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Dysnatremia in hospitalized patients: Prevalence and impact on outcome

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Abstract
Background/aim: Sodium is the major extracellular cation in the body and is therefore one of the most important osmotic ally active solutes. Disturbance of sodium balance, referred to as dysnatremia is a frequent finding in adults in the hospital in-patient setting, and accounts for the bulk of electrolyte disturbances in this patient population. Abnormal serum sodium concentrations are known to adversely affect physiologic function and an increasing body of evidence suggests that dysnatremia may be associated with adverse outcome. The aim of this study was to assess the prevalence of dysnatremia among hospitalized patient in King Khalid Hospital, Najera, and KSA (KKHN) on admission and to access the relation of the initial serum sodium concentration with mortality and length of stay (LOS) in hospitalized patients.
Material and methods: We conducted retrospective observational randomized study on random sample of patients admitted to inpatients departments during one year period starting 01.08.2014 up to 31.07.2015 through medical records review. terminally ill patients, those with advanced malignancy and very old patients above 75 years old were excluded (No. 740 patients including 483 males and 257 females). Serum sodium on admission, length of stay and outcome beside basic demographic data were extracted from medical records.
Results: 17.7 % of the study subjects (No. 131) had dysnatremia. The prevalence of hyponatremia is significantly higher than Hypernatremia (16.2 % vs. 1.48 % $P < 0.005$). Patients with Hypernatremia had significantly higher mortality rate than both patients with hyponatremia and normonatremia (36.3 % vs., 3.3 vs. 1.64 % respectively $P< 0.005$). Patients with hyponatremia had higher mortality rate than patients with normonatremia (3.3 % vs. 1.64 %), however the difference is not statistically significant ($P > 0.005$). Patients with normonatremia had longer mean LOS, followed by patients with hyponatremia then patients with Hypernatremia (5.16 vs. 4.74 vs. 2.67 days), however the difference is not statistically significant ($P> 0.005$)
Conclusion: The prevalence of dysnatremia in hospitalized patients in King Khalid Hospital, Najran, Saudi Arabia is comparable the documented prevalence in other studies. The prevalence of Hypernatremia is much less than hyponatremia, however it has significantly higher mortality rates. Patients with dysnatremia has shorter inpatient LOS, which may be attributed to higher mortality, however this impact is not statistically significant. Further work is needed to define the risk factors for the higher mortality in patients with dysnatremia.

Keywords: dysnatremia, hypernatremia, hyponatremia, length of stay, mortality

1. Introduction
Sodium homeostasis is controlled by combined action of the renal renin-angiotensin-aldosterone system, sympathetic neural and catecholamine activity, secretion of vasopressin from the neurohypophysis, and release of natriuretic peptides from myocardium [1].
Vasopressin secretion is controlled by osmoreceptors and baroreceptors, and the effects of vasopressin on the renal excretion of water are influenced by genetic polymorphisms [2, 3].
Aquaporins and ATP ases control the cell membrane water and sodium flux in the face of changes in extracellular ion concentration [4, 5].
Sodium disturbances (dysnatremias) resulting in hyponatremia and hypernatremia are a common problem in patients after hospital admission. Lack of access to free water, reliance on intravenous fluid and nutritional support, and the usually serious nature of their underlying disease are the main causes for impaired renal water handling. Sodium disturbances can occur in hospitalized patients. Prevention of the occurrence of dysnatremia can be done in many cases. Hospitalized patient are usually well monitored and blood samples are taken. Care must be taken about the maintenance of fluid and electrolyte balance [6].
The sodium disturbances, hyponatremia and hypernatremia, are common in patients admitted to intensive care. They are important markers of a critically ill patient's clinical status that often prompt changes to a patient's treatment, and they are associated with an increased risk of death [7].
Dysnatremia can be developed with patient admission to the hospital [8-9]. Physiological functions can be affected by abnormal serum sodium concentrations leading to adverse outcome [8-11]. Patients can be exposed to dysnatremia due to the nature of the disease upon admission and to lack of free access to water [10, 11, 12].
Hyponatremia is the most common electrolyte imbalance in hospitalized patients which can be resulted because of the underlying acute illness or as a consequence of therapeutic

interventions [13].

Hyponatremia is associated with increased morbidty and mortality, but whether the mortality is associated with hyponatremia itself or the underlying illness remains unclear [13].

Dysnatremia is a common problem among hospitalized patients which increases in mortality rates [14].

Dysnatremias increase mortality not only in patients were admitted with dysnatremia but only in developed dsynatremia during patient stay in the hospital [14].

Mortality rates in patients with dysnatremia range from 42% to 62% [15]. As the serum sodium level continues to rise, it has a prognostic impact justifying that once a dysnatremia has been detected, prompt treatment is needed [16].

$1.6 – $3.6 billion is the direct costs of hyponatremia in the US annually, and the potential increase in mortality associated with hyponatremia, a better understanding of hyponatremia is important [13].

2. Materials and methods

The study was conducted from August 2014 to July 2015 at The King Khalid Hospital, Najran, Saudi Arabia. The primary finding was mortality rates and length of stay. Terminally ill patients, those with advanced malignancy and very old patients above 75 years old were excluded from the study. Written informed consent from the patients' relatives was obtained for each subject. History and clinical examination were recorded for all patients. Age, sex, admitting diagnoses, comorbidities, serum sodium on admission, length of stay and the mortality rate of patients for each group beside basic demographic data of the subjects were recorded. The study was designed as an observational descriptive cross-sectional randomized study.

Subjects were classified into 3 groups according to further changes in their serum sodium levels during hospital stay. Group A was the normonatremia group, group B was the Hypernatremia and group C was the Hyponatremia group.

Normal serum sodium level with reference range (135 to 145 mmol/L) during the first day of their hospital admission. Hypernatremia was defined as a serum sodium concentration >145 mmol/L. Hyponatraemia was defined as a serum sodium concentration <135 mmol/L. Study results were compared to previously published studies focusing on prvelance, length of stay and mortality rates of dysnatremia in hospitalized patients.

3. Results

Statistics

A statistical package program was used to evaluate the data obtained from the study. All data were coded, checked, entered and analyzed using SPSS software version 17 Descriptive statistical methods (frequency, proportion, mean, and standard deviation) were used in the evaluation of research data. The Pearson chi-square test was used in comparing qualitative data. In comparing quantitative data, the one way Analysis of Variance (ANOVA) test was used in intergroup comparison of parameters when there was more than one group and Tukey's Post hoc test was used in determining the group causing a difference. The results were calculated at the 95% confidence interval, $P < 0.05$ significance level and $P < 0.01$ advanced significance level.

4. Results

Baseline characteristics of the patients are shown in Table 1. The normonatremia group included 29 females and 33males patients, The hypernatremia group included 44 females and 25males patients, and The hyponatrenia group included 51 females and 21males patients. The average age was 50.18 ±14.79 years in the normonatremia group, 50.87±14.5 years in the hypernatremia group and 50.71±14.42 years in the hyponatrenia group.

No statistically significant difference was found between the 3 groups in terms of age and sex ($P > 0.05$).

Patients with Hypernatremia had significantly higher mortality rate than both patients with hyponatremia and normonatremia (36.3 % vs., 3.3 vs. 1.64 % respectively $P< 0.005$). Patients with hyponatremia had higher mortality rate than patients with normonatremia (3.3 % vs. 1.64 %), however the difference is not statistically significant ($P>0.005$), as shown in Table 2.

Patients with normonatremia had longer mean LOS, followed by patients with hyponatremia then patients with Hypernatremia (5.16 vs. 4.74 vs. 2.67 days), however the difference is not statistically significant ($P> 0.005$), as shown in Table 3.

5. Discussion

Dysnatremia is associated with substantial morbidity and mortality. The identification of risk factors associated with the development of dysnatremia is important in determining preventive strategies. Data on prevalence and clinical profile of hyponatremias are scarce.

The present study was designed for evaluation of acquired sodium disturbances in hospitalized patients. The patients of the current study were classified into 3 groups according to further changes of serum sodium level during hospital stay: always normonatremia, acquire hyponatremia, and acquire hypernatremia.

The results of the current study showed that 17.7 % of the study subjects (No. 131) had dysnatremia. The prevalence of hyponatremia is significantly higher than Hypernatremia (16.2 % vs. 1.48 % $P < 0.005$).

The results of the present study agree with (Sakr *et al*., 2013) [14] who reported that in one study of all patients admitted to an ICU with a dysnatremia, 81.4% of the patients had hyponatremia while 18.6% had hypernatremia [14].

Goh reported that hyponatremia developed in approximately 30% of patients treated in intensive care unit, and is associated with mortality increase of 7 to 60 % [17].

Upadhyay in another study obtained that hyponatremia occurred in about 30–40% of hospitalized patients, which is even higher than previous estimates [18].

This variability of the prevalence in different centers may be due to interventions done to the hospitalized patients and may be due to severity and comorbidity of the original disease that may occur in the hospitalization period.

Iwasa, *et al*., and Ishikawa, *et al*., found that hypernatremia was less common than hyponatremia with an incidence of around 1% across the spectrum of all patients [19, 20].

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The results of the current study agree with (Lindner *et al*., 2007& Waite *et al*., 2013) who reported that mortality rates are greater for patients with hypernatremia when compared with normonatremic patients. Mortality rates are also higher in patients with hypernatremia upon admission [9-21].

Studies have demonstrated even small increases in serum sodium levels are correlated with an increase in risk for mortality [22].

Developing hypernatremia is closely associated with increased intensive care unit length of stay [9, 15, 21].

The results of the current studt agree with (Lindner *et al*., 2007) who reported that increases in serum sodium levels are linked with an increasing severity of disease, length of stay and mortality [9].

Patients with hyponatremia have been linked to an increased mortality rate as compared to those without hyponatremia [15].

It has also been found that even small decreases in serum sodium levels upon hospital admission can result in an increase in mortality rates [22].

Hyponatremia is manifest at the time of presentation to the emergency room or ambulatory care setting and may be asymptomatic or associated with relatively simple symptoms such as a nausea, headaches, and lethargy. Other neurological symptoms associated with hyponatremia including attention deficit, impaired balance or memory are frequently mild and often overlooked, but may result in significant morbidity, including higher rates of falls/fractures [13].

Despite its relative frequency among patients in the hospital setting, the prevalence of hyponatremia in the general population remains unknown, as does the clinical significance of the hyponatremia in the outpatient setting [13].

The perioperative period may be associated with a marked neurohumoral stress response, significant fluid losses and varied fluid replacement regimes. Acute changes in serum sodium concentration are therefore common. Disorders of plasma sodium concentration are common and are associated with increased hospital stay, resource utilization and mortality [22, 23].

Surgical patients may be particularly vulnerable, since the perioperative period is often characterized by a vigorous neurohumoral stress response, significant fluid losses and widely varying fluid replacement regimes. Previous studies have reported hospital outcomes associated with dysnatraemias present on admission, in specific medical or surgical subspecialties, in intensive care, or in mixed medical-surgical populations [22, 23].

Leung *et al.* reported increased mortality in patients with preoperative hyponatraemia using data from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) [24].

McCausland *et al.* described similar outcomes in dysnatraemic patients after orthopaedic surgery [23].

Knowledge of these factors, and closer attention to electrolyte

monitoring and fluid therapy in patients at increased risk, might attenuate any associated increase in mortality [7].

The results of the present study disagree with (Homoky, 2015) who reported that the study did not demonstrate a statistically significant difference in length of stay or mortality between normonatremic and dysnatremic patients [16].

Subjects with hyponatremia had significantly higher rates of hospitalization in the year preceding participation. Also, a five-fold increase in mortality risk among subjects with hyponatremia was reported [13].

After adjustment for age, gender, comorbidities and other factors that may affect mortality, hyponatremia remains associated with significantly increased risk of mortality in all subjects, suggesting an inherent adverse impact associated with a chronic hypotonic state beyond that of the underlying illness [13].

Recent small studies have shown similar associations of hyponatremia with all-cause mortality but have been limited to elderly patients in community settings [29, 30].

The clinical significance of hyponatremia in a nationally representative outpatient population of all adults aged ≥18 years, and demonstrates the increased mortality risk with hyponatremia even among subjects aged 18-50 [13].

Pre-admission and hospital acquired dysnatraemias are known to be associated with increased resource utilization and mortality in mixed medical-surgical and intensive care populations and more recently have been linked to mortality in two large cohorts of post-surgical patients [23, 24].

Sodium variability per se also predicted increased mortality in patients admitted to a surgical ICU [14].

We have shown that deviations from baseline greater than 5 mmol/l are associated with increased hospital mortality, even when preoperative values are normal. We selected the threshold of >5 mmol/l deviation from preoperative baseline because lesser changes are typical in stable, uncomplicated perioperative patients, and are known to be confounded by diurnal variation, blood glucose and protein concentrations, and laboratory imprecision [25-26].

Also, changes of this magnitude were not found to predict mortality in a large study of patients treated in surgical intensive care [14].

Although dysnatraemias may represent non-causal biomarkers of underlying neuroendocrine or inflammatory disorders, and correction may not necessarily provide benefit, clinical experience and published data strongly suggest that fluid management does affect outcomes and that dysnatraemia may be avoided [31-32].

Thus, sodium values may merit closer attention than they currently receive. While doses of potassium, glucose and even water are regularly adjusted in surgical patients, sodium is delivered at standard concentrations as long as serum values are normal. With greater consideration of the last-recorded sodium measurement and of easily measured sodium losses in urine and drains, some variability may be prevented, reducing osmotic shifts and associated effects on organ function, and improving outcomes [31].

In conclusion, acquired dysnatremia is a common problem in medical hospitalized patients with higher prevalence of hyponatremia compared with hypernatremia and many factors during hospital admission may participate in these acquired dysnatremia in hospital such as fever, comorbid conditions e.g Renal impairment, advanced liver disease, diuretics use and, the frequent use of hypotonic fluids. Moreover, the acquired dysnatremia carries a negative impact on the course of original disease, hospital stay and mortality of the patients in hospital.

Frequent serum sodium monitoring is suggested for early detection of dysnatremia, and attention should be paid toward injudicious use of diuretics and hypotonic fluids with hospitalized patients. Further studies are needed to address the impact of the severity of dysnatremia on patient outcome, and to determine whether correcting the serum sodium level could improve Th clinical outcomes in hospitalized patients.

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