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Admission dysnatremia in critically ill children

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Introduction

The serum sodium concentration is influenced by many factors such as body water, free water intake, urinary loss, secretion of anti-diuretic hormone (ADH), and underlying diseases.

Introduction: Many causes of admission to the pediatric intensive care unit (PICU) may potentially induce hyponatremia. This study was aimed at evaluating the incidence of admission dysnatremia in the PICU and its relationship with the underlying disease and demographic factors.

Materials and Methods: This observational prospective study was conducted in a 12-bed medical PICU in a tertiary governmental teaching hospital for six months. The study group comprised patients aged 1 month to 18 years. Patients who received intravenous fluid within 24 hours before admission were excluded. Serum sodium was checked on admission and concentrations below 135 and above 145 mEq/L were considered hyponatremia and hypernatremia, respectively.

Results: One hundred and ninety-five patients (117 males, 60%) were included in the study. The mean serum sodium level was $137.8 \text{ mEq/L} \pm 5.2$. Forty-two patients (20.5%) were hyponatremic and 10 (5.1%) were hypernatremic. The most prevalent diagnosis in hyponatremic patients was pulmonary diseases followed by renal diseases, central nervous system (CNS) diseases, diabetic ketoacidosis (DKA), gastrointestinal (GI) diseases, and cardiovascular and hematologic-oncologic diseases. Fifty percent of nephrologic patients were hyponatremic. Hyponatremia was found in 26.5%, 23.5%, 20%, 16.6%, and 14.2% of the children with lung diseases, DKA, hematologic-oncologic diseases, cardiovascular diseases, and CNS and GI diseases, respectively. Moreover, 20%, 16.6%, 11.7%, 7.1%, and 2.9% of the patients with infectious diseases, cardiovascular diseases, DKA, CNS diseases, and pulmonary diseases had hypernatremia, respectively.

Conclusions: Hyponatremia is frequent in our PICU. Patients suffering from renal diseases, pulmonary problems, DKA, and hematologic-oncologic diseases have a higher chance of hyponatremia ($\geq 20\%$).

Keywords: Sodium; Hyponatremia; Fluid Therapy; Children; Intensive Care.

Running Title: AKI in children with acute gastroenteritis

In recent years, researchers have focused on hyponatremia and hospital acquired hyponatremia, resulting in changes in intravenous fluid sodium administration to prevent/treat acute hyponatremia [1-5], a

condition which can potentially damage the brain by inducing brain swelling [6]. Sodium distribution is different between the peripheral circulation and the central nervous system (CNS). It moves freely in the extracellular fluid in the peripheral circulation but CNS endothelial junctions prevent free and rapid movement of sodium when the blood brain barrier is intact [7]. A rapid decrease of 5 mEq/L in serum osmolality causes a difference of 17.5% between the brain interstitium and the capillary lumen, resulting in brain edema [8]. ADH is an important body water hemostatic factor. It is secreted from the hypothalamus and acts on renal distal and collecting tubes. It increases water reabsorption and can potentially cause hyponatremia [9]. Many causes of admission in the pediatric intensive care unit (PICU) may potentially cause an increase in ADH secretion and lead to hyponatremia (Fig. 1) [10-12].

Hyponatremia occurs frequently in critically ill children. Any condition resulting in increased ADH, syndrome of inappropriate ADH secretion (SIADH), increased right atrial pressure, ineffective extra-cellular fluid, cerebral salt wasting, or increased sensitivity of renal tubes to ADH may cause hyponatremia. In addition, iatrogenic interventions, such as surgery, administration of hypotonic intravenous fluids, corticosteroids, mechanical ventilation, diuretics and some other medications, may cause in-hospital hyponatremia [13-17]. Hyponatremia may cause cerebral edema and its devastating complications; furthermore, treatment of hyponatremia and hypernatremia may be associated with mortality or morbidity. According to previous studies, the incidence of hyponatremia in the adult ICU varies between 14% to 29.7% [18, 19]. Hyponatremia may occur in 20-45% of severe pediatric illnesses [20-21].

In Iran, the prevalence of hyponatremia is 8.8% in pediatric acute CNS disorders [22]. On admission, hyponatremia and hypernatremia is found in 40.7% and 2.3% of the patients suffering from gastroenteritis, respectively [23]. A research in the PICU showed 8.7% arrival hyponatremia (serum sodium <130 mEq/L) [24]. These figures indicate major differences in the prevalence of hyponatremia in different studies. Although the high prevalence of hyponatremia in admitted children is not a novel story, the frequency of this situation on PICU admission and its relationship with the underlying diseases has not been evaluated in many centers like ours. The aim of the present study was to evaluate the incidence of dysnatremia at the time of admission to a tertiary medical PICU and its relationship with underlying diseases and demographic factors.

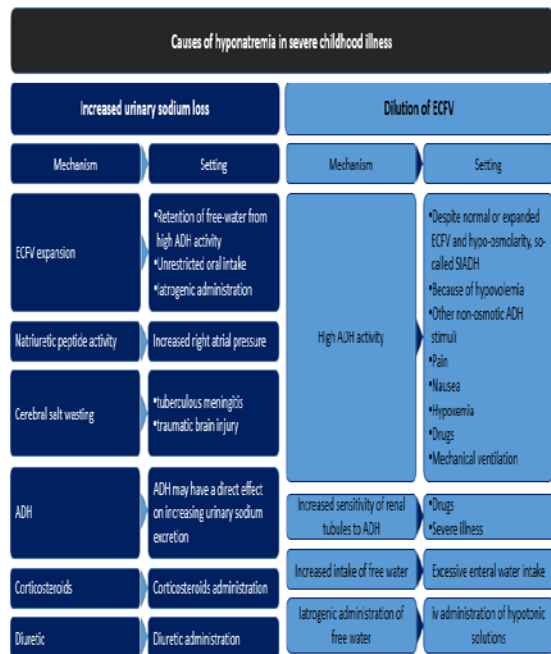


Figure 1. Causes of hyponatremia in severe pediatric diseases ECFV=extracellular fluid volume. ADH=antidiuretic hormone. SIADH=syndrome of inappropriate ADH secretion. From: Duke T, Molyneux EM. Intravenous fluids for seriously ill children: time to reconsider. Lancet. 2003;362(9392):1320-3.

Materials and Methods

This observational prospective study was conducted in a 12-bed medical PICU in a tertiary governmental teaching hospital from

May 2016 to November 2016. The study group comprised patients aged 1 month to 18 years admitted to the PICU.

All admitted patients were included in study except for those received intravenous fluid more than half of maintenance fluid needs within 24 hours before admission.

They were excluded because it could potentially affect the serum sodium concentration.

Half saline fluid is used in the emergency and non-intensive care wards as the maintenance fluid in this center, except in dehydrated patients for whom isotonic fluid is used.

The serum sodium concentration (mEq/L) was checked upon admission and concentrations below 135 and above 145 mEq/L were considered hyponatremia hypernatremia, respectively.

The patients' demographic characteristics including age, sex, weight, category of admission diagnosis, and admission serum sodium were documented from the patients' data files.

The following symptoms were considered related to dysnatremia only if they could not be explained by a different underlying disorder: weakness, nausea, emesis, cramps, seizures, somnolence, agitation, restlessness, headache, disorientation, confusion, coma, and syncope.

The study was approved by the Research Ethics Committee of Shiraz University of Medical Sciences (ir.sums.rec.1394.S1138) and conducted according to the tenets of the Helsinki Declaration. Because all measurements were performed as part of routine metabolic evaluation of the patients, confidentiality was observed and the medical team did not intervene in the treatment process, the study was waived from consent.

According to previous studies, the incidence of admission hyponatremia is about 14% in the adult ICU and 20-45% in severe pediatric illnesses [18-21]. We use 14% as the lowest incidence of serum sodium below 135 mEq/L in severely ill pediatric patients in the PICU. Thus, for the prevalence target, the sample size of the study was 185 if $p=0.14$, $z=1.96$ and $d=0.05$ using the following formula $[n = Z^2_{1-\alpha/2} \times P(1-P) / d^2]$.

$\alpha/2=1.96$ and $d=0.05$ using the following formula $[n = Z^2_{1-\alpha/2} \times P(1-P) / d^2]$.

Results

During six months, 263 patients were admitted to the PICU and 195 patients, including 117 (60%) males and 78 (40%) females, were enrolled in study. (Figure 2)

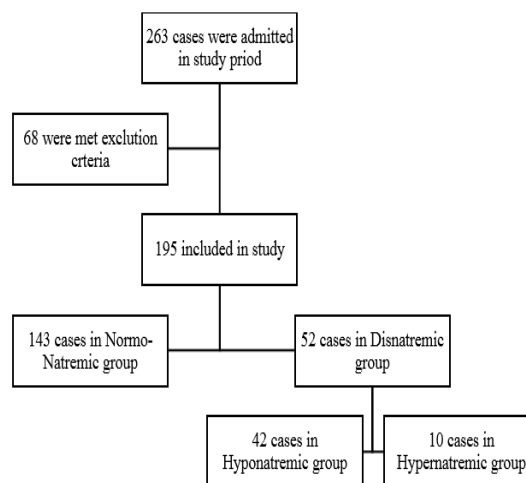


Figure 2. Flow diagram of patient selection

The mean age and weight of the subjects was 4.8 ± 5.1 years and 16.3 ± 14.1 kg, respectively. On the first day of admission, 35.6% of the patients were intubated. The mean serum sodium concentration was $137.8 \text{ mEq/L} \pm 5.2$ (range: 119 to 155 mEq/L).

The most frequent causes of PICU admission were pulmonary diseases (including pulmonary infections and inflammation) (34.9%) followed by CNS (including CNS infection) (14.4%) and gastrointestinal diseases (including diarrhea) (10.8%), respectively (Table 1).

Among hyponatremic patients, 10 (5.1%) had moderate to severe hyponatremia (serum sodium below 130 mEq/L). They comprised 4 pulmonary cases, 2 subjects with CNS diseases, 2 cases with renal diseases, and 2 cardiovascular patients.

The patients were divided into 3 separate age groups: 2 months-1 year, 1-5 years, and over 5 years. Serum sodium showed no significant difference according to age ($P=0.672$), sex ($P=$

0.459), and primary diagnosis on admission (P=0.34).

Forty-two patients (20.5%) were hyponatremic and 10 (5.1%) were hypernatremic. The most common diagnosis in patients with hyponatremia was pulmonary diseases followed by renal diseases, CNS diseases, DKA, GI diseases, and cardiovascular and hematologic-oncologic diseases. Fifty percent of the nephrologic patients were hyponatremic, and hyponatremia was found in 26.5%, 23.5%, 20%, 16.6%, and 14.2% of the children with lung diseases, DKA, hematologic-oncologic diseases, cardiovascular diseases, and CNS and GI diseases, respectively. Hyponatremia was not detected patients suffering from infectious diseases and multiple trauma. Moreover, 20%, 16.6%, 11.7%, 7.1%, and 2.9% of the patients with infectious diseases, cardiovascular diseases, DKA, CNS diseases, and pulmonary diseases had hypernatremia, respectively

The lowest mean serum sodium was seen in hematologic-oncologic patients (136.20 ±3.91 mEq/L), followed by renal (136.63 ±5.99 mEq/L) and pulmonary diseases (136.97 ±4.53 mEq/L). GI patients had the highest mean serum sodium (139.19 ±3.50 mEq/L) (Table 1).

No patients had signs or symptoms explained by hyponatremia or hypernatremia alone. However, weakness (5/40), nausea (10/40), emesis (17/40), seizures (6/40), irritability (13/40), confusion (5/40), and coma (4/40) were seen in hyponatremic patients. Four hypernatremic patients had emesis and one had seizures.

Study limitation: The duration of the study was rather short, and a longer research with follow-up on in-hospital dysnatremia may produce more valuable results. Furthermore, the result of this six-month study may be affected by the seasonal prevalence of some specific diseases like respiratory infections. We used incidence of admission hyponatremia in PICU for sample size calculations; thus, our findings may not truly reflect the situation of hypernatremia.

Discussion

The main finding of this study was that admission hyponatremia and hypernatremia was prevalent in our center. The overall

Table 1. Dysnatremia based on admission diagnosis

Category of admission diagnosis	N (%)	Mean serum sodium ± SD (mEq/L)	Na<135 mEq/L	Na>145 mEq/L
Lung	68 (34.9%)	136.97 ± 4.53	18/68 (26.5%)	2/68 (2.9%)
CNS	28 (14.4%)	138.57 ±4.92	4/28 (14.2%)	2/28 (7.1%)
GI	21 (10.8%)	139.19 ±3.50	3/21 (14.2%)	0/21 (0.0%)
DKA	17 (8.7%)	138.06 ±5.23	4/17 (23.5%)	2/17 (11.7%)
Renal	16 (8.2%)	136.63 ±5.99	8/16 (50.0%)	0/16 (0.0%)
Heart	12 (6.2%)	137.50 ±9.90	2/12 (16.6%)	2/12 (16.6%)
Hem.	10 (5.1%)	136.20 ±3.91	2/10 (20.0%)	0/10 (0.0%)
Infct.	10 (5.1%)	141.20 ±7.34	0/10 (0.0%)	2/10 (20.0%)
M.Trauma	4 (2.1%)	139.00 ±3.46	0/4 (0.0%)	0/4 (0.0%)
Other	9 (4.6%)	138.67 ±3.67	1/9 (11.1%)	0/9 (0.0%)
Total	195 (100%)	137.84 ±5.26	40/195 (20.5%)	10/195 (5.1%)

Lung: Pulmonary diseases, CNS: central nervous system diseases, GI: gastro-intestinal diseases, Renal: nephrologic diseases, Heart: cardiovascular diseases, Hem: hematologic-oncologic diseases, Infct.: infectious diseases, M.Trauma: multiple trauma

frequency of hyponatremia was 20.5% in the present study, which was higher in patients with renal diseases, pulmonary disorders, DKA, and hematologic-oncologic diseases.

General PICU population: Hasegawa et al reported hyponatremia in 17% of the hospitalized pediatric patients but Prasad et al. reported it in 30% of the pediatric patients admitted to the emergency department [25,26]. Kadivar et al. found admission hyponatremia in 8.7% of the PICU patients [24]. The type of PICU in this study which was a medical one, and defining hyponatremia as serum sodium below 135 mEq/L instead of 130 mEq/L could explain

the higher prevalence of hyponatremia in our study.

Renal diseases: Patients suffering from renal diseases have several risk factors for hyponatremia including impaired renal excretion of water, high plasma concentrations of arginine vasopressin, and use of diuretics specially thiazides. In our study, the rate of hyponatremia was as high as 50% in patients with renal diseases. When we reviewed those files, we found multiple risk factors for hyponatremia including severe nephrotic syndrome, end-stage renal disease complicated with volume overload, use of diuretics, and renal tubulopathy.

Pulmonary diseases: Admission hyponatremia was present in 26.5% of the patients with pulmonary diseases, which is almost consistent with the results of previous studies. Henna et al. found that 33% of children suffering from bronchiolitis were hyponatremic. Luu et al. reported hyponatremia in 22% of the cases with bronchiolitis in the PICU and Don et al. reported hyponatremia in 45.4% of the patients with community acquired pneumonia [27-29]. With regards to the prevalence of the pulmonary problems in included patients (34.9%), number of hyponatremic patients with pulmonary disease were higher in total cases, but prevalence of hyponatremia in this group (26.5%) was not the highest one.

Diabetic ketoacidosis: Hyponatremia was seen in 23.5% of the DKA cases without correcting sodium for hyperglycemia. The shift of water to the extracellular space and hyperlipidemia can cause pseudo-hyponatremia in DKA [30].

CNS diseases: Sorkhi et al. reported hyponatremia in 8.8% the pediatric patients suffering from acute CNS disorders [22]. In our study, the rate of hyponatremia was 14.2% in patients with CNS infections and other CNS diseases such as convulsion and encephalitis.

Gastro-intestinal diseases: In our study, 14.2% of the patients with GI diseases had admission hyponatremia, while Badeli et al. reported it in 2.3% of the subjects suffering from gastroenteritis. The reason for this

discrepancy could be the type of GI patients admitted to our center (mainly patients with gastroenteritis and liver diseases). Kim et al. reported a rate of 31% for hyponatremia in pre-transplant hepatic failure [31].

Cardiovascular diseases: Cardiovascular diseases, especially heart failure states, can lead to ineffective extravascular fluid, which can cause hyponatremia together with the use of diuretics and production of atrial natriuretic peptide. According to our findings, 16.6% of the cases with cardiovascular diseases had hyponatremia.

Unlike hyponatremia, hypernatremia is less common and is less addressed in previous studies in the PICU setting. Forman et al. reported a prevalence of 0.04% for hypernatremia (serum sodium above 150 mEq/l) in the general pediatric ward [32]. In a study by Moritz et al., hypernatremia (serum sodium above 150 mEq/l) was found in 1.4% of sodium values in a laboratory database [33]. In our study, the frequency of admission hypernatremia (serum sodium above 145 mEq/L) was 5.1% in critically ill children. Considering 150 mEq/L as the cut-off point for hypernatremia, there were only two hypernatremic patients in our study. Thus, the prevalence of serum sodium above 150 mEq/L was 1% in the present study. Seven out of 10 patients with serum sodium above 145mEq/L needed primary fluid resuscitation because of moderate to severe dehydration

Conclusions

Similar to previous studies, our results showed that admission hyponatremia is frequent in our critically ill children. Patients suffering from renal and pulmonary diseases, DKA, and hematologic-oncologic diseases had a greater chance of hyponatremia (equal to or above 20%). Considering the fact that hyponatremia is a common problem in critically ill patients, proper measures should be taken for its prevention, early detection, and prompt treatment.

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Conflict of Interest

None declared

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