

## Hyponatremia, bone mineral density and falls in the elderly; Results from AHAP study

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**Background.** Hyponatremia (HN) can be associated with osteoporosis, falls and bone fractures in the elderly. Recent researches demonstrated different results about the correlation of HN with bone mineral density and bone fractures.

**Methods.** This analytic research came from the AHAP project in northern IRAN. All people aged 60 years and over were included in the study. Individuals with severe comorbidities and then who had concurrent conditions which could have impact on bone mineral densities (BMD) such as long-term use of steroids, calcium and/or vitamin D supplements, bisphosphonates, calcitonin, thiazides and hormonal medications were excluded.

**Results.** One thousand and one hundred and thirteen older persons entered in the study. More than 10 percent of the participants had HN (serum Na<sup>+</sup> level  $\leq$  137mEq/L). No significant difference has been observed between hyponatremic and nonhyponatremic individuals about their balance abilities; bone mineral density; incidence of falls and/or bone fracture during the previous 6 months; dependency in activities of daily living; and osteoporosis.

**Conclusion.** HN was not a prevalent problem in older adults who met the inclusion criteria of this research. No significant difference has been observed between HN and bone mineral density and falls in the elderly.

**Key words:** Hyponatremia, Bone mineral density, Bone fracture, Osteoporosis, Aging.

### INTRODUCTION

Hyponatremia (HN) is a prevalent problem in the elderly [1-3]. Chronic diseases [3, 4] and concurrent use of certain medications such as diuretics [5] and antidepressants [6] put older people at greater risk of HN. Recent studies demonstrate that HN can be associated with osteoporosis, falls and fractures [1, 7-11]. The association of HN with falls and fractures might be independent of osteoporosis [12]. A case-control study conducted in the USA showed that chronic and recent HN were associated with osteoporosis (OR = 12.09, CI: 9.34-15.66) and fractures of extremities, pelvis or vertebrae (OR = 4.61, CI: 4.15-5.11) [9], while, another study conducted in the Netherlands represented that HN was not associated with lower bone mineral density (BMD), but it was associated with increased risk of nonvertebral bone fractures [11]. Other study conducted in the University of Michigan showed that hip osteoporosis occurred in 17.6 % of patients with HN as compared to 6.6 % of patients with normal serum sodium level, but osteoporosis

was higher in younger age group (less than 55 years) as compared to older adults [13]. Considering different results in previous studies which may be due to the region where study participants were living and different underlying conditions; outcome variables which have been measured in the study protocol; and cut-off points of serum sodium concentration for determination of HN, this research has been proposed to assess the association of HN with bone density and falls in older population of Amirkola, Northern Iran.

### MATERIALS AND METHODS

This analytic research came from the Amirkola Health and Ageing Project (AHAP) [14]. All people aged 60 years and over were included in this study. Exclusion criteria were serious disease which did not permit to the elderly to follow the study examinations, and concurrent conditions which could have impact on bone mineral density such as long-term use of steroids at least for one month, calcium

and/or vitamin D supplements, bisphosphonates, calcitonin, thiazides and hormonal medications.

The collected data included age, gender, habitual behaviors (smoking, alcohol consumption, and physical activity); history of falls and bone fracture during the previous 6 months and the number of falls, if occurred; self-reported comorbid physical and mental disorders and medications they were currently taking. Weight and height were measured to calculate body mass index (BMI) as  $\text{weight}/(\text{height})^2$ .

The participants' static and dynamic balance abilities were measured with Berg Balance Scale (BBS). This test has 14 items and a five-point scale, ranging from 0-4. "0" indicates the lowest and "4" the highest level of function. The scores in the range of 41-56 suggest "low fall risk", 40-21 "medium fall risk" and 0-20 can be interpreted as "high fall risk" [15]. The validity and reliability of Persian version of this scale have been confirmed in Iran [16].

Data on physical activity was measured using Physical Activity Scale for Elderly (PASE) and was collected through interviews [17, 18]. The validity and reliability of this questionnaire (Cronbach's alpha coefficient of 0.97) were evaluated in an Iranian study [19]. The total score for each individual was calculated as between 0 and 400; higher scores meant higher physical activity levels. In this research, the scores greater than 150 were considered as having physical activity [20, 21].

The number of daily living activities which the participants needed help for doing was measured with ADL (activities of daily living) index. This index includes bathing, dressing, toileting, transferring, continence, and eating for measurement of the severity of disability [22].

Bone mineral density (BMD) was measured with DXA (dual-energy x-ray absorptiometry scan), by Lexxos densitometer (made in France). DXA measurements were performed at the neck of left femoral bone and lumbar vertebrae (L2-L4) and the result was expressed as T-scores. T-scores indicate the number of standard deviations (SD) by which the bone mass value deviated from the mean of a group of young normal controls [12]. T-scores  $\leq -2.5$  SD suggest osteoporosis,  $-2.5 < \text{T-score} \leq -1$  SD represent osteopenia; and T-scores greater than -1 can be defined as normal BMD [23].

Serum sodium concentration was assessed by photoelectric flame photometer device. Serum  $\text{Na}^+$  level  $\leq 137$  mEq/L was considered as HN [24].

Data analysis was performed with SPSS software version 18. Final results were presented as

descriptive statistics (mean and SD) and analytic statistics derived from t-test, chi-square, and one-way ANOVA. Odds ratio (OR) was used to show the additive risk of main outcome measures (such as balance disturbance, falls, fractures and osteoporosis) in the patients with hyponatremia.

This research was approved in the Ethics Committee of Babol University of Medical Sciences as registration code of MUBABOL.REC.1394.62.

## RESULTS

One thousand and one hundred and thirteen older persons ( $\geq 60$  years) were eligible and entered the study (68.9% of total): 622 (55.9%) male and 491 (44.1%) female. One hundred and fifteen individuals (10.3%) had HN. The baseline characteristics of the participants divided into normal and abnormal serum sodium concentrations are presented in Table 1. Significant differences have been observed between the two groups about their serum potassium and BUN levels and the percent of hypertensive patients ( $p < 0.05$ ). Nearly 2.5% of the participants had balance disorders.

Physical activity, the history of falls and bone fracture during the previous six months, disability in daily living activities, and presence of osteoporosis were compared between the two groups (with HN and without HN). The results are presented in Table 2. No significant differences have been observed between the two groups in the occurrence of falls and/or bone fracture during the previous 6 months; dependency in activities of daily living; and osteoporosis ( $p > 0.05$ ).

Serum sodium concentration has been compared among the three groups (normal, with osteopenia and osteoporotic patients) according to gender and their BMD T-scores. Results are presented in Table 3. Three hundred and eighty four persons (34.5%) had osteoporosis. No significant difference has been observed between males and females about serum sodium concentration, according to their BMD T-scores ( $p > 0.05$ ).

The association between serum sodium level and balance test, the occurrence of falls and bone fracture during the previous six months and disability in daily living activities is presented in Table 4. Mean of serum sodium concentration had no significant difference between the elderly who had lower ability to balance ( $p = 0.97$ ), the older people who had disability in daily living activity ( $p = 0.56$ ), the elderly who had falls ( $p = 0.16$ ) or bone fracture ( $p = 0.26$ ) in the previous 6 months.

*Table 1*  
Baseline characteristics of the participants based on their serum sodium level

Variable	Serum sodium concentration		p-value
	≤ 137 mEq/L N = 115	> 137 mEq/L N = 998	
Age	68.6 ± 6.8	68.5 ± 7.1	0.83
Number (percent) with diabetes mellitus	34 (9.9)	308 (90.1)	0.78
Number (percent) with hypertension	58 (8.6)	613 (91.4)	0.02
Number (percent) with self-reported cardiovascular disorders	27 (10.0)	244 (90.0)	0.82
Number (percent) with hepatic disorders	2 (10.0)	18 (90.0)	0.96
Number (percent) with renal disorders	0	0	0
Number (percent) with drug history of corticosteroids	8 (10.0)	72 (90.0)	0.73
Number (percent) with history of hormone replacement therapy	2 (10.5)	17 (89.5)	0.81
Mean of serum calcium level	9.35 ± 0.45	9.24 ± 0.43	0.77
Mean of serum phosphorus level	4.11 ± 0.60	3.92 ± 0.60	0.71
Mean of serum potassium level	4.05 ± 0.38	4.19 ± 0.26	< 0.001
Mean of serum BUN	19.43 ± 6.47	18.09 ± 5.49	0.004
Mean of serum creatinine	1.02 ± 0.26	0.95 ± 0.21	0.19
Body Mass Index	26.7 ± 4.0	27.3 ± 4.7	0.14
Berg Balance Scale score	51.7 ± 7.1	51.6 ± 6.2	0.95
Femoral Bone Mineral Density	0.84 ± 0.2	0.84 ± 0.2	1
Vertebral Bones Mineral Density	0.87 ± 0.2	0.86 ± 0.2	0.55

*Table 2*  
Prevalence of disability, falls, bone fracture and osteoporosis based on serum sodium concentration

Variable		Serum sodium concentration		OR (95% CI)	p-value
		≤ 137 mEq/L N (%)	> 137 mEq/L N (%)		
Occurrence of falls during the previous 6 months	yes	19 (9.2)	187 (90.8)	1.13 (0.73-1.74)	0.56
	no	96 (10.6)	811 (89.4)	0.97 (0.89-1.06)	
Occurrence of bone fracture during the previous 6 months	yes	33 (10.6)	227 (89.4)	0.96 (0.71-1.31)	0.83
	no	82 (10.2)	721 (89.8)	1.01 (0.89-1.14)	
Dependent in activities of daily living	yes	4 (14.8)	23 (85.2)	0.66 (0.23-1.88)	0.60
	no	111 (10.2)	975 (89.8)	1.01 (0.97-1.04)	
Osteoporosis	yes	39 (10.2)	345 (89.8)	1.01 (0.77-1.33)	0.88
	no	76 (10.4)	653 (89.6)	0.99 (0.86-1.13)	
To have physical activity	yes	91 (10.8)	751 (89.2)	0.95 90.86-1.05)	0.35
	no	24 (8.9)	247 (91.1)	1.18 (0.81-1.72)	

*Table 3*  
Serum sodium concentration, Gender and Bone Mineral Density

Gender	BMD groups	Number of people in this group	Serum sodium concentration (mean ± SD)	p-value
Male	Normal	176	140.2 ± 2.2	0.33
	With Osteopenia	347	140.3 ± 2.5	
	With Osteoporosis	99	139.9 ± 2.2	
Female	Normal	52	140.5 ± 2.0	0.14
	With Osteopenia	154	139.8 ± 2.2	
	With Osteoporosis	285	140.2 ± 2.5	
Total	Normal	328	140.2 ± 2.1	0.82
	With Osteopenia	501	140.1 ± 2.4	
	With Osteoporosis	384	140.1 ± 2.4	

*Table 4*  
Serum sodium concentration, balance test, the history of falls and bone fracture and disability in daily living activities

Variable	Groups	Number of people in this group	Serum sodium concentration (mean ± SD)	p-value
Score of Berg Balance Test	< 50	271	140.1 ± 2.4	0.97
	≥ 50	842	140.1 ± 2.3	
Dependent in activities of daily living	yes	27	139.9 ± 2.6	0.56
	no	1086	140.2 ± 2.3	
Occurrence of falls during the previous 6 months	yes	206	140.0 ± 2.2	0.16
	no	907	140.2 ± 2.4	
Occurrence of bone fracture during the previous 6 months	yes	310	140.0 ± 2.4	0.26
	no	803	140.2 ± 2.3	

## DISCUSSION

More than 10 percent of people aged 60 years and over had hyponatremia (serum  $\text{Na}^+$  level  $\leq 137$  mEq/L). No significant difference has been observed between hyponatremic and non-hyponatremic individuals about their balance abilities; bone mineral density; incidence of falls and/or bone fracture during the previous 6 months; dependency in activities of daily living; and osteoporosis. Mean of serum sodium concentration had no significant difference between the elderly who had lower physical activity; disability in daily living activity; and occurrence of falls or bone fracture in the previous 6 months. Considering BMD T-scores, no significant difference has been observed between two genders about their serum sodium concentration.

Nearly, one third of body sodium is stored in the bone [25]. The association of HN with balance impairment, falls and bone fractures in the elderly can be justified by different mechanisms including increase unsteady gait related to cognitive impairment; bone resorption and its fragility [1, 7, 8, 25], furthermore, another research presented that the sustained low extracellular sodium ion concentrations could directly stimulate osteoclastogenesis and that hyponatremia-induced oxidative stress might be involved in the mechanism [26].

In the research of Kinsella [12] which was conducted using the laboratory data related to 1408 females (aged 18 years and over, mean age of 61 years), 4.2% of the participants had serum sodium concentration less than 135 mEq/L; HN was found in 8.7% of the patients who had previous bone fracture compared to 3.2% of subjects who did not have the history of fracture. Hyponatremic patients had a 2.86 fold increased OR for fracture occurrence which was a different result compared to the present study. In the research of Hoorn [11], consistent with our research, HN was not associated with lower BMD but it was associated with increased risk of bone fractures. Hoorn [11] and Usala [9] showed that more decline in serum  $\text{Na}^+$  concentration may be needed to make osteoporosis in the elderly, while in our research mean of serum  $\text{Na}^+$  concentration in the subjects with osteoporosis was  $140.1 \pm 2.4$  (which is defined as nonhyponatremia). In Hoorn's study, individuals with HN had more recent falls (23.8% *versus* 16.4%), which is different with our result. This difference may be attributed to study design and considering underlying causes of HN in the elderly; for example, we had excluded the people who consumed diuretics. These causes of HN can have more impact on falls and osteoporosis.

In the research of Karanchi [24] in which, similar to our study, serum  $\text{Na}^+$  level  $\leq 137$  mEq/L was considered as cut-off point for HN, it was presented that HN was associated with a three-fold increased risk of osteoporosis, which is different from our result; on the other hand, consistent with our study, there was no significant difference between hyponatremic and nonhyponatremic older adults about the recent bone fracture and BMD of hip and femoral bones. Also, in Karanchi's research, BMD was higher at lumbar vertebrae (L2-L4) of hyponatremic subjects. This difference in the results may be due to study designs; in our research, concurrent conditions which could have impact on BMD were considered as exclusive criteria, while in Karanchi's study, frail older adults entered in the research.

In our study, mean of serum  $\text{Na}^+$  concentration in the three groups of BMD was about 140 mEq/L which is consistent with the studies of Hoorn [11] and Kinsella [12].

In the research of Usala in the USA [9], it was shown that HN was associated with chronic osteoporosis (OR = 3.97), recent osteoporosis (OR = 3.06), chronic bone fractures (OR = 4.61), and recent fractures (OR = 3.05) which is different from our results. This difference may be attributed to study design and individual characteristics of participants.

In our study, no significant association has been observed between serum  $\text{Na}^+$  concentration and incidence of falls; which is different with Ahamed's study in Australia [27]. Ahamed studied the patients aged  $\geq 65$  years admitted with HN during a 6-month period and demonstrated the prevalence of HN as 22%. In that research, HN was associated with the admission diagnoses of cardiovascular and metabolic disorders, use of diuretics and comorbidities. HN was associated with falls (OR = 3.12), and the increased odds of falling were similar for mild and moderate to severe HN. Duration of patients follow-up and inclusion criteria of the study can be the causes of the difference in the results. In our study, the frail elderly who could not refer to undergo laboratory tests, or had comorbid disorders which could have impact on BMD such as long-term use of diuretics had been excluded.

In this study, serum potassium concentration was significantly lower in the patients who had lower serum sodium level; also, serum BUN was higher in this group. This result can be representative for the maintenance mechanism of serum sodium concentration in association to potassium and total body water [28-30]. Adrogué mentioned in his study

that hyponatremia can be representative of excess of water relative to the sodium and potassium stores. Also, water retention usually results from impairment of renal excretion of electrolytes free water [29].

One of limitations of our study was that we examined recent HN; not chronic HN. It is suggested to be considered in future studies.

## CONCLUSION

No significant difference has been observed between hyponatremia and bone mineral density

and falls in the elderly. On the other hand, HN was not a prevalent problem in older adults who did not have serious comorbid disorder or severe disability or the individuals who did not consume medications which could have impact on serum sodium concentration.

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**Conflict of interest.** The authors declare that there are no conflicts of interest.

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**Introducere.** Hiponatremia (HN) se poate asocia cu osteoporoză și cu fracturi în cadrul populației vârstnice. Mai multe studii recente au arătat legătura dintre HN și densitatea osoasă și fracturile.

**Metode.** A fost realizat un studiu analitic cuibărit în cadrul cohortei AHAP din nordul Iranului. Toți pacienții peste 60 de ani au fost incluși în studiu. Au fost excluși indivizii cu comorbidități severe precum și cei care ar putea fi avut anumite condiții ce ar fi interferat cu densitatea mineral-osoasă cum ar fi consumul de glucocorticoizi, suplimentare cu calciu/vitamina D, terapie cu bisfosfonați, calcitonină, tiazide precum și medicație hormonală.

**Rezultate.** 1113 de pacienți în vârstă de 60 ani și peste au fost recrutați. Mai mult de 10% au avut hiponatremie (niveluri serice ale  $\text{Na}^+ \leq 137 \text{ mEq/L}$ ). Nu s-au găsit diferențe semnificative între pacienții hiponatremici și cei normonatremici.

**Concluzii.** HN nu a avut o prevalență foarte mare la pacienții vârstnici care au îndeplinit criteriile de includere în studiu. Nu au fost găsite diferențe semnificative între HN și densitatea minerală sau fracturile la pacienții vârstnici.

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