

# Does hyponatremia pose a risk factor for hip fractures in the elderly? Can a primary physician prevent it?

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## ABSTRACT

**Objective:** Fracture around the hip is amongst the most common and serious fractures in the elderly, which leads to significant morbidity and mortality. In literature, many authors noted that even mild hyponatremia adversely affects bone, leading to an increased incidence of fractures. We aim to determine whether chronic hyponatremia (>90-day duration) increases the risk of hip fracture in the elderly and whether primary care physicians can help to prevent it. **Materials and Methods:** During the period from January 2020 to March 2022, we identified 145 patients aged between 65 and 90 years who were admitted to the hospital with hip fractures following a fall and compared them with 140 healthy controls. We recorded sodium (Na) serum levels in all included patients at the time of arrival and consequently for 3 days and compared them with those of controls. Logistic regression was used to calculate odds ratios (ORs). We measured serum Na levels for 3 days and took the average to ascertain hyponatremia. **Result:** In the study, the odds of hyponatremia were 70.3% with a confidence interval of 95% versus 3.6% in controls ( $P = 0.05$ ). Age and hyponatremia were strongly associated with hip fractures following a fall. With a 5-year increase in age, the univariate OR for hip fracture increased by 5.67 ( $P < 0.0001$ ). After adjusting for age, cases were nearly six times more likely to be hyponatremic than controls (OR = 4.90,  $P = 0.04$ ). **Conclusion:** In our study, we noted that even mild chronic hyponatremia in old age increased the chance of falls. Addressing hyponatremia in the elderly may reduce the risk of falls and minimize hip fractures.

**Keywords:** Elderly patients, fall, hip fracture, hyponatremia

## Introduction

A serum sodium (Na) level of <135 mmol/L is considered hyponatremia. Mohan *et al.*<sup>[1]</sup> conducted a population-based, cross-sectional study in the United States (US) and discovered that 14,697 adults aged  $\geq 18$  years participated in the National Health and Nutrition Examination Survey between 1999 and 2000, and the prevalence of hyponatremia was 1.72%. Women (2.09%)

had a higher prevalence of hyponatremia, which increases with age, according to researchers. It was shown that hyponatremia affects 10% of elderly adults who live at home and 20% of those admitted to a small hospital.<sup>[2]</sup> The most feared outcome of hyponatremia is hyponatremic encephalopathy, which causes frequent falls and is associated with high morbidity and mortality.<sup>[3,4]</sup> Usala *et al.*<sup>[5]</sup> associated osteoporosis with hyponatremia. In 2002, McPherson *et al.*<sup>[6]</sup> noted that in symptomatic chronic severe hyponatremia, the orthopaedic injury was a common presentation. Mild or asymptomatic hyponatremia is associated with muscular pain and osteoporosis and may increase the risk of fractures. Many authors have observed that it is a very common electrolyte disturbance in patients who

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sustain hip fractures.<sup>[7-9]</sup> Tolouian *et al.*<sup>[10]</sup> recorded that among hyponatremic patients, hip fractures are common in the geriatric group who have high mortality (14–36%) within 1 year of the fracture. The fracture neck femur possesses high morbidity and mortality in the elderly, and it is approximately 11–23% at 6 months and 22–29% at 1 year from injury.<sup>[11]</sup> According to a study, hyponatremia is a prevalent electrolyte imbalance in the elderly that might go unnoticed with an incidence of approximately 1% and a prevalence of 3–4%, and it can be as high as 30% in patients in the Intensive Care Unit.<sup>[12]</sup>

Therefore, this study aimed to investigate the prevalence of hyponatremia in elderly patients with hip fractures. We also aimed to find whether a primary care physician can prevent this medical condition and reduce the chances of falls and subsequent fractures of the hip.

## Materials and Methods

The study was conducted in a tertiary care hospital in Guwahati, Assam, India, between January 2020 and March 2022 in the Department of Orthopaedics. The study was approved by our Hospital Ethics Committee. Being a retrospective nature of this study, informed consent was not applicable.

### Sample and study architecture

A total of 285 patients were included, of which 145 fell and developed hip fractures and were the study group, whereas 140 healthy persons in the same age bracket were the control group. Our study is a retrospective cohort study that included 145 patients admitted to the orthopaedic department with hip fractures following a fall who were aged >65 years and had a plasma Na level collected from laboratory data during the study. While doing analysis we compared patients with chronic hyponatremia, with plasma Na <135 mmol/L for 90 days, to eunatremic patients. Patients with only one Na level <135 mmol/L or irregular serum Na were excluded from the analysis; however, we included their data in a secondary analysis [Table 1]. During the course of our study, we noted that 25 patients with hip fractures too had normal Na levels. We measured serum Na by an indirect ion-selective electrode (ISE) method and using the same analytical instrumentation (i.e., Beckman Coulter AU5800; Beckman Coulter Inc., Brea, CA, USA) (ref range 135–145 mmol/L).

### Statistical analysis

The study used SPSS 19.0 software for all statistical analyses, and a two-sided *P* value < 0.05 was considered significant. We expressed categorical variables as frequencies and proportions and were compared with Fisher's exact tests or  $\chi^2$ . The continuous variables are expressed as means and standard deviations or medians and interquartile ranges, and the results thus obtained were compared between groups using the *t*-test or Mann–Whitney *U*-test if there were non-normal distributions. The predictive value of hyponatremia was also investigated using the receiver operating characteristic (ROC) curve.

**Table 1: Risk factors for hip fracture in the elderly**

<b>History of Falls</b>
<b>Sex</b>
<b>Body mass index</b>
<b>Ethnicity</b>
<b>Femoral neck BMD</b>
<b>Smoking</b>
<b>Diabetes</b>
<b>Parent fractured hip</b>
<b>Low Serum vitamin D levels</b>
<b>Poor or Low calcium intake</b>
<b>Prolonged immobilization due to any medical or surgical condition</b>
<b>Early menopause (&lt;40 years)</b>
<b>Organ transplantation</b>
<b>Rheumatoid arthritis</b>
<b>Hyponatremia</b>

Several methodologies were utilized to investigate the association between long-term chronic hyponatremia and hip fractures. The correlation between chronic hyponatremia and fractured hip was estimated by several approaches. Crude unadjusted incidence rates (per 100,000 person/years) of hip fractures keeping a 95% confidence interval (CI) were estimated for patients with and without prolonged hyponatremia.

This study used logistic regression to create a hyponatremia propensity score,<sup>[13]</sup> which considered variables, such as age, gender, congestive heart failure, history of chronic renal disease, or hepatic failure and use of medication, such as antidepressants and antipsychotics, steroidal medication, thiazide diuretics and anticonvulsants, all of which can cause hyponatremia.

The World Health Organization (WHO) has developed a country-specific fracture risk assessment tool (FRAX) that can be used to determine the likelihood of a hip or other bone fracture occurring in the following 10 factors. This tool can be used to predict the likelihood of a hip or other bone fracture occurring in the next 10 years.<sup>[14]</sup> Important clinical risk factors, such as a history of falls, have not yet been included in the FRAX algorithms because they have not been confirmed to be true. This means that there has not been much investigation into hyponatremia as a risk factor for hip fractures.

We adjusted the Na values for age, gender, diabetes, hypertension, chronic heart disease, and chronic renal disease, as well as comorbidities and medications in the propensity score model and individual risk factors included in the FRAX, to further assess the validity of our study, because these variables may provide additional prognostic information and improve confounding control beyond their inclusion in integrated risk scores.

## Results

There are numerous risk factors for femoral necks, such as low bone mineral density (BMD), history of injury, history of alcohol and smoking, as well as the person's age, gender, body mass index (BMI), inflammatory joint disease, glucocorticoid use, and secondary osteoporosis [Table 1].

In the study group of 145 patients, 102 (70.3%) were detected to have prolonged chronic mild hyponatremia, 18 (12.4%) had severe hyponatremia, whereas 25 (17.2%) had normal Na levels. The mean plasma Na levels were  $118.80 \pm 2.37$  mmol/L in the study group and  $142.68 \pm 4.5$  mmol/L in the eunatremic group (control) ( $P < 0.001$ ) [Table 2].

The mean plasma Na measurements were 3 (interquartile range [IQR] 1) for the hyponatremic group and 2 (IQR 4) for the eunatremic group. The median follow-up for the hyponatremic group was 120 days (range 50–200 days) and for the eunatremic group was 160 days (range 50–260 days). Thus, finally, among 145 hip fracture patients, 120 (82.7%) were found to be hyponatremic at the time of admission [Table 3].

As illustrated in Figure 1, both males (136 mmol/L and IQR 134–143 mmol/L vs. 139 mmol/L and IQR 137–145 mmol/L) and females (137 mmol/L and IQR 134–143 mmol/L vs. 142 mmol/L and IQR 136–140 mmol/L) had statistically significant differences in serum Na between the study population and controls in patients aged over 65 years. A comparison of serum sodium in the study and control groups is shown in Figure 1.

In the whole study population, the odds ratio (OR) of hyponatremia causing fracture was 2.02 (95% CI, 1.52–2.79) and 1.94 (95% CI, 1.32–2.82) in patients <65 years.

Hyponatremia has a very high area under the curve for predicting hip fracture when ROC curve analysis was performed ( $P \leq 0.0001$ ; 95% CI, 0.783–0.9216) [Figure 2]. People with serum Na levels less than 127 mmol/L had a 1.00 positive predictive value and a 0.56 positive predictive value for predicting hip fractures. There was a linear connection between serum Na levels in patients with hip fractures ( $r^2 = 0.012$ ,  $P = 0.001$ ) [Figure 3].

After a multivariate analysis in which hip fracture was entered as the dependent variable and serum Na, age, and gender

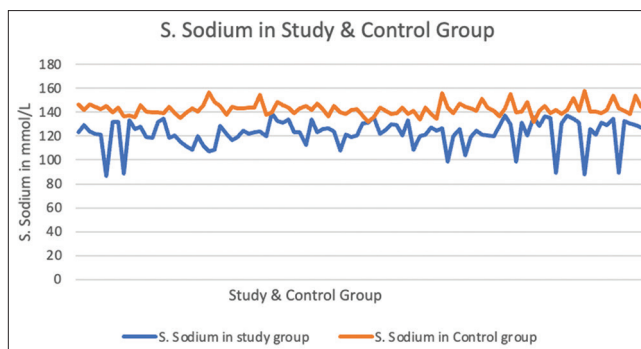


Figure 1: Comparison of serum sodium in study and control groups

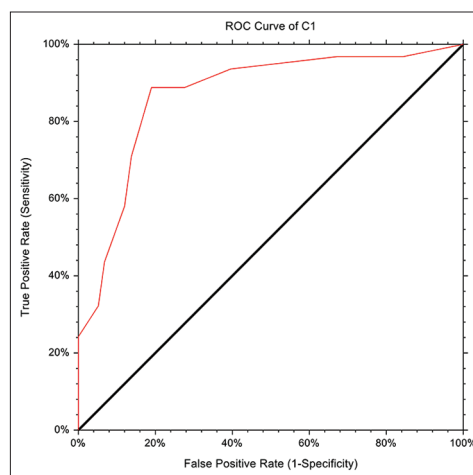


Figure 2: ROC curve showing the detection of serum sodium in study group patients against healthy controls. ROC, receiver operating characteristic; AUC, area under the curve

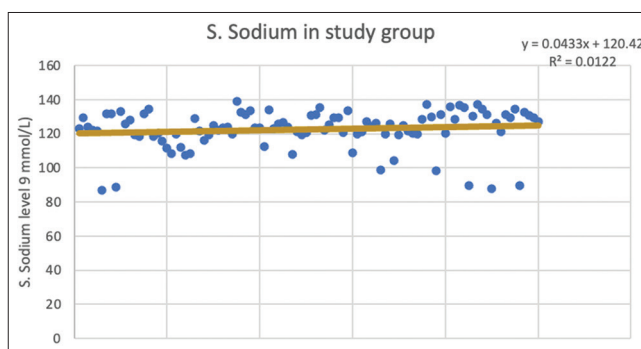


Figure 3: Correlation and regression between serum sodium concentration in patients with hip fracture

Table 2: Mean serum sodium levels in study and control groups

Characteristics	Control group	Study group n=145			P
		Hypo	Sever hyponatremia	Normo Na	
(n)	140	102 (70.3%)	18 (12.4%)	25 (17.2%)	<0.001
Age, mean $\pm$ standard deviation	76.3 $\pm$ 17.8	76.3 $\pm$ 18.2	77.9 $\pm$ 17.9	74.6 $\pm$ 19.5	<0.001
M/F	41/99	79/23	11/7	12/13	<0.001
Mean sodium (mmol/L)	142.68 $\pm$ 4.5 (131.2–157.3)	118.80 $\pm$ 2.37 (84.3–131.4)	88.54 $\pm$ 12.73 (84.3–111.8)	139.66 $\pm$ 34.56 (139.3–146.8)	<0.001

Hypo=Hyponatremia, NormoNa=Normal Serum Sodium

were entered as independent variables, a lower serum Na value remained a significant predictor of hip fracture (beta coefficient = 0.023).

## Discussion

Various studies have indicated that elderly patients who have suffered a hip fracture have a higher risk of hyponatremia than those who have not [Table 4]. Hoorn *et al.*<sup>[15]</sup> examined 5,208 elderly patients in their study, of whom 7.7% were hyponatremic. It was discovered that hyponatremic patients had a higher adjusted OR of developing vertebral and non-vertebral fractures. The values were 1.34 and 1.61, respectively. Sandhu *et al.*<sup>[9]</sup> obtained similar results when they analyzed the incidence of hyponatremia in 364 elderly patients referred to an emergency room with and without a fracture. The fracture group exhibited a considerably higher risk of hyponatremia (9.1 vs. 4.1%), with a mean serum Na level of 131.2 mmol/L. Kinsella *et al.*<sup>[16]</sup> examined 1,408 women who had bone densitometry and discovered that 18% of them had

fractures and 4.2% had hyponatremia. Patients with fractures exhibited a substantially higher incidence of hyponatremia than those without (8.7 vs. 3.2%), and hyponatremic patients had 2.25 times increased adjusted OR for the occurrence of fracture. Ayus and Arief<sup>[17]</sup> reported that 19% of women with chronic hyponatremia after menopause had a broken bone in their arms or legs.

Tolouian *et al.*<sup>[10]</sup> compared serum Na levels on the admission of 249 patients with hip fractures because of falls with those who were scheduled for hip replacement surgery as a control group. He noted a higher 16.9 versus 4.6% prevalence of hyponatremia in the study group as compared with controls ( $P = 0.03$ ). Kengne *et al.*<sup>[18]</sup> compared the incidence of hyponatremia (Na <135 mmol/L) in 513 elderly patients admitted with a fracture to a sex- and age-matched control group of otherwise normal patients and discovered that the fracture group had a significantly greater incidence of hyponatremia (13 vs. 3.9%), with an adjusted OR of 4.16 for fracture associated with hyponatremia.

According to Verbalis *et al.*<sup>[19]</sup> the OR was 2.87 times more among adults with mild hyponatremia (mean serum Na 133 mEq/L) in the development of osteoporosis than in those without hyponatremia. They also found a significant correlation between serum Na and BMD of the femoral neck in hyponatremia patients.

Cervellin *et al.*<sup>[20]</sup> attempted to find the prevalence of hyponatremia in patients with an intracapsular femoral neck fracture. They included 491 elderly patients aged  $\geq 65$  years and 380 controls. A higher prevalence of hyponatremia was recorded in patients with hip fractures.

Kuo *et al.*<sup>[21]</sup> discovered in a retrospective study that hyponatremia is associated with severe outcomes from falls in the elderly,

**Table 3: Demographic and baseline values in study and control groups**

Baseline characteristics	Study group Chronic hyponatremia (n=120)	Control group Normonatremia (n=140)	P
Plasma sodium, mean (SD), mmol/L	118.80±2.37	142.68±4.5	<0.001
Age, mean (SD), years	77.5	78.2	<0.001
Body mass index, mean (SD)	27±2.37	29±2.34	<0.001
Diabetes mellitus, (n)	28	37	0.343
Hypertension	47	56	0.623
CKD	16	29	0.421
IHD	29	18	0.417

CKD=Chronic kidney disease, IHD=Ischemic heart disease

**Table 4: Various studies revealed an association between low sodium and fractures in the elderly**

Author	Study design	Mean serum Na+ level	No. of patients	Result
Sandhu <i>et al.</i> <sup>[9]</sup>	A case-control study comparing the incidence of mild hyponatremia (Na <135 mmol/L) in elderly patients (>65 years) with and without large bone fractures.	131±2	728	9.1% incidence of hyponatremia in patients with fractures versus 4.1% in controls.
Tolouian <i>et al.</i> <sup>[10]</sup>	Case-control study; patients admitted for hip fracture secondary to fall compared to patients admitted for elective hip or knee replacement	131±2	249	The prevalence of hyponatremia was 16.9% in the study versus 4.6% in controls ( $P=0.03$ ). OR=4.80; $P=0.04$
Hoorn <i>et al.</i> <sup>[15]</sup>	Cross-sectional cohort study; incidence of falls and fractures in an elderly population with and without hyponatremia (Na <136 mmol/L)	133.4±2	5,208	23.8% incidence of falls in hyponatremic versus 16.4% in those without. OR of V/non-V fracture in HyNa 1.39 and 1.78, respectively.
Kinsella <i>et al.</i> <sup>[16]</sup>	Cross-sectional cohort study; incidence of hyponatremia (Na <135 mmol/L) in women with and without a fracture who underwent previous bone densitometry measurement.	132.2±1.8	1,408	8.7% incidence of hyponatremia in women with fracture versus 3.2% in those without.
Ayus and Arief <sup>[17]</sup>	Prospective study of postmenopausal women with chronic symptomatic HyNa (Na <130 mmol/L)	111±12	53	19% presented with orthopedic trauma.
Kengne <i>et al.</i> <sup>[18]</sup>	Case-control study; the prevalence of hyponatremia in elderly patients (>65 years) presenting with and without bone fracture.	131±3	1,026	13% incidence of hyponatremia in fracture patients versus 3.9% in controls.
Verbalis <i>et al.</i> <sup>[19]</sup>	Cross-sectional cohort study; evaluation of BMD in patients >50 years with hyponatremia (Na <135 mmol/L) versus normonatremic controls in the NHANES III	133±2	Not known	Adjusted OR of osteoporosis in hyponatremia adults was 2.87 times than in controls.

with a higher Injury Severity Score, longer hospital stays, and a greater probability of death. Renneboog *et al.*<sup>[22]</sup> examined 122 persons (average age  $72 \pm 13$  years), with asymptomatic chronic hyponatremia and sustained falls and 244 healthy controls, in their study. These researchers claimed that mild chronic hyponatremia causes many people to fall, possibly because they have difficulty walking and focusing. Fehlberg *et al.*<sup>[23]</sup> also discovered that hyponatremia is a risk factor for falls, particularly in patients with serum Na levels  $<126$  mEq/L. Corona *et al.*<sup>[24]</sup> recently conducted a review of 15 research studies and concluded that hyponatremia is associated with an increased risk of falls and bone fractures, particularly in the elderly.

In our study, we analysed a retrospective cohort using various methodologies with multiple designs and analytic approaches. For the main analysis, tight procedures were employed to ensure that pseudo hyponatremia, which is induced by hyperglycaemia, did not enter. It also employed propensity score methods to ensure that older patients with distinct hyponatremia risk factors were excluded from the main analysis because they were more likely to develop hyponatremia. Patients with hyponatremia have a higher risk of death because they are more prone to frequent falls, and they are also more likely to break their hips. Hyponatremia is an indication of mortality in patients with cirrhosis or heart failure, thus long-term hyponatremia and hip fracture estimations may be too low.

### Limitations of the study

Our study has several weaknesses, including a limited number of patients with long-term chronic hyponatremia. Our design was constrained, and this is how it turned out. Retrospective studies are susceptible to residual confounding because they employ information from electronic medical records to seek potential confounders and do not account for all possible factors that could have been associated with chronic hyponatremia, such as H2 blockers and NSAIDs. This study did not take into account all these potential influences. Because of the lack of racial/ethnic diversity in our study, the findings may not be extended to all populations. More research is required to corroborate our findings that persons with chronic hyponatremia are at a higher risk of hip fractures.

### Role of primary care physician

Hyponatremia is a quite common medical condition in the elderly that leads to frequent giddiness and falls. In developing countries, this is generally ignored and labelled as an age-related weakness, especially in middle-class and lower socioeconomic families. A primary healthcare giver can sensitize people about hyponatremia, which is easily preventable and can reduce the chance of falls and resulting hip fractures.

### Conclusion

Mild chronic hyponatremia of  $>90$  days in older patients was found to be a risk factor for hip fracture; however, it was not the

only factor. This suggests that a longer duration of hyponatremia increases the risk of hip fractures.

However, there is still a lot of disagreement on how to manage mild hyponatremia, particularly in the elderly. Various studies and evidence suggest that rapid repair of chronic hyponatremia is associated with severe neurological issues, such as cerebral oedema and confusion; hence, this should be avoided. Although this study cannot prove a link between mild hyponatremia and dementia, it raises concerns with regard to the current protocol and treatment guidelines for mild hyponatremia in the elderly.

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### Conflicts of interest

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