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Evaluation of the frequency of hyponatremia and risk factors among hospitalized geriatric patients.

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Abstract

Hyponatremia is an electrolyte imbalance common in clinical practice and is associated with impaired quality of life and survival. The aim of this study is to investigate hyponatremia-associated clinical characteristics in a hospitalized geriatric patient population. Hyponatremia was categorized as mild, moderate and severe based on serum Na levels. The relationships between severity of hyponatremia and patient age, sex, duration of hospital stay, time of hyponatremia onset and outcome were studied. A total of 978 patients aged 65 years and above were evaluated. Hyponatremia was detected in 176 patients (18%). Moderate (HR: 4.5, 95% Cl: 0.213-0.542, p<0.001) and severe hyponatremia (HR: 2.5, 95% Cl: 0.077-0.606, p<0.001) were significantly more frequent in patients with hyponatremia at the time of hospitalization. Of the etiological factors, the most common was acute renal damage and iatrogenic causes. The most common comorbidities were diabetes mellitus and hypertension. The impact of polypharmacy and impaired oral intake on hyponatremia in the geriatric population was clearly seen. We demonstrated that patients with diabetes and hypertension are at a higher risk of developing hyponatremia, and showed a significant relationship between severity of hyponatremia and the time that hyponatremia was diagnosed.

Keywords: Hyponatremia, Geriatric patient, Etiology, Comorbidity, Hyponatremia severity.

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Introduction

Hyponatremia is one of the most frequent electrolyte imbalances seen in clinical practice which is often defined as a serum sodium (Na) measurements of <135 mEq/L [1, 2]. The exact prevalence and incidence is not known. While it is seen in 15-30% of hospitalized patients, more than 50% of the overall hyponatremic population consists of hospitalized patients [3, 4].

In hyponatremia cases, it should first be established if the patient is genuinely hyponatremic (hypo-osmolar hyponatremia) or pseudo-hyponatremic (iso-osmolar hyponatremia) which is observable in conditions such as hyperlipidemia and hyperproteinemia [5].

While hyponatremia can affect all age groups, its incidence seems to be higher in the elderly due to the impaired response of water and electrolyte homeostasis to dietary and environmental alternations [6]. The higher frequency of hyponatremia in the elderly population was also shown to be associated with presence of comorbidities, physiological changes in glomerular filtration rate, altered water metabolism and polypharmacy [7-9].

There are very few studies investigating the incidence and prevalence of hyponatremia and addressing to risk factors associated with hyponatremia and offering up-to-date information in our country. The objective of our study was to determine the frequency and etiology of hyponatremia and comorbidities in the hospitalized elderly and to investigate the relationship between severity of hyponatremia and demographic characteristics, hospitalization and mortality.

Methods

A total of 978 patients aged 65 years and above was evaluated in our study and included 176 geriatric patients, serum sodium levels of whom were <135 mEq/L at the time they presented, or dropped below 135 mEq/L over the period of hospital stay.

Patient files were reviewed retrospectively. Age, sex, the time hyponatremia was diagnosed, regular medications and medications given while the patient was hospitalized, chronic condition history if present, diagnoses leading to hyponatremia and volume status were documented. Duration of hospital stay and outcome (improvement, death) were indicated.

Patients were identified from determined sodium values of hospitalized patients, which were sent electronically from the chemistry department. Sodium values were determined with ion-selective electrodes (Hitachi 917, Roche, according to the manufacturer's instructions) and in all of these samples plasma osmolality and plasma glucose concentration were determined simultaneously. In all patients the first step consisted of the exclusion of pseudo-hyponatraemia, through analysis of plasma osmolality, total protein, triglyceride and cholesterol concentrations. The patients were grouped according to the severity of hyponatremia as follows: sodium levels of 126-135 mEq/L were considered mild hyponatremia, sodium levels of 116-125 mEq/L as moderate hyponatremia and sodium levels of ≤ 115 mEq/L as severe hyponatremia [10].

The World Health Organization considers individuals aged 65 years and older within the psychogeriatric age group. Gerontologists classify people aged 65 to 74 years as early old age, people aged 75 to 84 years as old age and people aged 85 years older as late old age (senility) [11]. The patients were distributed into three groups based on these data. The frequency of hyponatremia for the internal medicine clinic of our hospital, hyponatremia etiologies and comorbidities were calculated as percentage rates. The relationships between severity of hyponatremia and patient age, sex, duration of hospital stay, time of hyponatremia onset and outcome were studied.

Statistical analysis

SPSS 22.0 software was used for statistical analyses of the data. The data were summarized as percentages and means. Hyponatremia prevalence in the hospitalized geriatric population was calculated. The relationships between hyponatremia severity and age groups, sex, duration of hospital stay and outcome were studied using the chi-square, independent student's T test and Mann Whitney U tests. Comorbidities and hospitalizations were presented as percentages. The results were evaluated by hazard ratio and 95% confidence interval. In these analyses, p values <0.05 were considered statistically significant.

Results

A total of 978 patients aged 65 years and older that admitted in hospital were enrolled. Of the hospitalized patients, 530 (54%) had one or more electrolyte imbalances. Hyponatremia was detected in 176 (18%). The lowest and highest Na values were 98 mEq/L and 134 mEq/L, respectively, with a mean Na of 125.9 mEq/L. Mild, moderate and severe hyponatremia were identified in 121 (68.7%), 41 (23.2%) and 14 (7.9%) of the patients, respectively. Mean age of patients was 76.1 ± 7.2 years (65-95 years) overall, and was 75.8 ± 7.3 years (65-95 years) in women and 76.7 ± 7.2 years (65-92 years) in men. Age range was 65-74 years for 84 patients (47.7%), 75-84 years for 66 (37.5%) and ≥ 85 for 26 patients (14.8%). Hyponatremia was considerably more common among females (female/male: 109/67; 61.6% versus 38.4%). Duration of hospital stay was ranging between one day and 50 days, with a mean duration of hospital stay of 9.9 days. Hyponatremia was detected during hospital stay in 113 (64.2%) of the 176 patients diagnosed with hyponatremia while 63 (35.8%) of the patients developed hyponatremia between days 1 and 25 of hospitalization (5.2 days on average). Hundred fourty four (81.8%) patients were discharged from the internal medicine clinical service and laboratory parameters with improvement, while 15 (8.5%) died during stay the hospital's internal medicine clinical service. Seventeen (9.6%) patients required intensive care during hospital stay. Of the patients treated in the intensive care unit, one was discharged with improvement, whereas 16 patients died. As a result, one hundred fourty five (82.4%) patients were discharged from the hospital with improvement, while thirty one (17.6%) patients were died. There is not significant relationship between severity of hyponatremia and mortality. But the mortality rate is significantly high in patients who stay in intensive care unit ($p<0.001$).

The relationships between severity of hyponatremia and demographic characteristics, duration of hospital stay, time of hyponatremia onset and outcome were examined: no significant relationship observed between female and male gender, age groups, duration of hospital stay or outcome, while severity of hyponatremia and time of hyponatremia onset were significantly related. Of the 113 (64.2%) patients diagnosed with hyponatremia at the time of hospitalization, 64 (56.6%) had mild hyponatremia, 37 (32.8%) had moderate hyponatremia and 12 (10.6%) had severe hyponatremia. On the other hand, of the 63 (35.8%) patients who developed hyponatremia following hospitalization, 57 (90.4%) developed mild hyponatremia, 4 (6.4%) moderate hyponatremia and 2 (3.2%) severe hyponatremia. Among the patients diagnosed with hyponatremia at the time of hospitalization, moderate hyponatremia (Hazard ratio: 4.5, 95% Cl: 0.213-0.542, $p<0.001$) and severe hyponatremia (Hazard ratio: 2.5, 95% Cl: 0.077-0.606, $p<0.001$) was significantly more frequent (With reference to patients diagnosed with hyponatremia after hospitalization). The relationship between hyponatremia severity and age is shown in Table 1 and the relationship with sex and duration of hospital stay is given in Table 2.

Table 1: *Relationship between hyponatr emia se verity and groups. *p: significance.*

Age	Total N	Mild; N (%)	Moderate; N (%)	Severe; N (%)	P*
65-74	85	57 (67.1)	18 (21.1)	10 (11,8)	Referen ce
75-84	65	42 (64.6)	20 (30.7)	3 (4.7)	0,61
≥85	26	22 (84.6)	3 (11.5)	1 (3.9)	0,11

Table 2: *Relationship between hyponatremia severity and sex, duration of hospital stay, time of hyponatremia diagnosis and mortality. *p: significance.*

		Total N	Mild; N(%)	Moderate; N(%)	Severe; N(%)	P*
	Female	109	72 (66)	28 (25.6)	9 (8.4)	0,59
Sex	Male	67	49 (73.1)	13 (19.4)	5 (7.5)	
	1-5 days	56	35 (62.5)	15 (26.7)	6 (10.8)	
	6-10 days	62	40 (64.5)	17 (27.4)	5 (8.1)	0,89
	11-20 days	42	32 (76.2)	9 (21.4)	1 (2.4)	0,06
Duration of hospital stay	≥ 21 days	16	14 (87.5)	0 (0)	2 (12.5)	0,20
	At time of hospitalization	113	64 (56.6)	37 (32.8)	12 (10.6)	<0.001
Hyponatremia diagnosed	After hospitalization	63	57 (90.4)	4 (6.4)	2 (3.2)	
	Improvement	145	96 (66)	35 (24)	14 (10)	0,50
Outcome	Death	31	22 (71)	8 (25)	1 (4)	

The rates of etiology of hyponatremia were as follows; thirty eight patients (23.3%) had infection, 87 (47.7%) had acute renal damage (ARD), 22 (12.5%) had acute cardiac failure (ACF), 3 (1.7%) had encephalopathy, 4 (2.2%) had hypovolemic shock, 7 (3.9%) had malignancies, 128 (72.7%) had iatrogenic factors, 8 (4.5%) had chronic lung disease (CLD) and 39 (22.2%) had impaired oral intake and malnutrition (Figure 1).

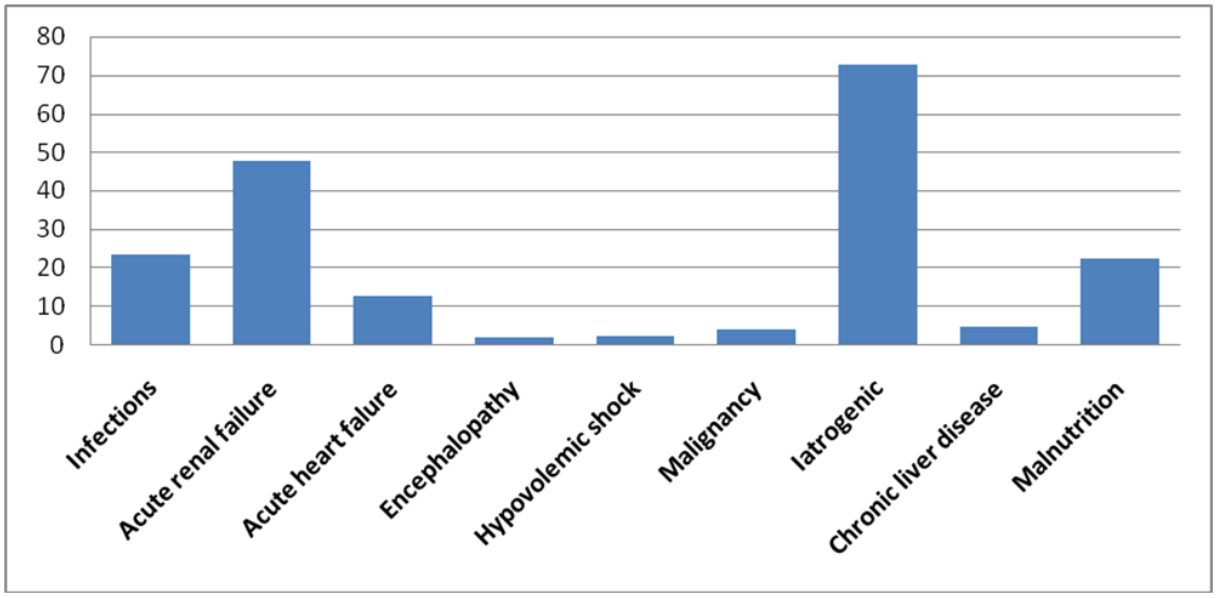

Figure 1: *Etiology in hyponatremia.*

By volume status, 103 (58.5%) patients were hypervolemic, 30 (17%) were euvolemic and 43 (24.5%) had hypovolemic hyponatremia.

Current comorbidities of the patients with hyponatremia were. Ninety two patients (52.2%) had diabetes mellitus (DM), 130 (73.8%) had hypertension (HT), 30 (17%) had malignancies, 41 (23,3%) had coronary artery disease (CAD), 60 (34%) had congestive heart failure (CHF), 87 (49.4%) had chronic kidney disease (CKD), 13 (7.4%) had CLD, 32 (18.1%) had chronic obstructive pulmonary disease (COPD) or asthma, 10 (5.7%) had psychiatric conditions, 12 (6.8%) had thyroid dysfunction, 23 (13%) had neurologic conditions, 15 (8.5%) had cardiac arrhythmias, 11 (6.2%) had benign prostate hyperplasia (BPH)

and only one 1 (0.5%) patient had chronic skin disease (Figure 2).

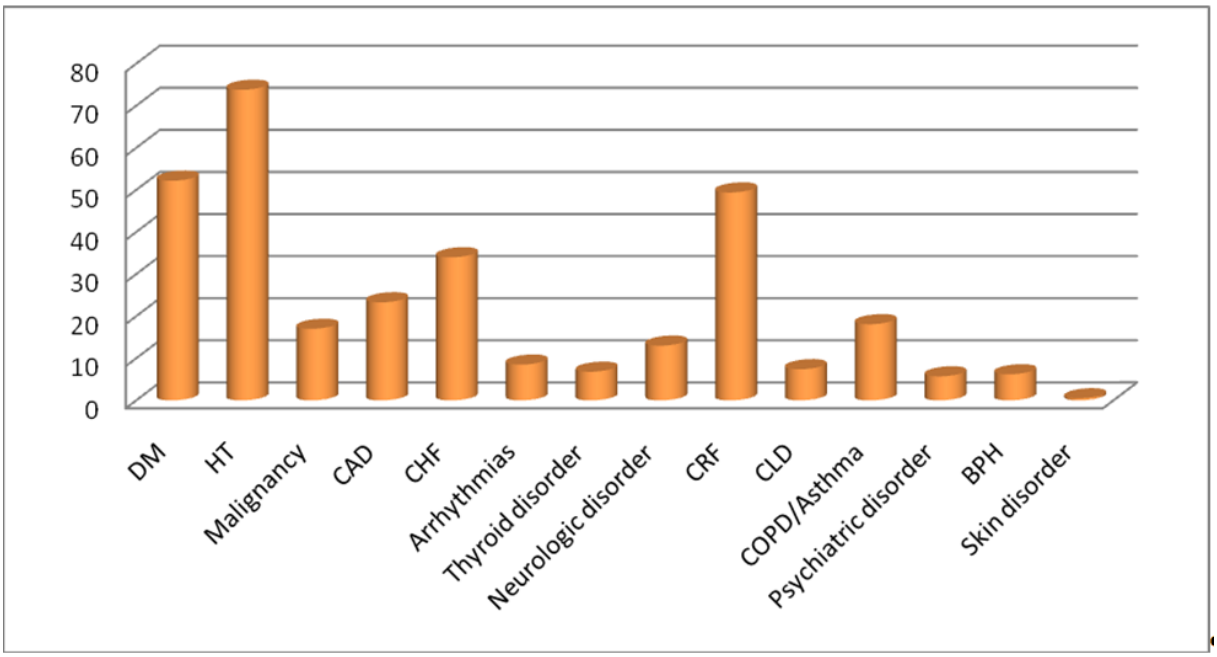

Figure 2: *Comorbidities in hyponatremic patients (DM: Diabetes Mellitus, HT: Hypertension, CAD: Coronary Artery Disease, CHF: Chronic Heart Failure, CRF: Chronic Renal Failure, CLD: Chronic Liver Disease, COPD: Chronic Obstructive Lung Disease, BPH: Benign Prostatic Hypertrophy).*

Discussion

The present study clearly indicated that hyponatremia in elderly population is not uncommon. Also we demonstrated that time of onset of hyponatremia is significantly related to the severity of hyponatremia. Additionally the rate of mortality among geriatric patients with hyponatremia in intensive care unit is remarkable.

Hyponatremia is the most common electrolyte disorder, particularly in the geriatric population and among hospitalized patients [12]. Although there are conflicting reports on the incidence and prevalence of hyponatremia due to the differences in the considered criteria as well as in the age ranges and populations studied, values ranging from 2.5 to 30% have been reported from the previous studies [3]. In their 3-year prospective study involving 98.411 adults hospitalized patients, Waikar et al. (2009) identified hyponatremia in 14.290 (14.5%) patients at the time of hospitalization and noted further 5093 patients developing hyponatremia during hospital stay (19.7% in total). Gosch et al. (2012) reported a value of 16.7% in their study with 2280 hospitalized geriatric patients. In our study, consistent with the literature, 530 (54%) of the 978 hospitalized patients aged 65 years and older had at least one electrolyte disorder and 176 (18%) developed hyponatremia [13, 14].

There is a lack of consensus regarding the severity of hyponatremia and different studies considered different ranges. In the Singapore study, 36% of the patients had Na values of 126-135 mEq/L (mild hyponatremia), 5% had Na values of 116-125 mEq/L (moderate hyponatremia) and 1.2% had Na values of <116 mEq/L (severe hyponatremia) [10]. Based on the same values, mild hyponatremia was less common and moderate and severe hyponatremia were more common in our study compared to the Singapore study.

We found out that the risk of moderate and severe hyponatremia was significantly higher in the patients diagnosed with hyponatremia at the time of hospitalization. In a study by Hawkins (2003) and Anderson et al. (1985), moderate and severe hyponatremia were significantly more frequent among patients with hospital-acquired hyponatremia [10, 15]. This suggests an impact of poor health care services, irregular follow-up and multiple drug use in the geriatric population. Also hyponatremia during hospital stay may be detected in routine checks, therefore at an earlier stage.

Despite conflicting results have been reported from studies investigating the relationships between risk of hyponatremia development and severity of hyponatremia and age and sex, the studies generally reported increased rates of hyponatremia with increasing age [16]. Women are at a higher risk of developing hyponatremia associated with psychotropic and the diuretic drug was given the lower body weight as a characteristic of the gender [17]. In our study, moderate and severe hyponatremia was more common in the female compared to male gender, although the relationship was not statistically significant.

While many studies have reported inappropriate antidiuretic hormone (ADH) syndrome as the most common cause of hyponatremia, multiple factors may cause hyponatremia in the geriatric population. In their study, Padhi et al. (2014) reported the most common cause of hyponatremia as the inappropriate

ADH syndrome (IADHS) (36.2%), followed by severe sepsis (21.5%), trauma (21.1%) and ARD (5.9%) [18]. In a study by Rao et al. (2010), the most common cause was IADHS (30%) and the other factors were medications (24%) and renal losses (21%), respectively [19]. In contrast with other studies, drug-induced hyponatremia, impaired oral intake and malnutrition and ARD-associated hyponatremia was significantly more frequent in our study.

One of the leading reasons that hyponatremia is more common in the geriatric population is the comorbidities. Mohan et al. (2013) identified comorbidities in 73% of the patients who developed hyponatremia. Of these patients, 51% had HT, 16% had DM, 13% had thyroid disorders, 17% had COPD, 15% had malignancies and 19% had psychiatric disorders while 27% had no comorbidities [20]. Because of elderly age group in our study, DM, HT, CAD, CKD and malignancies were more frequent compared to the other studies.

Gray et al. (2014) found that patients with hyponatremia were hospitalized for significantly longer durations compared to normo-natremic patients, while Lim et al. (2001) did not determine a significant relationship between sodium levels and duration of hospital stay in their study in the geriatric population [21, 22]. No significant relationship was determined in our study. Even though previous studies have found out longer durations of hospital stay for hyponatremic patients compared to normo-natremic patients, the relationship between hyponatremia severity and duration of hospital stay in hyponatremic patients is not clear. This observation suggests that underlying comorbidities rather than severity of hyponatremia is the major determinant of hospital stay.

An increased risk of mortality has been demonstrated for hyponatremic patients in previous studies. Mortality rate was 20% in a study by Clayton et al. (2006) enrolling 108 severely hyponatremic patients, 27% in a study conducted in England with 104 patients and 20% in a study by Rao et al. (2010) in the geriatric population [19, 23, 24]. Consistent with the available data, mortality rate was 17.6% in our study.

In addition to correcting the serum sodium, the management of hyponatraemia must always include treatment of the underlying cause. Severe or symptomatic hyponatraemia should be treated as a medical emergency. While fluid restriction is the initial treatment of choice in asymptomatic patients, more active and urgent treatment is required in the symptomatic patient with severe euvolaemic hyponatraemia. Hypertonic saline should only be used in symptomatic patients with very low serum sodium concentrations. Hypervolaemic hyponatraemia should be easily recognizable by history, clinical examination and the results of renal and liver function tests. The management is to treat the underlying disease process and will usually include fluid restriction and diuretic therapy. The history and clinical examination will be supported by biochemistry consistent with hypovolaemia with hypovolaemic hyponatraemia. Treatment consists of volume expansion with isotonic saline [25, 26].

Conclusion

There is a growing geriatric population in our country and this patient population is at higher risk of fluid electrolyte balance due to organic and functional changes in the organism that occur with age. Because comorbidities and polypharmacy are more common, and geriatric population; especially in intensive care, is under remarkable risk of hyponatremia related mortality, they require urgent and appropriate management. To reduce hyponatremia-associated hospitalization, morbidity, mortality and health care costs, older patients should be monitored against hyponatremia at the time of hospitalization as well as during the hospital stay. Further studies with larger sample are essential to reach more precise conclusion.

Conflict of Interest

The author has no conflict of interest.

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