to evaluate the multiple aspects of the possible link between hyponatremia and different types of hip fracture.

After a visual check of the pre- and postsurgical radiographs to confirm the diagnosis, and the serum sodium concentrations measured upon admission, on the day before surgery, on the days after surgery (calculated as mean of values of the days until discharge), and every 48 h thereafter until hospital discharge, were analyzed.

Serum sodium concentrations were determined by indirect potentiometry using the SYNCHRON[®] System (Beckman Instruments, Brea, CA, USA). The measuring equipment was calibrated with known standards each week, using the protocol suggested by the manufacturer.

The means of the serum sodium concentrations at the time points listed above were calculated using the “average” feature of Microsoft Excel. The prevalence of hyponatremia was calculated using the “sort and filter” and “conditional formatting” features of Microsoft Excel. For the purposes of this investigation, hyponatremia was defined as a serum sodium concentration <135 mmol/L [1] that occurred at least once during a patient’s hospital stay from admission to discharge.

The χ^2 test with the Yates correction was performed to compare prevalence across groups. Statistical significance was set at $p < 0.05$.

Table 2. Mean serum sodium concentration and prevalence of hyponatremia in each group

	Serum sodium concentration ^a , mmol/L				
	study population	female ECPFF	female ICPFF	male ECPFF	male ICPFF
At admission	138.9±3.6	139±3.4	138.7±4.0	138.7±3.6	139.7±3.4
Presurgery day	138.5±3.8	138.6±4	138.3±3.8	138.4±3.3	138.9±3.2
Postsurgery days	139.4±3.8	139.4±3.2	138.9±4.6	140.1±4.1	139.4±3.3
At discharge	139.9±4.6	140.5±3.9	139.4±4.1	139.5±6.6	140.3±3.3
Mean total	139±3.9	139.2±3.7	138.7±4.1	139.1±4.3	139.5±3.4
	Prevalence of hyponatremia				
	study population	female ECPFF	female ICPFF	male ECPFF	male ICPFF
At admission	9%	8%	11%	10%	5%
Presurgery day	13%	14%	17%	9%	8%
Postsurgery days	6%	6%	9%	0%	8%
At discharge	10%	8%	6%	19%	10%
Mean total	10%	9%	11%	9%	8%

ECPFF, extracapsular proximal femoral fracture; ICPFF, intracapsular proximal femoral fracture.

^a Expressed as mean ± SD.

Results

Of the 334 patients, there were more females ($n = 236$, 71%) than males ($n = 98$, 29%), with a ratio of 2.4:1. In both female and male patients, there were more extracapsular proximal femoral fractures, 157/236 (67%) and 60/98 (61%), respectively than intracapsular proximal femoral fractures, 79/236 (33%) and 38/98 (39%), respectively. Overall, the prevalence of hyponatremia in the total population was 19% (64/334). There were no statistically differences across groups (Table 1).

There were no statistically significant differences between the admission and the presurgery groups (29/327, due to missing data vs. 34/262, due to missing data; $p = 0.164$), or between the postsurgery and hospital discharge groups (14/235, due to missing data vs. 14/137, due to missing data; $p = 0.215$).

A statistically significant difference was found between the pre- and- postoperative groups (34/262, due to missing data vs. 14/235, due to missing data; $p = 0.043$).

The highest value of mean serum sodium concentration (140.5 mmol/L) was during the hospital discharge phase in females with extracapsular proximal femoral fracture group, and the lowest value (138.3 mmol/L) was during the presurgery phase in the female intracapsular proximal femoral fracture group (Table 2). There was a decrease in the mean serum sodium concentration in all

groups between admission and the presurgery phase but an increase from the presurgery to the postsurgery phase, and a further increase from the postsurgery to the hospital discharge phase (except in males with intracapsular proximal femoral fracture) (Table 2).

Discussion

In this study, the prevalence of hyponatremia in patients with proximal femoral fractures was high. The prevalence of hyponatremia was 18% for female patients with extracapsular proximal femoral fracture, 22% for female patients with intracapsular proximal femoral fracture, 20% for male patients with extracapsular proximal femoral fracture, and 18% for male patients with extracapsular proximal femoral fracture.

The mean 19% prevalence of hyponatremia in the total population was lower than the 26% reported by Cumming et al. [22]. This discrepancy could be due to the type of population studied. It is noteworthy that the study population in Cumming et al. [22] was not restricted to femoral fractures, but included all types of fragility fractures in elderly patients.

In our study, there was a 9.4% prevalence of hyponatremia in elderly patients with intracapsular fracture upon admission, lower than the 22% reported by Cervellin et al.

[23]. This discrepancy could be due to the larger number of patients in their study ($n = 491$ vs. $n = 334$ in ours).

Mild chronic hyponatremia should not be viewed as a benign condition [11] because it is caused by multiple comorbidities or pharmacologic treatments (e.g., antihypertensives, antidepressants, and antiepileptics), and can lead to several pathologies and even death, both in and out of hospital [6–8, 24–26]. Even mild hyponatremia in the elderly should be considered a risk factor for falls [21].

Since the serial assessment of serum sodium concentration is a simple, inexpensive, and rapid biochemical test, it seems reasonable to suggest that clinicians should investigate the presence of hyponatremia in all elderly patients taking medications potentially involved in the pathogenesis of hyponatremia, and plan an effective clinical management through awareness of the adverse effects of certain drugs on serum sodium levels [27].

The treatment of mild hyponatremia remains an open question, especially in the elderly. Several lines of evidence suggest that rapid correction of chronic hyponatremia may be associated with severe complications, especially serious neurologic injury in patients undergoing fluid restriction [28]. For the general management of chronic hyponatremia, Spasovski et al. [29] recommend to stop nonessential fluids, medications, or other factors that can lead to hyponatremia. They also suggest a cause-specific treatment and to not use treatment with the sole aim of increasing serum sodium concentration.

A safer strategy may be represented by the administration of a new class of drugs, the vasopressin antagonists

or vaptans, which are capable of correcting hyponatremia in different clinical conditions [30], though data on major clinical outcomes are still conflicting and somewhat lacking [31].

Finally, it is unclear whether treating hyponatremia improves patient outcomes. Even if it is decided to treat hyponatremia, it is often unclear which treatment option is most appropriate [29].

The limitations of this study were missing data because in many patients serum sodium concentration was not systematically assessed during the hospital stay, and also the lack of data on the etiology of hyponatremia in each patient.

Conclusion

In this study, the prevalence of hyponatremia was 19%, so it was indeed a frequent occurrence in the elderly patients with hip fractures. Serum sodium concentrations should be routinely assessed in elderly patients with hip fractures and the hyponatremia corrected accordingly.

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References

- 1 Moritz ML, Ayus JC: The pathophysiology and treatment of hyponatraemic encephalopathy: an update. *Nephrol Dial Transplant* 2003;18:2486–2491.
- 2 Gankam Kengne F, Andres C, Sattar L, et al: Mild hyponatremia and risk of fracture in the ambulatory elderly. *QJM* 2008;101:583–538.
- 3 Soiza RL, Talbot HSC: Management of hyponatraemia in older people: old threats and new opportunities. *Ther Adv Drug Saf* 2011; 2:9–17.
- 4 Tambe AA, Hill R, Livesley PJ: Post-operative hyponatraemia in orthopaedic injury. *Injury* 2003;34:253–255.
- 5 Upadhyay A, Jaber BL, Madias NE: Incidence and prevalence of hyponatremia. *Am J Med* 2006;119(7 suppl 1):S30–S35.
- 6 Soiza RL, Hoyle GE, Chua MP: Electrolyte and salt disturbances in older people: causes, management and implications. *Rev Clin Gerontol* 2008;18:143–158.
- 7 Ayus JC, Wheeler JM, Arieff AI: Postoperative hyponatremic encephalopathy in menstruant women. *Ann Intern Med* 1992;117: 891–897.
- 8 Ayus JC, Achinger SG, Arieff A: Brain cell volume regulation in hyponatremia: role of sex, age, vasopressin, and hypoxia. *Am J Physiol Renal Physiol* 2008;295:F619–F624.
- 9 Clayton JA, Le Jeune IR, Hall IP: Severe hyponatraemia in medical in-patients: aetiology, assessment and outcome. *QJM* 2006;99:505–511.
- 10 Ellison DH, Berl T: Clinical practice. The syndrome of inappropriate antidiuresis. *N Engl J Med* 2007;356:2064–2072.
- 11 Ayus JC, Moritz ML: Bone disease as a new complication of hyponatremia: moving beyond brain injury. *Clin J Am Soc Nephrol* 2010;5:167–168.
- 12 Kruse C, Eiken P, Verbalis J, et al: The effect of chronic mild hyponatremia on bone mineral loss evaluated by retrospective national Danish patient data. *Bone* 2016;84:9–14.
- 13 Renneboog B, Musch W, Vandemergel X, et al: Mild chronic hyponatremia is associated with falls, unsteadiness, and attention deficits. *Am J Med* 2006;119:71.e1–e8.
- 14 Verbalis JG, Barsony J, Sugimura Y, et al: Hyponatremia-induced osteoporosis. *J Bone Miner Res* 2010;25:554–563.
- 15 Hoorn EJ, Rivadeneira F, van Meurs JBJ, et al: Mild hyponatremia as a risk factor for fractures: the Rotterdam Study. *J Bone Miner Res* 2011;26:1822–1828.
- 16 Ayus JC, Arieff AI: Pulmonary complications of hyponatremic encephalopathy. Noncardiogenic pulmonary edema and hypercapnic respiratory failure. *Chest* 1995;107:517–521.

- 17 Cumming K, McKenzie S, Hoyle GE, et al: Prognosis of hyponatremia in elderly patients with fragility fractures. *J Clin Med Res* 2015; 7:45–51.
- 18 Carriero FP, Christmas C: In the clinic. Hip fracture. *Ann Intern Med* 2011;155:ITC6-1–ITC6-15; quiz ITC6-16.
- 19 Tinetti ME, Williams CS: Falls, injuries due to falls, and the risk of admission to a nursing home. *N Engl J Med* 1997;337:1279–1284.
- 20 Morley JE: Is it possible to prevent injurious falls? *Eur Geriatr Med* 2014;5:75–77.
- 21 Tolouian R, Alhamad T, Farazmand M, et al: The correlation of hip fracture and hyponatremia in the elderly. *J Nephrol* 2012;25:789–793.
- 22 Cumming K, Hoyle GE, Hutchison JD, et al: Prevalence, incidence and etiology of hyponatremia in elderly patients with fragility fractures. *PLoS One* 2014;9:e88272.
- 23 Cervellin G, Mitarittono M, Pedrazzoni M, Picanza A, Lippi G: Prevalence of Hyponatremia in Femur Neck Fractures: A One-Year Survey in an Urban Emergency Department. *Adv Orthop*. DOI: 10.1155/2014/397059.
- 24 Friedman E, Shadel M, Halkin H, et al: Thiazide-induced hyponatremia. Reproducibility by single dose rechallenge and an analysis of pathogenesis. *Ann Intern Med* 1989;110:24–30.
- 25 Spigset O, Hedenmalm K: Hyponatremia in relation to treatment with antidepressants: a survey of reports in the World Health Organization data base for spontaneous reporting of adverse drug reactions. *Pharmacotherapy* 1997;17:348–352.
- 26 Asconapé JJ: Some common issues in the use of antiepileptic drugs. *Semin Neurol* 2002;22: 27–39.
- 27 Liamis G, Milionis HJ, Elisaf M: A review of drug-induced hyponatremia. *Am J Kidney Dis* 2008;52:144–153.
- 28 Vaidya C, Ho W, Freda BJ: Management of hyponatremia: providing treatment and avoiding harm. *Cleve Clin J Med* 2010;77: 715–726.
- 29 Spasovski G, Vanholder R, Alolio B, et al: Clinical practice guideline on diagnosis and treatment of hyponatraemia. *Nephrol Dial Transplant* 2014;29(suppl 2):i1–i39.
- 30 Schrier RW, Gross P, Gheorghide M, et al: Tolvaptan, a selective oral vasopressin V2-receptor antagonist, for hyponatremia. *N Engl J Med* 2006;355:2099–2112.
- 31 Gross PA, Wagner A, Decaux G: Vaptans are not the mainstay of treatment in hyponatremia: perhaps not yet. *Kidney Int* 2011;80:594–600.