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Original Article

Sodium levels on admission are associated with mortality risk in hospitalized patients

Amit Akirov [a,b,*], Talia Diker-Cohen [a,b,c], Tali Steinmetz [b,d], Oren Amitai [a,b], Ilan Shimon [a,b]

[a] Institute of Endocrinology, Beilinson Hospital, Petach Tikva, Israel
[b] Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel
[c] Internal Medicine A, Beilinson Hospital, Petach Tikva, Israel
[d] Department of Nephrology and Hypertension, Beilinson Hospital, Petach Tikva, Israel

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ABSTRACT

Aims: Abnormal sodium values are common among hospitalized patients. We aimed to investigate the association of admission sodium values and mortality.
Methods: Historical prospectively data of adult patients hospitalized to medical wards between January 2011 and December 2013. Admission sodium values were classified to five categories: severe hyponatremia (<125 mEq/L), mild hyponatremia (125–135 mEq/L), normal sodium values (135–145 mEq/L), mild hypernatremia (145–150 mEq/L) and severe hypernatremia (>150 mEq/L). Main outcomes were length of hospitalization, in-hospital mortality and mortality at the end-of-follow-up.
Results: The cohort included 27,889 patients (mean age 67 ± 18 years, 52% males). The total follow-up was 1065 days. Most patients had normal sodium values (76%), 22% had hyponatremia, 3% had hypernatremia. Mean age increased with increase in severity of hyponatremia or hypernatremia. Median length of hospitalization was longer with mild and severe hypernatremia (7 and 5 days, respectively) or with mild and severe hyponatremia (4 and 4 days, respectively), compared to normal sodium levels (3 days). Compared to in-hospital mortality with normal sodium levels (5%), mortality was higher with mild and severe hyponatremia (9% and 14%, respectively) and was highest with mild (28%), and severe hypernatremia (52%). Mortality rate at the end of follow-up was 28% with normal sodium levels, 44% and 48% with mild and severe hyponatremia, 66% and 90% with mild and severe hypernatremia, respectively.
Conclusions: Abnormal sodium values on admission were associated with longer hospitalization and increased short- and long-term mortality. Mortality risk was higher with hypernatremia, compared to hyponatremia.

1. Introduction

Abnormal sodium levels are very common electrolyte disturbances in hospitalized patients. Numerous studies indicated hyponatremia and hypernatremia are associated with adverse outcomes in patients admitted to intensive care units [1–3].

Hyponatremia is generally defined as a serum sodium levels of <135 mEq/L [4,5]. Hyponatremia on admission was associated with increase by >50% in in-hospital mortality [6–8]. Waikar et al. reported the risk of mortality is evident even in patients with mild hyponatremia [9]. Hyponatremia is often associated with heart disease, malignancies, renal, pulmonary and neurologic diseases [5,9].

Hypernatremia, defined as sodium levels higher than 145 mEq/L, was reported in 2% of patients presenting to emergency department [1]. Alsirafy et al. reported over 60% death rate in patients with high sodium levels on admission [10].

Several studies proved the prognostic value of admission sodium levels for different conditions, including community acquired pneumonia, hip fracture, stroke, myocardial infarction and heart failure [11–18]. The mortality risk associated with hyponatremia was particularly strong in patients with cardiovascular disease and malignancy [9].

In the present study with a large cohort of hospitalized patients, the association between the entire spectrum of admission sodium levels and important hospitalization outcomes, including length of admission, all-cause in-hospital mortality and mortality at the end of follow-up was evaluated.

2. Methods

The study was conducted in a large 1300-bed university-affiliated tertiary medical center. Most of admissions to the 10 medical wards are through the emergency department. All patient data are recorded in electronic medical charts (based on the same database platform used in the community primary care facilities). Deaths are entered into the hospital's mortality database, which is updated according to the population registry of the Ministry of the Interior.

* Corresponding author at: Institute of Endocrinology, Rabin Medical Center-Beilinson Hospital, Petach Tikva 49100, Israel.
E-mail address: amitak@clalit.org.il (A. Akirov).

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For the present study, historical prospectively collected observational data were extracted from the medical records of all patients admitted for any cause to the hospital's medical wards between January 1, 2011 and December 31, 2013. Mortality data were obtained up to June 1, 2015. Self-reported data regarding alcohol use, smoking and body mass index, as well as co-morbidities were also collected from the database.

We excluded patients without blood sodium measurement on admission. In patients with multiple admissions, only the first was analyzed. Sodium values were corrected according to glucose values in patients with hyperglycemia, based on a correction factor of 1.6 mEq/L for every 100 mg/dL increase in serum glucose levels.

To reduce the probability that serum sodium levels were affected by hospital treatment, we focused on measurements performed, within the first 24 h of admission. Serum sodium values were classified into the following five categories: severe hyponatremia (<125 mEq/L), mild hyponatremia (125–135 mEq/L), normal sodium values (135–145 mEq/L), mild hypernatremia (145–150 mEq/L) and severe hypernatremia (>150 mEq/L).

Outcome measures included length of admission, in-hospital mortality and mortality at the end of follow-up according to sodium values on admission.

The study was approved by the Institutional Review Board.

2.1. Statistical analysis

The statistical analysis for this paper was generated using SAS Software, Version 9.4.

Continuous variables were presented by mean ± SD. Categorical variables were presented by (N, %).

ANOVA was used to compare the value of continuous variables between sodium level groups and the Chi-Square test was used to compare the value of categorical variables between these study groups.

ANOVA was also used to analyze length of hospitalization. In-hospital mortality was analyzed by logistic regression. Overall survival, by study groups, was analyzed by the KM model.

Overall survival, by study groups, adjusted for covariates was analyzed by the Cox proportional hazards model. Two sided p values < 0.05 were considered statistically significant.

3. Results

3.1. Study cohort

There were 73,796 admissions to the 10 medical wards during the study period. After exclusion of repeat admissions (40,076 admissions), and patients with no measurement of sodium values within 24 h of admission (5831 patients), the final study cohort consisted of 27,889 patients.

Mean age of the cohort was 67 ± 18 years, 14,397 (52%) were male. Most patients had normal sodium values on admission (21,109, 76%), 22% of patients had hyponatremia, mostly mild hyponatremia (5515 patients, 20%), and 2% of patients had severe hyponatremia (515 patients). Hypernatremia on admission was evident in 3% of the patients (750 patients) (Table 1).

The most common discharge diagnoses in the cohort were diseases of the circulatory system (8586/27,889 patients, 31%), infectious diseases (6479/27,889 patients, 23%), and diseases of the gastrointestinal and genitourinary system (3963/27,889 patients, 14%). Disease of the gastrointestinal and genitourinary system was the most common discharge diagnosis in patients with severe hyponatremia (47%), while infectious disease was the most common diagnosis with mild hyponatremia (36%). In patients with sodium levels above 145 mEq/L, the common diagnoses were infectious diseases (44%), diseases of the genitourinary and digestive tract (16%) and diseases of the circulatory system (15%) (Table S1 in the Supplementary Appendix).

3.2. Length of hospitalization

The mean length of hospitalization was 5 ± 7 days, with longer length of stay in patients with mild or severe hypernatremia (9 ± 11 and 10 ± 12 days, respectively), while the shortest length of stay was evident in patients with normal sodium levels (5 ± 7 days). In patients with mild and severe hyponatremia, the mean length of stay was 6 ± 7 days and 6 ± 6 days, respectively (Table 2).

In patients hospitalized for diseases of the circulatory system (8586 patients), length of hospitalization was longer in all patients with abnormal sodium levels on admission (n = 1073 patients), compared to patients with normal sodium (7513 patients). In patients with severe hyponatremia the length of stay was 3.1 days longer and in patients with severe hypernatremia it was 9.5 days longer.

3.3. Mortality

Complete follow-up data at 12 months were available for all patients, with first patient censored after 1.4 years. The mean ± SD total follow-up from admission was 1065 days (518–1613 days).

3.3.1. In-hospital mortality

Overall in-hospital mortality was 6.6% (1832/27,889).

Compared to in-hospital mortality in the group of patients with normal sodium levels on admission (5%), in-hospital mortality was significantly higher in patients with mild and severe hyponatremia (9% and 14%, respectively). Highest in-hospital mortality risk was evident in patients with mild (28%), and severe hypernatremia (52%) (Table 2).

Compared to patients with normal admission sodium levels, the unadjusted odds ratio for in-hospital mortality were highest with severe hypernatremia (OR = 22.1, 95% CI = 17.3–28.2).

Table 1
Baseline characteristics. Baseline characteristics and comorbidities.

	Severe hyponatremia (Na < 125)	Mild hyponatremia (Na 125–135(	Normal sodium (Na 135–145)	Mild hypernatremia (Na 145–150)	Severe hypernatremia (Na > 150)
Patients' characteristics, n (%)	515 (2%)	5515 (20%)	21,109 (76%)	476 (2%)	274 (1%)
Age, mean (years) (median)	75 ± 15 (77)	70 ± 17 (74)	66 ± 19 (68)	76 ± 20 (80)	82 ± 13 (85)
Men, n (%)	177 (34%)	2729 (50%)	11,136 (53%)	239 (50%)	116 (42%)
Smoking (%)	38 (9%) (missing = 73)	664 (14%) (missing = 731)	3317 (18%) (missing = 2242)	49 (13%) (missing = 88)	15 (7%) (missing = 57)
Alcohol (%)	4 (1%) (missing = 49)	114 (2%) (missing = 797)	444 (2%) (missing = 2487)	4 (1%) (missing = 86)	5 (2%) (missing = 56)
BMI, median	25 ± 5	25 ± 5	26 ± 5	26 ± 8	24 ± 7
Co-morbidities, n (%)					
Malignancy	130 (25%)	1285 (23%)	2960 (14%)	70 (15%)	38 (14%)
Hypertension	276 (54%)	2572 (47%)	9478 (45%)	245 (51%)	149 (54%)
Ischemic heart disease	88 (17%)	1198 (22%)	4906 (23%)	120 (25%)	63 (23%)
Congestive heart failure	64 (12%)	596 (11%)	2154 (10%)	65 (14%)	40 (15%)
Chronic renal failure	39 (8%)	543 (10%)	1803 (9%)	66 (14%)	35 (13%)
Cerebrovascular disease	27 (5%)	456 (8%)	1993 (9%)	73 (15%)	54 (20%)

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