Int Urol Nephrol (2013) 45:265–273
DOI 10.1007/s11255-012-0307-9

NEPHROLOGY - ORIGINAL PAPER

Clinical features, outcome and cost of hyponatremia-associated admission and hospitalization in elderly and very elderly patients: a single-center experience in Turkey

K. Turgutalp · O. Ozhan · E. Gok Oguz · M. Horoz · A. Camsari · A. Yilmaz · A. Kiykim · M. Arici

Received: 8 June 2012 / Accepted: 24 September 2012 / Published online: 11 October 2012

Abstract
Purpose Hyponatremia is a common electrolyte disorder in hospitalized patients. Clinical features, outcome and cost of hyponatremia-associated admission and hospitalization in elderly and very elderly patients are not well known.
Methods Elderly (>64 years) patients admitted to the emergency department (ED) and hospitalized between January 1, 2010, and December 31, 2010, were evaluated. Hyponatremia was defined as serum sodium level below 135 mmol/L. Hyponatremic patients were divided into two groups: group 1 ($n = 150$, 65–74 years old) and group 2 ($n = 103$, >74 years old).
Results A total of 4,960 patients above 65 years of age admitted to ED and hospitalized were included. Prevalence of ED in group 1 and group 2 was 4.1 % (150/3,651) and 7.8 % (103/1,309), respectively ($p < 0.001$). Vomiting and diarrhea were the most important complaints. A total of 111 (43.8 %) patients were being treated with renin–angiotensin system (RAS) blockers. Mortality, morbidity and hospital cost increased in parallel to decrease in serum Na^+ level and increase in age. Group 2 subjects had not only higher intensive care need ($p < 0.01$) and mortality rates ($p < 0.01$), but also higher hospital cost burden ($p < 0.05$) compared to group 1. Alzheimer's disease was one of the most common co-morbidity in patients, particularly in group 2 (5.3 % vs. 21.3 %, $p < 0.001$).
Conclusion Hyponatremia-associated hospitalization is an important and potentially lethal condition in elderly and very elderly patients. Clinicians should be careful when prescribing RAS blockers and diuretics in elderly patients.

Keywords Hyponatremia · Elderly · Prevalence · Mortality · Hospital cost

K. Turgutalp (✉) · E. Gok Oguz · M. Horoz · A. Kiykim
Division of Nephrology, Department of Internal Medicine, School of Medicine, Mersin University, 33079 Mersin, Turkey
e-mail: k.turgutalp@hotmail.com

O. Ozhan
Division of Endocrinology and Metabolism, Department of Internal Medicine, School of Medicine, Mersin University, Mersin, Turkey

A. Camsari
Department of Cardiology, School of Medicine, Mersin University, Mersin, Turkey

A. Yilmaz
Department of Neurology, School of Medicine, Mersin University, Mersin, Turkey

M. Arici
Nephrology Unit, Department of Internal Medicine, School of Medicine, Hacettepe University, Ankara, Turkey

Background

Hyponatremia is the most common electrolyte disorder in hospitalized patients, particularly in elderly patients [1]. It is well known that there are several physiologic changes that occurred in the elderly such as reduced total body water volume, glomerular filtration rate and urinary concentrating ability, changes in aldosterone concentration, decrease in thirst, decrease in free water clearance and increased atrial natriuretic peptide concentration. Such changes have been related to increased tendency to develop hyponatremia in the elderly [1].

Extensive data are available about the clinical features, related factors, outcome and cost of hospital-acquired hyponatremia. The prevalence of hospital-based hyponatremia is up to 25 %. Hyponatremia is also a common condition in elderly people living in nursing houses [2]. The cost burden and accompanying problems related to hyponatremia such as psychiatric disorders, delirium, tuberculosis, surgery and drug use in hospitalized patients as well as in subjects living in nursing houses were well known [3]. On the other hand, data about the prevalence, cost burden, clinical courses and related factors for patients with hyponatremia-associated admission and hospitalization are not well defined in the elderly. Limited number of studies has revealed the prevalence of as 8–11 % in elderly subjects [4].

People above 65 years of age comprised 7.2 % of Turkey's population, and there are 70,000 people above 90 years of age to date [5]. By the time of 2050, 730 % increase in the elderly is expected [5]. In this sense, the specific clinical problems in elderly people along with their management should be well defined. The aim of this study was to exhibit the clinical features, results and cost of hyponatremia-associated hospitalization in elderly subjects.

Patients and methods

People above 65 years of age admitted to the emergency department (ED) of Mersin University Hospital and hospitalized between January 1, 2010, and December 31, 2011, were assessed, retrospectively. The study design was approved by local ethical committee (date: November 23, 2009; reference number: 119).

A repeated serum Na^+ level which had been measured less than 135 mmol/L was defined as hyponatremia. In our hospital practice, all patients with hyponatremia admitted to ED have been consulted to the nephrologists. Serum Na level between 130 and 135 was accepted as mild hyponatremia, whereas values between 120 and 130 were accepted as moderate hyponatremia. Serum Na^+ level which had been measured less than 120 mmol/L was accepted as severe hyponatremia.

In our country, average life expectancy is 74 years [5]. Patients were divided into two groups as "elderly" (group 1, 65–74 years) and "very elderly" (group 2, >74 years). Study subjects had not been admitted to another hospital in preceding 2 weeks before the admission.

Demographic data

Admission reasons, nutritional status, clinical symptoms and signs, neurologic examination, co-morbidities and medication history were assessed. The admission complaints of patients were represented by ICD 10 codes. Volume status and vital signs at the time of admission were obtained, except in 5 patients in group 1 and 4 patients in group 2. Patients were divided into three groups according to their systolic blood pressure on admission. Subjects were defined as hypotensive if they had systolic blood pressures less than 100 mmHg. Systolic blood pressure between 100 and 140 mmHg was defined as normotensive unless the subjects were not receiving any antihypertensives. Finally, if patients had systolic blood pressures above 140 mmHg or if they were already under antihypertensive treatment, they were classified as hypertensive.

Katz's scoring system that measured patients' ability of performing daily activities by themselves such as urine continence, walking, feeding, changing clothes and fulfilling toilet needs had been measured in study subjects, except in 8 patients in group 1 and 4 patients in group 2 [6]. Patients having Katz's score above 12, between 2 and 12, and below 2 were accepted as "full independent", "partially dependent" and "dependent", respectively. Mental status had been recorded with Folstein's mini mental state examination (MMSE) [7] scoring system in study subjects, except 8 patients in group 1 and 4 patients in group 2. Patients having MMSE score above 23, between 17 and 23, between 12 and 17, and below 12 were accepted as "normal", "mildly impaired", "mild to severely impaired" and "severely impaired", respectively.

The patients' volume status on admission had been recorded in all study subjects. Causes of hyponatremia, time to normalization of Na^+ levels, neurologic findings, complications, outcome, causes of mortality, need for ventilator support and intensive care, and hospital cost were assessed in all study subjects.

Laboratory tests

Serum Na^+ and plasma glucose levels, serum blood urea nitrogen (BUN), creatinine, potassium, magnesium, chloride, calcium, phosphate, serum albumin, TSH (thyroid-stimulating hormone), liver enzymes, vitamin B12, arterial blood gases, CRP levels, free cortisol levels as well as urine density, and Na^+ levels in 24-h urine had been measured on admission in all subjects. Serum Na^+ levels had been measured every 2–4 h until normalization of serum Na^+. Specific tests for special conditions had been measured in selected patients.

Neurologic examination had been performed in all subjects. Mental status examination had been performed by MMSE, and motor abnormalities had been investigated by neurologic examination and Katz score. Autonomic instability including tachycardia, diaphoresis, blood pressure changes, cranial nerve examination and respiratory abnormalities had been recorded in neurologic examination. Diagnosis of Alzheimer's disease (AD) had been based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV-TR) [8]. Computed tomography or magnetic resonance imaging of the head had been performed only in patients with focal neurologic deficit.

Statistical methods

Shapiro–Wilk test was used to test the numeric data in terms of its convenience for normal distribution. While parametric tests were used for the assessment of variables showing normal distribution, nonparametric tests were used if normal distribution was not detected. For the comparison of the two independent categoric groups in terms of numeric variables, either Student's *T* or Mann–Whitney *U* tests were used according to the distribution of the data. For the comparison of categoric variables where more than two independent groups were involved, one-way analysis of variance (ANOVA) test was applied. For the ANOVA test results revealing statistical significance, Tukey's HSD among the post hoc tests was performed. Pearson's chi-square test was applied according to the assumptions in the comparisons of two categoric variables. For testing a possible linear association between two numeric variables, Spearman-Rho test was used. Paired sample test was applied to assess the differences in consecutive values. Type 1 error was determined to be 0.05, and for the statistical analysis, MedCalc 11.5 statistic program was applied.

Results

Between January 1, 2010, and December 31, 2011, 4,960 patients above 65 years of age had been admitted to the emergency department. The prevalence of hyponatremia-associated hospitalization in group 1 and group 2 was 4.1 % (150/3,651) and 7.8 % (103/1,309), respectively ($p < 0.001$), and the overall prevalence was found to be 5.1 % ($n = 253$, 253/4,960). There was no significant gender difference between the groups ($p > 0.05$). Clinical and laboratory parameters of group 1 and group 2 are shown in Tables 1 and 2, respectively.

Distribution according to the severity of severe, moderate and mild hyponatremic subjects in group 1 was 58, 28 and 14 %, respectively ($p < 0.05$). However, distribution according to the severity of severe, moderate and mild hyponatremic subjects in group 2 was 60, 25 and 15, respectively ($p < 0.05$). In both of the groups, most of the subjects had been admitted to the hospital due to severe hyponatremia.

Most common reasons for admission are shown in Fig. 1, and most common co-morbidities are listed in Table 3. When groups 1 and 2 were compared, group 2 subjects were found to be more hypotensive than group 1 (70 % vs. 52.4 %, $p < 0.01$).

Hypovolemic hyponatremia was the most common type of hyponatremia in both groups, and it was significantly higher than other types ($p < 0.05$). Hypovolemic hyponatremia and hypervolemic hyponatremia were more common in group 2 as compared to group 1 ($p < 0.05$) (Table 1). On the other hand, most of the patients suffering from severe hyponatremia were diagnosed with hypovolemic hyponatremia ($p < 0.05$).

Table 1 Clinical features of the groups

	Group 1 ($n = 150$)	Group 2 ($n = 103$)	p
Age	69.45 ± 3.5	82.35 ± 5.2	<0.05
Gender (female/male)	72/78	57/46	NS
Systolic blood pressure (mmHg)	126.6 ± 31.4	112.1 ± 42.0	<0.05
Diastolic blood pressure (mmHg)	75.2 ± 19.6	66.9 ± 14.5	<0.05
KATZ score	2.5 ± 1.8	1.1 ± 0.9	<0.001
MMSE score	21.1 ± 8.1	11.3 ± 6.2	<0.001
Hypovolemic hyponatremia (%/n)	59.9/89	65/67	<0.05
Normovolemic hyponatremia (%/n)	14.1/22	14.5/15	NS
Hypervolemic hyponatremia (%/n)	26/39	20.5/21	<0.05
Time to Na^+ level normalization			
0–24 h (%/n)	18.7/28	16.5/17	NS
24–48 h (%/n)	39.3/59	42.7/44	NS
48–72 h (%/n)	25.3/38	25.2/26	NS
>72 h (%/n)	16.7/25	15.5/16	NS
AKI (%)	13.3	20.3	<0.01
Dialysis in patients with AKI (%)	35	58.3	<0.001
NIC (%/n)	58.6/88	79.6/82	<0.01
NVS (%/n)	19.3/29	35.9/37	<0.01
Length of hospital stay (day)	9.56 ± 7.1	11.80 ± 8.2	<0.05
Fully healed subjects (%/n)	68.7/102	48.6/50	<0.001
Mortality rate (%/n)	31.3/48	51.4/53	<0.001
Cost (USD)	1,524.4 ± 719.1	1,745.7 ± 756.9	<0.01

NIC need for intensive care, *NVS* need for ventilator support, *NS* not significant, *MMSE* mini mental state examination, *USD* US dollars, *AKI* acute kidney injury

The most common hyponatremia-associated conditions are shown in Table 4. In group 1, renin–angiotensin system (RAS) blockers (ACE inhibitors and angiotensin receptor blockers) + thiazide diuretic use, and diarrhea were the most common reasons. On the other hand, oral intake impairment, vomiting and diarrhea were the most common reasons in group 2. Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) had been detected only in a few patients (3.3 % vs. 6.7 % in group 1 and 2, respectively) ($p < 0.05$). When classified according to the severity of hyponatremia, RAS blockade, diuretic use and diarrhea coexistence were the most common related factors for hyponatremia in group 1. Oral intake impairment, vomiting and diarrhea coexistence, on the other hand, were the most common reasons for group 2 regardless of the severity of hyponatremia.

Katz's and MMSE scores between groups are shown in Table 1. Katz's and MMSE scores negatively correlated with length of hospital stay ($p < 0.05$, $r = -0.39$ for Katz's and $r = -0.41$ for MMSE scores) and with cost ($p < 0.05$, $r = -0.33$ for Katz's and $r = -0.37$ for MMSE scores). No relation was detected between the scores and other parameters such as need for intensive care and ventilator support, clinical complications, and mortality rates. Katz's and MMSE scores were not significantly different between genders ($p > 0.05$). The Katz's scores of severe, moderate and mild hyponatremic subjects in group 1 were 2.3 ± 1.1, 2.7 ± 1.2 and 2.9 ± 1.2, respectively ($p < 0.05$ for all). However, in group 2, the Katz's scores for severe, moderate and mild hyponatremic patients were found to be 0.9 ± 0.3, 1.1 ± 0.4 and 1.8 ± 0.7, respectively ($p < 0.05$ for all). While the minimum Katz's score was detected in group 2 subjects with severe hyponatremia ($p < 0.05$), the maximum Katz's score was found in group 1 subjects with mild hyponatremia ($p < 0.05$). The MMSE scores of patients with severe, moderate and mild hyponatremia in group 1 were 19.2 ± 5.6, 23.1 ± 6.1 and 26.2 ± 6.3, respectively ($p < 0.05$ for all). The MMSE scores of the subjects with severe, moderate and mild hyponatremia in group 2, on the other hand, were found to be 9.4 ± 3.1, 11.1 ± 4.2 and 18.6 ± 5.4, respectively ($p < 0.05$ for all). The minimum MMSE score was in group 2 patients with severe hyponatremia ($p < 0.05$), and the maximum was in group 1 subjects with mild hyponatremia ($p < 0.05$).

Recorded complications in hospital were assessed in all subjects. In group 1 and group 2, 40.7 % ($n = 61$) and 26.2 % ($n = 27$) of subjects had no complication ($p < 0.001$), respectively. Acute kidney injury (AKI) and systemic bacterial infection had been

Table 2 Laboratory features of the groups

	Group 1 ($n = 150$)	Group 2 ($n = 103$)	p
Plasma glucose levels (mg/dL)	83.65 ± 3.5	82.35 ± 5.2	NS
Potassium (mEq/L)	4.6 ± 0.4	4.8 ± 0.5	NS
Magnesium (mg/dL)	2.1 ± 0.9	2.2 ± 1.0	NS
Chloride (mEq/L)	101.4 ± 19.6	100.5 ± 14.5	NS
Na^+ level on admission (mmol/L)	119.0 ± 6.8	118.5 ± 7.0	NS
Serum creatinine (mg/dL)	0.84 ± 0.79	1.45 ± 0.72	<0.05
Hemoglobin (gr/dL)	13.1 ± 1.1	12.5 ± 1.7	NS
Calcium (mg/dL)	9.3 ± 1.8	9.2 ± 1.6	NS
Phosphate (mg/dL)	3.7 ± 0.7	5.6 ± 1.6	<0.05
Albumin (g/dL)	3.9 ± 0.7	3.8 ± 0.6	NS
TSH (μIU/mL)	3.2 ± 1.1	3.4 ± 1.2	NS
ALT (U/L)	26.3 ± 1.4	27.2 ± 1.5	NS
AST (U/L)	29.5 ± 1.7	27.4 ± 1.5	NS
Vitamin B12 (pg/mL)	214 ± 28	231 ± 32	NS
CRP (mg/L)	3.2 ± 0.2	3.5 ± 0.3	NS
Cortisol (nmol/L)	215 ± 38	219 ± 26	NS
Urine density	1,020.5 ± 5.5	1,021 ± 5.6	NS
Na + levels in 24 h urine	72.8 ± 12.1	71.6 ± 11.9	NS
Arterial blood gases Ph	7.41 ± 0.03	7.40 ± 0.02	NS
Serum blood urea nitrogen (mg/dL)	32.2 ± 4.5	42.5 ± 5.8	<0.05

TSH thyroid-stimulating hormone, *ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *CRP* C-reactive protein

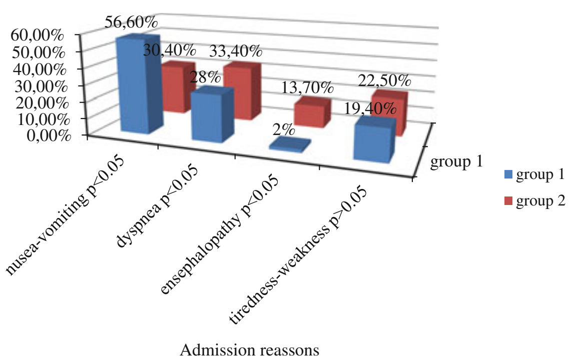

Fig. 1 Admission reasons according to the groups

Table 3 Co-morbidities in groups

Co-morbidity	Group 1 (n/%)	Group 2 (n/%)	p
Alzheimer's disease	8/5.3 %	22/21.3 %	<0.05
Hypertension	29/19.3 %	14/13.6 %	<0.05
Heart failure	26/17.3 %	22/22.3 %	NS
Diabetes mellitus	29/19.3 %	14/13.6 %	<0.05
Cancer	4/2.6 %	8/7.7 %	<0.05

RAS renin–angiotensin system, *NS* not significant

Table 4 The most common hyponatremia-associated conditions in groups

Conditions	Group 1 (n/%)	Group 2 (n/%)	p
RAS blockers + thiazide diuretic use + diarrhea	50/33.3	21/20.3	<0.01
RAS blockers + thiazide diuretic use + OII	40/26.6	19/18.4	<0.01
OII + vomiting + diarrhea	39/26	33/32	<0.05
Loop diuretic use + vomiting	11/7	15/14.5	<0.05
RAS blockers (without diuretic) + vomiting	10/6	13/12.6	<0.05

OII oral intake impairment

developed in 13.3 % of the group 1 subjects and 20.3 % of the group 2 subjects ($p < 0.01$). Hemodialysis had been performed in 7 of 20 patients (35 %) in group 1 and 14 of 24 patients (58.3 %) in group 2 ($p < 0.001$).

The need for intensive care and ventilator support was higher in group 2 than in group 1 ($p < 0.01$) (Table 1). The need for ventilator support and intensive care unit was higher in patients with severe hyponatremia in both group 1 and group 2 than in others ($p < 0.05$). Eighty-four percentage of patients who had need for ventilator support had died. The mortality rate of the patients who had need for intensive care and ventilator support was significantly higher in both groups ($p < 0.001$).

Time to normalization of Na^+ levels for all groups is shown in Table 1. While time to normalization of Na level had been 24 h in patients with acute onset hyponatremia, chronic onset hyponatremia had been normalized slowly accordingly with a normalization speed of 0.5–1.0 mmol/h. In group 1, 92 % ($n = 26$) of the patients whose serum Na^+ levels had been normalized within 0–24 h were suffering from severe hyponatremia, whereas remaining 7.3 % ($n = 2$) were suffering from moderate hyponatremia ($p < 0.05$). In group 1, 32.2 % ($n = 19$), 32.2 % ($n = 19$) and 35.6 % ($n = 21$) of the subjects whose serum Na^+ levels had been normalized within 24–48 h were suffering from severe, moderate and mild hyponatremia, respectively ($p > 0.05$), and 47.3 % ($n = 18$) and 52.4 % ($n = 20$) of the subjects whose serum Na^+ levels had been normalized within 48–72 h were suffering from severe and moderate hyponatremia, respectively ($p > 0.05$). Finally, 96 % ($n = 24$) and 4 % ($n = 1$) of the patients in group 1 whose serum Na^+ levels had been normalized within more than 72 h were suffering from severe and moderate hyponatremia ($p < 0.05$). In group 2, 88.2 % ($n = 15$) and 17.2 % ($n = 2$) of the subjects whose serum Na^+ levels had been normalized within 0–24 h were suffering from severe and moderate hyponatremia, respectively ($p < 0.05$). In group 2, 43.1 % ($n = 19$), 25 % ($n = 11$) and 31.8 % ($n = 14$) of the patients whose serum Na^+ levels had been normalized within 24–48 h were suffering from severe, moderate and mild hyponatremia, respectively ($p > 0.05$). In group 2, 50 % ($n = 13$), 42.3 % ($n = 11$) and 7.7 % ($n = 2$) of the subjects whose serum Na^+ levels had been normalized within 48–72 h were suffering from severe, moderate and mild hyponatremia, respectively ($p > 0.05$). Finally, 87.5 % ($n = 14$) and 12.5 % ($n = 2$) of the subjects in group 2 whose serum Na^+ levels had been normalized within more than 72 h were suffering from severe and moderate hyponatremia, respectively ($p < 0.05$). In patients where Na^+ levels had been normalized within 0–24, 24–48, 48–72 and more than 72 h, complication rates were found to be 55.2, 37.7, 33.3 and 55.7 %, respectively. Metabolic encephalopathy (from lethargy to coma) rates were 9.3, 6, 7.3 and 46 % in group 1 and 18, 10, 9 and 58 % in group 2 ($p < 0.05$ for all comparisons). Mortality rates for the mentioned time to normalization regardless of the age were as follows: 53.1 % for 0–24 h, 32.4 % for 24–48 h, 41.3 % for 48–72 h and 48.7 % for after 72 h. Mortality rates were higher in patients with rapid correction within 24 h or too slow correction (>72 h) of the hyponatremia ($p < 0.05$).

Mean length of hospital stay for group 1 and group 2 is shown in Table 1. Mean length of hospital stay for all subjects was found to be 9.32 ± 9.2 days. The mean length of hospital stay for fully healed patients was 10.7 ± 5.5 days and 14.9 ± 6.2 days for died subjects ($p < 0.05$). Length of stay in the hospital in group 1 patients with severe, moderate and mild hyponatremia was 10.5 ± 2.4, 9.8 ± 2.1 and 5.1 ± 1.2 days, respectively. When group 2 is assessed, the length of stay for the severe, moderate and mild hyponatremic subjects was detected to be 13.1 ± 3.4, 11.9 ± 2.9 and 6.7 ± 1.7 days, respectively. The longest length of hospital stay was observed in group 2 patients with severe hyponatremia and AKI ($p < 0.005$). The minimum length of stay in the hospital was detected in group 1 subjects with mild hyponatremia ($p < 0.05$). There was no significant difference with respect to cause of hospital duration in both groups ($p > 0.05$). There was a negative correlation between the length of hospital stay, and Katz's and MMSE scores ($p < 0.05$, $r = -0.39$ and $r = -0.41$, respectively).

A total of 101 patients had died. Group 2 had a significantly higher mortality rate than group 1 ($p < 0.001$) (Table 1). The exitus ratio distributions in group 1 according to the severity of hyponatremia were as follows: severe hyponatremic 54.2 % ($n = 26$), moderate hyponatremic 37.5 % ($n = 18$) and mild hyponatremic 8.3 % ($n = 4$); however, in group 2, they were as follows;: severe hyponatremic 58.4 % ($n = 31$), moderate hyponatremic 32.2 % ($n = 17$) and mild hyponatremic 9.4 % ($n = 5$). Severe hyponatremic subjects with AKI in group 2 had the highest mortality rate (58.4 %, $p < 0.05$). The minimum mortality rate was in group 1 patients with mild hyponatremia ($p < 0.05$). Both age and Na^+ levels on admission were seen an important factor on mortality ($p < 0.05$). In terms of mortality, there was no significant difference between genders in both groups ($p > 0.05$).

Hospital cost is shown in Table 1. The median hospital costs in group 1 subjects with severe, moderate and mild hyponatremia were $1{,}621.2 \pm 723.1$, $1{,}568.3 \pm 683.7$ and $1{,}034.4 \pm 452.2$ USD, respectively. On the other hand, in group 2, they were $1{,}832.4 \pm 783.1$, $1{,}692.4 \pm 695.7$ and $1{,}499.1 \pm 627.4$ USD for patients with severe, moderate and mild hyponatremia, respectively. The subjects who had the lowest hospital cost were the ones in group 1 patients with Na^+ levels between 130 and 135 mmol/L ($p < 0.05$). On the other hand, group 2 subjects with Na^+ levels less than 120 mmol/L and AKI had the highest hospital cost. Mean cost of a hyponatremic subject was found to be $1{,}614 \pm 729$ US dollars

(USD). Controlling for age, sex and co-morbid conditions, hyponatremia was a significant independent predictor of total hospital cost.

Discussion

This study revealed that hyponatremia-associated admission and hospitalization prevalence in very elderly patients is higher than in elderly patients. We observed that the need for intensive care and ventilator support as well as the hospital cost and mortality rates was higher in very elderly patients than in elderly patients. It has been reported that hospital-based hyponatremia is common in female elderly patients and that females tolerated hyponatremia better than males [1]. In our study, there was not a significant gender difference in both elderly and very elderly patients.

Decrease in thirst, poor self-care and some drug therapies (RAS blockers, diuretics) may cause impaired regular oral intake of water and nutrients and may cause hyponatremia in elderly persons. It has been demonstrated that the prevalence of drug-induced hyponatremia increases with age [9]. Diuretics are one of the most common causes of hyponatremia in elderly patients [10]. Passare et al. [9] have underlined in their study that the use of not only diuretics but also several other drugs may cause hyponatremia in elderly patients. RAS blockers have a modest natriuretic effect regardless of diet Na^+ content [11]. Some older papers reported that lisinopril and enalapril may cause hyponatremia [12]. Rarely, ACE inhibitors may cause hyponatremia via syndrome of inappropriate secretion of antidiuretic hormone [13]. Moreover, it is known that thiazide diuretic use even at low dosages as in combined preparation (ACE inhibitors plus thiazide, ARB plus thiazide) may lead to severe fatal hyponatremia particularly in elderly subjects [14]. Sharabi et al. [15] have reported in their study that hyponatremia risk increases up to 10- and 16-fold in patients using thiazide diuretics with ages above 65 and 75 years, respectively, as compared to young patients. In the present study, treatment with thiazide diuretics and RAS blockers (ACE inhibitors, angiotensin II receptor blockers and their diuretic combinations) in both groups, particularly in the very elderly group, was commonly encountered. Yawar et al. [13] have found that there are many causes of hyponatremia; however, single use of diuretics, ACE inhibitors or ARBs is the most common cause with a proportion of 30 %. While 6 % of our elderly subjects had been using RAS blockers without diuretics, it was 12.6 % for our very elderly subjects. De Vecchis et al. [16], in their case–control study where 57 patients under at least 175 mg oral loop diuretic treatment with congestive heart failure were involved, had detected that 19 patients developed hyponatremia at the end of 6-month follow-up. When our subjects are assessed, we have detected that 7 % of elderly and 14.5 % of very elderly hyponatremic subjects were under loop diuretic treatment. The cause-and-effect relationship between RAS blockers and hyponatremia is not an aim of this study, but physicians should be careful about prescribing RAS blockers and diuretics in elderly and very elderly persons. SIADH is one of the most common causes of hyponatremia in the elderly [1]. As an interesting finding, SIADH had been diagnosed in a few of our patients. We expected that SIADH had been overlooked in our subjects.

Chronic disease and disorders, and multidrug therapy related to these conditions are common in elderly persons. In some observational studies, it has been detected that hyponatremia was detected on admission in 47 % of cancer patients [17]. Zilberberg et al. [18] demonstrated that hyponatremic patients had a higher co-morbidity index than patients with normal Na^+. Antecedent heart disease, diabetes mellitus, hypertension and Alzheimer's disease were the most common co-morbidities in our subjects, particularly in very elderly patients. There is no doubt about the contributions of such co-morbidities in development of ED, but their impact on outcome and cost remains not clear. Prerenal acute kidney injury (AKI) is common in patients presenting with hyponatremia, and diuretics were one the causes of AKI [19]. Development of acute kidney injury (AKI) and systemic bacterial infection, and need for renal replacement therapy (hemodialysis) were higher in very elderly patients than in elderly patients.

Terzian et al. [20], in their study where 4,123 geriatric hyponatremic subjects were evaluated, have shown that mortality rates were increased approximately twofold in hyponatremic subjects compared to non-hyponatremic ones. It has been reported that mortality associated with hyponatremia is higher in males than in females (33.3 % vs. 9.1 %). The mortality rate was 38 and 51.4 % in elderly and very elderly patients, respectively, in our study. There was no gender difference in mortality. While some studies have been documented that Na^+ levels on admission are related to mortality [21], others did not [22]. We found that there was a significant relation between mortality, morbidity and cost, and Na^+ levels on admission in our elderly and very elderly patients. This relation was more prominent in patients with Na^+ levels on admission less than 120 mmol/L. On the other hand, time to normalization of hyponatremia is another important factor that related mortality and morbidity. In our subjects, mortality rate was higher in patients having time to normalization of hyponatremia less than 24 h or greater than 72 h than in others. On the other hand, mortality rate was higher in patients who required dialysis than in others. Shorr et al. [23] have evaluated 6,117 patients (mean age 74.4 years) who had serum Na^+ levels less than 130 mmol/L as severe hyponatremic and 18,445 patients (mean age 74.3 years) with Na^+ levels between 130 and 135 mmol/L as non-severe hyponatremic subjects. In their study, they also have stated that severe hyponatremic and non-severe hyponatremic patients had mean costs of 11.109 and 10.033 USD, respectively. For our severe hyponatremic subjects, the hospital costs were 1,621.2 ± 723.1 and 1,832.4 ± 783.1 US dollars, respectively, for elderly and very elderly subjects. On the other hand, for elderly and very elderly patients with mild hyponatremia, hospital cost was 1,034.4 ± 452.2 US dollars and 1,499.1 ± 627.4 US dollars, respectively. The most influential factors for cost were serum Na^+ levels on admission, time to normalization of hyponatremia and age.

Conclusion

Hospitalization-required hyponatremia is more common in very elderly persons than in elderly persons. We found that impaired oral intake, Alzheimer's disease, and RAS blocker and diuretic use were the most common associates. Length of hospital stay, AKI, severe infection, need for intensive care and mechanical ventilation as well as cost and mortality rates are higher in very elderly subjects than in elderly subjects.

Acknowledgments None.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Rao MY, Sudhir U, Anil Kumar T, Saravanan S, Mahesh E, Punith K (2010) Hospital-based descriptive study of symptomatic hyponatremia in elderly patients. J Assoc Physicians India 58:667–669
2. Chen LK, Lin MH, Hwang SJ, Chen TW (2006) Hyponatremia among the institutionalized elderly in 2 long-term care facilities in Taipei. J Chin Med Assoc 69(3):115–119
3. Callahan MA, Do HT, Caplan DW, Yoon-Flannery K (2009) Economic impact of hyponatremia in hospitalized patients: a retrospective cohort study. Postgrad Med 121(2):186–191
4. Miller M, Carter JM, Fredlander DA, Carter JM (1996) Apparent idiopathic hyponatremia in an ambulatory geratric population. J Am Geriatr Soc 44:404–408
5. http://www.tuik.gov.tr/PreHaberBultenleri.do?id=8428
6. Soto ME, Secher M, Gillette-Guyonnet S, van Kan GA, Andrieu S, Nourhashemi F, Rolland Y, Vellas B (2012) Weight loss and rapid cognitive decline in community-dwelling patients with Alzheimer's disease. J Alzheimers Dis 28(3):647–654
7. Pihlajamaki M, Jauhiainen AM, Soininen H (2009) Structural and functional MRI in mild cognitive impairment. Curr Alzheimer Res 6:179–185
8. American Psychiatric Association (2000) Diagnostic and statistical manual of mental disorders (IV-TR), 4th edn-text revised. Washington, DC
9. Passare G, Viitanen M, Törring O, Winblad B, Fastbom J (2004) Sodium and potassium disturbances in the elderly: prevalence and association with drug use. Clin Drug Investig 24(9):535–544
10. Liamis G, Milionis H, Elisaf M (2008) Blood pressure drug therapy and electrolyte disturbances. Int J Clin Pract 62(10):1572–1580
11. Schoolwerth AC, Sica DA, Ballermann BJ, Wilcox CS (2001) Renal considerations in angiotensin converting enzyme inhibitor therapy: a statement for healthcare professionals from the council on the kidney in cardiovascular disease and the council for high blood pressure research of the American heart association. Circulation 104:1985–1991
12. Hume AL, Jack BW, Levinson P (1990) Severe hyponatremia: an association with lisinopril? DICP 24(12): 1169–1172
13. Yawar A, Jabbar A, Haque NU, Zuberi LM, Islam N, Akhtar J (2008) Hyponatraemia: etiology, management and outcome. J Coll Physicians Surg Pak 18(8):467–471
14. Chow KM, Kwan BC, Szeto CC (2004) Clinical studies of thiazide induced hyponatremia. J Natl Med Assoc 96:1305–1308
15. Sharabi Y, Illan R, Kamari Y, Cohen H, Nadler M, Messerli FH, Grossman E (2002) Diuretic induced hyponatraemia in elderly hypertensive women. J Hum Hypertens 16(9):631–635

16. De Vecchis R, Ariano C, Esposito C, Giasi A, Cioppa C, Cantatrione S (2012) In right or biventricular chronic heart failure addition of thiazides to loop diuretics to achieve a sequential blockade of the nephron is associated with increased risk of dilutional hyponatremia: results of a case-control study. Minerva Cardioangiol. Jul 5. (Epub ahead of print)
17. Doshi SM, Shah P, Lei X, Lahoti A, Salahudeen AK (2012) Hyponatremia in hospitalized cancer patients and its impact on clinical outcomes. Am J Kidney Dis 59(2):222–228
18. Zilberberg MD, Exuzides A, Spalding J, Foreman A, Jones AG, Colby C, Shorr AF (2008) Epidemiology, clinical and economic outcomes of admission hyponatremia among hospitalized patients. Curr Med Res Opin 24(6):1601–1608
19. Adams D, de Jonge R, van der Cammen T, Zietse R, Hoorn EJ (2011) Acute kidney injury in patients presenting with hyponatremia. J Nephrol 24(6):749–755
20. Terzian C, Frye EB, Piotrowski ZH (1994) Admission hyponatremia in the elderly: factors influencing prognosis. J Gen Intern Med 9:89–91
21. Kim JH, Lee JS, Lee SH, Bae WK, Kim NH, Kim KA, Moon YS (2009) The association between the serum sodium level and the severity of complications in liver cirrhosis. Korean J Intern Med 24(2):106–112
22. Kang SH, Kim HW, Lee SY, Sun IO, Hwang HS, Choi SR, Chung BH, Park HS, Park CW, Yang CW, Kim YS, Choi BS (2012) Is the sodium level per se related to mortality in hospitalized patients with severe hyponatremia? Clin Nephrol 77(3):182–187
23. Shorr AF, Tabak YP, Johannes RS, Gupta V, Saltzberg MT, Costanzo MR (2001) Burden of sodium abnormalities in patients hospitalized for heart failure. Congest Heart Fail 17(1):1–7