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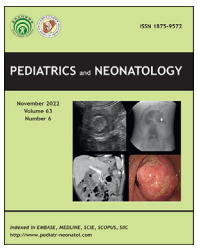

Original Article

# Serum electrolyte abnormalities in pediatric patients presenting to an emergency department with various diseases: Age-related differences

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**Key Words**
age-related differences;
children;
pediatric emergency department;
serum electrolyte abnormalities

*Background:* This study evaluated the prevalence and frequency of serum electrolyte abnormalities (SEAs) in children presenting to a pediatric emergency department (PED) with various diseases.
*Methods:* Pediatric patients (≤18 years) with blood electrolyte panels obtained in the PED of Lin-Kou Chang Gung Memorial Hospital, Taiwan, in the 5 years from January 1, 2016, to August 31, 2021, were enrolled in this retrospective observational study. Patients were divided into three age groups: Group A, < 4 years; Group B, 4–11 years; and Group C, 12–18 years. The associations between SEAs and clinical diseases in children and age-related differences were assessed.
*Results:* This study included 182,058 pediatric patients visiting our PED over a 5-year period. A total of 250 (0.14%) patients with SEAs were included in the analysis. The study population consisted of 127 boys and 123 girls with a median (IQR) age of 9.0 (3.2–14.1) years. Hospital admission was required in 86.4% (n = 216) of the patients, and 32.4% (n = 81) of them were admitted to the pediatric intensive care unit (PICU). The median (IQR) hospital stay and PICU stay was 6.5 (4.0–11.0) and 4.0 (3.0–8.0) days, respectively. The PICU stay was longer in Group A ($p < 0.05$) and shorter in group C ($p < 0.05$). Hyponatremia was the most common SEA in group A (46.3%, n = 31), while hypokalemia was common in groups B (54.2%, n = 52) and C (32.2%, n = 28). Gastrointestinal, renal, and endocrine diseases were common clinical conditions associated with SEAs in pediatric patients in our PED.

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*Conclusion:* The detection rate of SEAs in patients in the PED was 0.14%. Hyponatremia was a common SEA in pediatric patients aged <4 years, while the most common electrolyte disorder in those >4 years old was hypokalemia. In infants and young children, SEAs were associated with a longer PICU stay.
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## 1. Introduction

Serum electrolyte abnormalities (SEAs) are severe sequelae of many diseases.[1] A number of diseases and their comorbidities can cause various SEAs in different age groups, which may increase the risks of hospital admission and mortality.[2] In critically ill children, SEAs can affect clinical outcomes and they are associated with high rates of pediatric intensive care unit (PICU) admission.[3] SEAs pose a challenge to pediatricians, particularly in the pediatric emergency department (PED), because they can be caused by both mild clinical conditions and life-threatening events.[4] Early identification with appropriate interventions in cases of serum sodium, potassium, calcium, and phosphorus abnormalities is crucial for pediatric patients in the PED.[4] There have been a number of reports regarding the clinical roles of SEAs in adult patients in the emergency department.[2] However, surprisingly little information is available regarding SEAs in patients in the PED. We assessed the clinical spectrum of patients presenting with SEAs at a PED and the associations between age and medical conditions over a 5-year period.

## 2. Materials and methods

### 2.1. Participants and study design

This retrospective observational study was conducted in patients (≤18 years) who visited the PED of Lin-Kou Chang Gung Memorial Hospital (CGMH), a pediatric tertiary care hospital in Taiwan, during the 5-year period between January 1, 2016, and August 31, 2021. Patients with incomplete clinical records and/or electrolyte panel data were excluded. This study was approved by the local institutional review board (No. 202002448A3) of Lin-Kou CGMH, Taiwan, and was conducted in accordance with the tenets of the Declaration of Helsinki.

Demographic information (sex, age, and underlying medical issues), laboratory findings, clinical presentation, and hospital and/or PICU stays were evaluated. We collected laboratory data, including serum creatinine and electrolyte levels, and information on clinical presentations and diagnoses. The patients' height and serum creatinine levels were used to calculate the estimated glomerular filtration rate (eGFR) for the creatinine-based bedside Schwartz equation.[5–8] Blood samples from each patient were obtained using a BD Insyte™ intravenous indwelling catheter (22 or 24 G; Becton Dickinson, Franklin Lakes, NJ, USA) and were stored at ambient temperature in BD Vacutainer Blood Collection Tubes (Becton Dickinson) containing plasma separating tube (PST) gel and lithium heparin. The blood samples in the BD Vacutainer Blood Collection Tubes (Becton Dickinson) were immediately sent to the clinical laboratory for biochemical analysis. Our clinical laboratory was available 24 h a day. Biochemical data were measured using a Roche Cobas 6000 Chemistry Analyzer (MYCO Instrumentation, Inc., Bonney Lake, WA, USA).

We calculated the numbers of patients who presented with hypernatremia, hyponatremia, hyperkalemia, hypokalemia, hypocalcemia, and hyperphosphatemia. The normal values were based on the respective reference ranges of our central laboratory. Hypernatremia and hyponatremia were defined as serum sodium levels >150 mEq/L and <135 mEq/L, respectively.[9–11] Hyperkalemia and hypokalemia were defined as serum potassium levels >5.5 mEq/L and <3.5 mEq/L, respectively.[10,12] Hypocalcemia was defined as a total serum calcium level <8 mg/dL.[10] Hyperphosphatemia was defined as a serum phosphate level >5 mg/dL.[10]

Patients with SEAs were divided into three age groups according to the definitions of the Centers for Disease Control and Prevention (CDC) (https://www.cdc.gov/parents/index.html), Group A, < 4 years; Group B, 4–11 years; and Group C, 12–18 years, and the associations between underlying clinical diseases and electrolyte disorders in the different age groups were assessed.

The data were collected, reviewed, de-identified, and analyzed anonymously by the authors. The requirement for informed consent was waived by the ethics committee due to the anonymized nature of the data and scientific purpose of the study.

### 2.2. Statistical analyses

Descriptive statistics are presented for the representation of certain data (e.g., demographics). Univariate summaries are provided for continuous variables (e.g., mean ± SD for serum electrolytes; median and interquartile range [IQR] for age, serum creatinine, eGFR, length of stay [LOS] in the hospital, and LOS in the PICU), whereas frequencies and percentages are used to summarize categorical variables (e.g., sex, associated disease). Student's t-test and the $\chi 2$ test with Fisher's exact test were used to test the significance of differences in continuous and categorical variables, respectively. Statistical comparisons of the mean values of serum creatinine, eGFR, LOS in the hospital and in the PICU between different ages with SEAs were performed by an ANOVA test for parametric data, and significant data were further analyzed using post hoc testing. All analyses

**Table 1** Characteristics of the pediatric patients and the patterns of serum electrolyte abnormalities in.three different age groups.

| | <4 yrs (Group A) | 4 – 11 yrs (Group B) | 12 – 18 yrs (Group C) | Total |
|---|---|---|---|---|
| **Demographics** | | | | |
| Total patients (M/F) | 67 (49/18) | 96 (52/44) | 87 (26/61) | 250 (127/123) |
| Age, Median (IQR) (yrs) | 1.5 (0.8–2.7) | 8.4 (6.2–10.4) | 15.5 (13.9–16.5) | 9.0 (3.2–14.1) |
| Serum Cr, Median (IQR) (mg/dL) | 0.3 (0.3–0.5) | 0.5 (0.4–0.8) | 0.9 (0.6–2.3)$^{\theta,\Psi}$ | 0.6 (0.4–1.0) |
| Ped. eGFR, Median (IQR) (ml/min/ 1.73 $m^2$)[a] | 95 (58.3–110.0) | 88.7 (61.2–105.0) | 67 (26.7–98.4)$^{\theta,\Psi}$ | 84.2 (49.0–106.0) |
| **Serum electrolyte abnormalities** | | | | |
| Hypernatremia (mEq/L) | | | | |
| Patients numbers (%) | 3 (4.5%) | 0 (0%) | 0 (0%) | 3 (1.2%) |
| Mean ± SD | 162.00 ± 11.53 | NA | NA | 162.00 ± 11.53 |
| Hyponatremia (mEq/L) | | | | |
| Patients numbers (%) | 31 (46.3%) | 25 (26.0%) | 22 (25.3%) | 78 (31.2%) |
| Mean ± SD | 126.81 ± 7.26 | 129.24 ± 3.19 | 128.77 ± 5.59 | 128.14 ± 5.78 |
| Hyperkalemia (mEq/L) | | | | |
| Patients numbers (%) | 15 (22.4%) | 16 (16.7%) | 25 (28.7%) | 56 (22.4%) |
| Mean ± SD | 6.23 ± 0.80 | 5.68 ± 0.43 | 5.94 ± 0.63 | 5.95 ± 0.65 |
| Hypokalemia (mEq/L) | | | | |
| Patients numbers (%) | 16 (23.9%) | 52 (54.2%) | 28 (32.2%) | 96 (38.4%) |
| Mean ± SD | 2.68 ± 0.77 | 2.88 ± 0.46 | 2.8 ± 0.37 | 2.82 ± 0.50 |
| Hypocalcemia (mg/dL) | | | | |
| Patients numbers (%) | 1 (1.5%) | 1 (1.0%) | 6 (6.9%) | 8 (3.2%) |
| Mean ± SD | 6.1 ± 0 | 7.8 ± 0 | 5.65 ± 0.87 | 5.98 ± 1.05 |
| Hyperphosphatemia (mg/dL) | | | | |
| Patients numbers (%) | 1 (1.5%) | 2 (2.1%) | 6 (6.9%) | 9 (3.6%) |
| Mean ± SD | 11.1 ± 0 | 9.25 ± 2.62 | 9.68 ± 1.76 | 9.74 ± 1.76 |
| **Outcomes** | | | | |
| Numbers of admission (M/F) | 58 (42/16) | 80 (40/40) | 78 (21/57) | 216 (103/113) |
| LOS in hospital, Median (IQR) (days) | 6.0 (4.0–11.0) | 6.0 (4.0–10.0) | 7.0 (5.0–12.8) | 6.5 (4.0–11.0) |
| Numbers of admission to ICU (M/F) | 26 (16/10) | 24 (11/13) | 29 (7/22) | 81 (34/47) |
| LOS in PICU, Median (IQR) (days) | 6.0 (3.0–14.5)$^{\Psi,\phi}$ | 4.0 (2.0–6.0) | 4.0 (3.0–6.0) | 4.0 (3.0–8.0) |

yrs: year-old; M: male; F: female; IQR: interquartile range; Cr: Creatinine; Ped: Pediatric; eGFR: estimated glomerular filtration rate; NA: not applicable; LOS: length of stay; PICU: pediatric intensive care unit;
$^{\theta}p < 0.05$ vs Group A; $^{\Psi}p < 0.05$ vs Group B; $^{\phi}p < 0.05$ vs Group C.
[a] Pediatric eGFR (ml/min/1.73 $m^2$) in accordance with creatinine-based "Bedside Schwartz" equation.[5–8]

were performed using SPSS ver. 26.0 (SPSS Inc., Chicago, IL, USA) and $p < 0.05$ was taken to indicate statistical significance.

## 3. Results

### 3.1. Characteristics of serum electrolyte abnormalities of pediatric patients in different age groups

A total of 182,058 pediatric patients who were brought to our PED during the 5-year study period were included in the study (Table 1). This population included 250 (0.14%) pediatric patients with SEAs consisting of 127 (50.8%) boys and 123 (49.2%) girls with a median (IQR) age of 9.0 (3.2—4.1) years. Group A consisted of 67 (26.8%) patients younger than 4 years with a median (IQR) age of 1.5 (0.8—2.7) years. Group B consisted of 96 (38.4%) patients aged 4—11 years with a median (IQR) age of 8.4 (6.2—10.4) years. Group C consisted of 87 (34.8%) patients 12—18 years old with a median (IQR) age of 15.5 (13.9—16.5) years. Group C had a higher serum creatinine level ($p < 0.05$ vs. both Groups A [95% Confidence Intervals (CI): 1.045—4.228] and B [95% CI: 1.108—4.006]) and poorer pediatric eGFR than the other groups ($p < 0.05$ vs. both Groups A [95% CI: 1.759—36.550] and B [95% CI: 2.932—34.616]).

Overall, hypokalemia was the most common SEA in 96 (38.4%) patients, followed by hyponatremia in 78 (31.2%) and hyperkalemia in 56 patients (22.4%). Hypernatremia, hypocalcemia, and hyperphosphatemia were seen in 3 (1.2%), 8 (3.2%), and 9 (3.6%) cases, respectively (Table 1).

The rate of patients with hypernatremia in Group A was 4.5% (n = 3). There were no cases of hypernatremia in either Group B or C.

Hyponatremia was the most common SEA in Group A (46.3%, n = 31) ($p < 0.05$ vs. both Groups B and C), followed by hypokalemia in 16 (23.9%) patients, hyperkalemia in 15 (22.4%), hypernatremia in 3 (4.5%) patients ($p < 0.05$ vs. both Groups B and C), hypocalcemia in 1 (1.4%) patient, and hyperphosphatemia in 1 patient (1.4%) (Table 1 and Fig. 1).

In Group B, the most common SEA was hypokalemia, which was seen in 52 (54.2%) patients ($p < 0.05$ vs. both Groups A and C), followed by hyponatremia in 25 (26%), hyperkalemia in 16 (16.7%), hyperphosphatemia in 2 (2.1%), and hypocalcemia in 1 (1.0%) patient (Table 1 and Fig. 1).

The most common SEA in Group C was hypokalemia, which was seen in 28 (32.2%) patients. Hyperkalemia was detected in 25 (28.7%) patients ($p < 0.05$ vs. both Groups A and B), hyponatremia was seen in 22 (25.3%) patients in Group C, with hypocalcemia in 6 (6.9%) patients, and hyperphosphatemia in 6 (6.9%) patients (Table 1 and Fig. 1).

A total of 216 (86.4%) patients required admission to hospital. The median (IQR) LOSs in the hospital were 6.5 (4.0—11.0), 6.0 (4.0—11.0), 6.0 (4.0—10.0) and 7.0 (5.0—12.8) days for the whole cohort, and Groups A, B, and C, respectively. Among the hospitalized patients, 32.4% (n = 81) had a severe clinical presentation that required admission to the PICU, and the median (IQR) LOS in the PICU was 4.0 (3.0—8.0) days. Group A had the longest LOS in the PICU (median [IQR]: 6.0 [3.0—14.5] days) ($p < 0.05$ vs. both Groups B [95% CI: 1.431—6.790] and C [95% CI: 1.210—7.161]), while there was no statistical difference for LOS in the PICU between Group B (median [IQR]: 4.0 [2.0—6.0] days) and Group C (median [IQR]: 4.0 [3.0—6.0] days) (Table 1).

### 3.2. Relations between underlying clinical diseases and serum electrolyte abnormalities in different age groups

Many clinical diseases are associated with SEAs, including acute gastroenteritis, rotavirus infection, norovirus

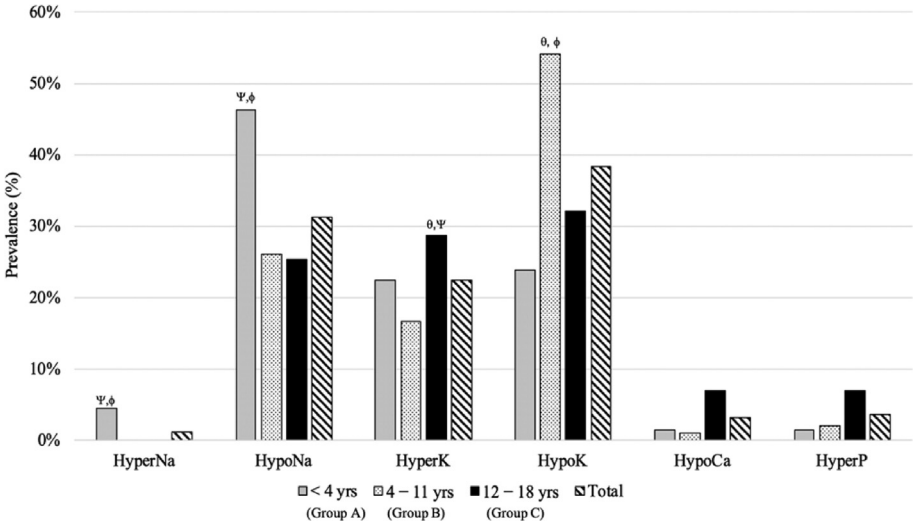


**Figure 1** Serum electrolyte abnormalities in different age groups. Hypernatremia (HyperNa), hyponatremia (HypoNa), hyperkalemia (HyperK), hypokalemia (hypoK), hypocalcemia (HypoCa) and hyperphosphatemia (HyperP) in <4 yrs (Group A, gray column), 4 – 11 yrs (Group B, dotted column), 12 – 18 yrs (Group C, black column) and all patients group (slash column). yrs: years old; $^{\theta}$ $p < 0.05$ vs Group A; $^{\Psi}$ $p < 0.05$ vs Group B; $^{\Phi}$ $p < 0.05$ vs Group C.

infection, *Salmonella* infection, volvulus with ischemic bowel changes, infantile hypertrophic pyloric stenosis, urinary tract infection, urosepsis, acute kidney injury, acute on chronic kidney disease, renal function impairment due to antibody mediated rejection in kidney transplant recipients, hemolytic uremic syndrome, renal tubular acidosis, hypokalemia periodic paralysis, Gitelman syndrome, Bartter syndrome, mitochondrial disorder-related secondary Fanconi syndrome, nephrogenic diabetes insipidus, diabetic ketoacidosis, primary adrenal insufficiency, complex convulsions, tumor lysis syndrome, Sjogren syndrome and rhabdomyolysis. The most common diseases in our pediatric patients related to SEAs were gastrointestinal (GI) disease in 102 patients (40.8%), followed by renal disease in 78 patients (31.2%), and endocrine disease in 31 patients (12.4%). Other conditions seen in our cohort were neurological disease (5.6%, n = 14), oncological disease (3.6%, n = 9), heart disease (1.6%, n = 4), allergy-immunology-rheumatology disease (0.8%, n = 2), child abuse (0.4%, n = 1), inborn error of metabolism (1.2%, n = 3), out-of-hospital cardiac arrest (OHCA) (0.8%, n = 2), and hemolysis of blood samples (1.6%, n = 4) (Fig. 2 and Table 2).

Various diseases have been reported to be associated with SEAs in the three age groups examined in this study (Table 2 and Fig. 3). GI and renal diseases are common in pediatric patients of all ages seen with SEAs in the PED. There were no significant differences in SEAs caused by GI disease between the different age groups. Renal disease showed a greater likelihood of causing SEAs in Group A ($p < 0.05$ vs. Group B [95% CI: 0.156–0.652]) and Group C ($p < 0.05$ vs. Group B [95% CI: 1.513–5.874]). The incidence of SEAs related to endocrine disease increased significantly with age (95% CI: 1.034–5.146; $p < 0.05$).

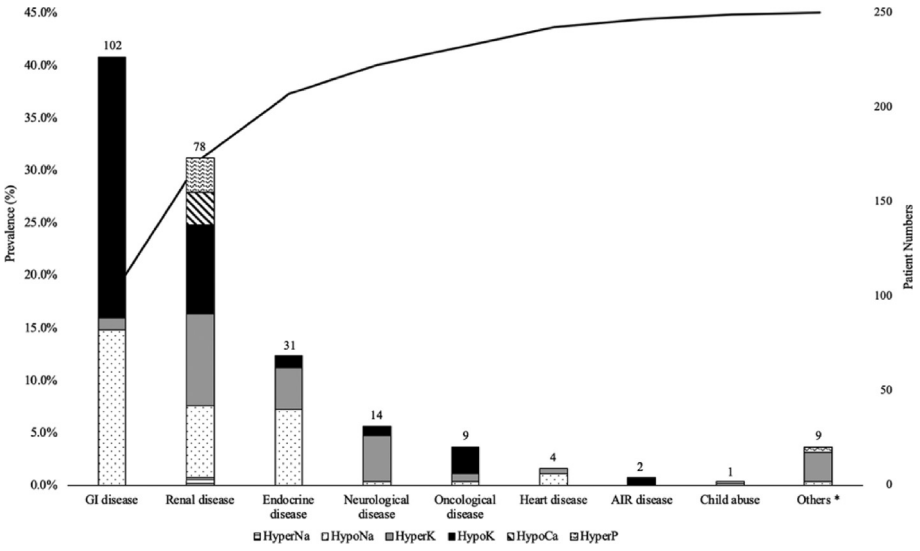


**Figure 2** Underlying clinical diseases and serum electrolyte abnormalities. The numbers of hypernatremia (HyperNa), hyponatremia (HypoNa), hyperkalemia (HyperK), hypokalemia (HypoK), hypocalcemia (HypoCa) and hypophosphatemia (HyperP) in different clinical diseases. * Others included blood sample hemolysis, out-of-hospital cardiac arrest (OHCA), inborn error of metabolism. GI: gastrointestinal; AIR: Allergy-immunology-rheumatology.

**Table 2** Underlying clinical diseases associated with serum electrolyte abnormalities in pediatric patients of three different age groups in the emergency department.

| Associated disease | <4 yrs (Group A) | 4 – 11 yrs (Group B) | 12 – 18 yrs (Group C) | Total |
|---|---|---|---|---|
| GI disease (%) | 43.3 | 47.9 | 31 | 40.8 |
| Renal disease (%) | 40.3 | 17.7 | 39.1 | 31.2 |
| Endocrine disease (%) | 0 | 11.5 | 23 | 12.4 |
| Neurological disease (%) | 9 | 6.3 | 2.3 | 5.6 |
| Oncological disease (%) | 0 | 6.3 | 3.4 | 3.6 |
| Heart disease (%) | 0 | 4.2 | 0 | 1.6 |
| AIR disease (%) | 0 | 1 | 1.1 | 0.8 |
| Child abuse (%) | 1.5 | 0 | 0 | 0.4 |
| Others[a] (%) | 6 | 5.2 | 0 | 3.6 |

GI: gastrointestinal; AIR: Allergy-immunology-rheumatology.
[a] Others included blood sample hemolysis, out-of-hospital cardiac arrest (OHCA), inborn error of metabolism.

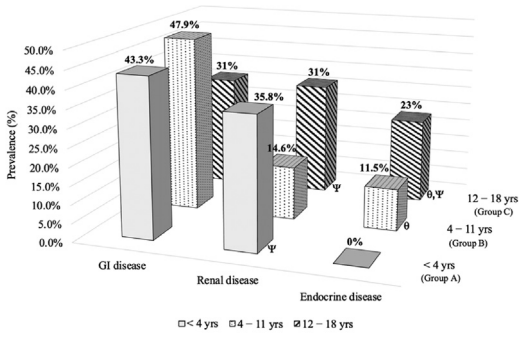


**Figure 3** The three most common problems in pediatric patients with serum electrolyte abnormalities presenting to the pediatric emergency department. GI, renal and endocrine disease in <4 yrs (Group A, gray column), 4 – 11 yrs (Group B, dotted column) and 12 – 18 yrs (Group C, slash column). GI: gastrointestinal; yrs: years old; $^{\theta}$ $p < 0.05$ vs Group A; $^{\Psi}$ $p < 0.05$ vs Group B; $^{\Phi}$ $p < 0.05$ vs Group C.

## 4. Discussion

The detection rate of SEAs in the PED was 0.14%, the rate of admission of children with SEAs was 86.4%, and 32.4% were critically ill and required PICU care.[4] The most common SEAs observed were dysnatremia and dyskalemia,[13] the rates of which were related to age.[2]

No children aged 4—11 years or 12—18 years had hypernatremia. Three hypernatremia cases were found in children aged <4 years; these were child abuse with excessive dietary sodium (n = 1), Pierre Robin syndrome (n = 1), and mitochondrial disorder-related secondary Fanconi syndrome (n = 1). Hypernatremia is not commonly found in patients with Pierre Robin syndrome, and there have been few previous reports in rare cases in specific clinical conditions.[14,15] Few studies have addressed the possibility of hypernatremia in patients with secondary Fanconi syndrome related to mitochondrial disorders.[16,17] Hyponatremia was also frequently found in Group A in the present study. This may have been because hyponatremic dehydration is relatively common in young children with GI disorders, particularly acute viral gastroenteritis.[18—20] Inappropriate intravenous hypotonic saline solutions or oral rehydration with either diluted milk or low-sodium fluids for young children with fluid loss can also lead to dilutional hyponatremia.[18,19] Hyperkalemia was noted at a higher rate in Group C. The risk factors for hyperkalemia include renal function impairment caused by acute kidney injury, chronic kidney disease, end-stage renal disease, renal dysfunction after renal transplantation, diabetic ketoacidosis, rhabdomyolysis, tumor lysis syndrome, and nonsteroidal anti-inflammatory drug (NSAID)-related nephrotoxicity.[21—26] Hypokalemia occurred more frequently in Group B. This group showed higher rates of dehydration and GI illness, which are associated with volume contraction due to secondary hyperaldosteronism with subsequent hypokalemia.[23] The numbers of patients with hypocalcemia and hyperphosphatemia were small in this study population, and there were no significant differences in their incidence rates between the three groups.

Overall, GI, renal, and endocrine diseases were common causes of SEAs in all three age groups. GI disease was the main clinical condition related to electrolyte imbalance in all age groups examined here.[19,20,23] SEAs associated with renal disorders were more common in Groups A and C than in Group B (both $p < 0.05$) because renal tubule immaturity is associated with lower rates of solute and water transport in infants and young children than in adolescents and adults to maintain electrolyte homeostasis.[27,28] Other salt-loss syndromes with transient tubular resistance to aldosterone related to obstructive uropathy, acute pyelonephritis, tubulointerstitial nephritis with or without a predisposing renal and urinary tract system malformation were also described.[27,29—31] Renal function impairments caused by acute kidney injury, chronic kidney disease, end-stage renal disease, renal dysfunction after renal transplantation, rhabdomyolysis, and NSAID-related nephrotoxicity were more common causes of SEAs in teenagers than in the other age groups examined.[21—26] The rate of SEAs caused by endocrine disease increased with age because diabetic ketoacidosis is more common in teenagers due to their poor compliance with dietary instructions and insulin therapy for type 1 diabetes mellitus. The increased incidence and hospitalization rates, particularly in older children and adolescents, are due to worsening glycemic control, which is associated with marked comorbidity.[22,32—36]

### 4.1. Limitations

This was a retrospective study, so we could not be sure that the data were complete. In addition, this study included only cases from a single tertiary care hospital, and the numbers of patients with SEAs were relatively small. Additional multicenter studies of larger cohorts are required to clarify the clinical presentations of SEAs in the PED associated with different diseases in different age groups and to identify factors related to SEAs in pediatric patients in the PED.

## 5. Conclusions

The rate of pediatric patients with SEAs in the PED was 0.14%, and the rate of hospital and PICU admissions of children with SEAs was 86.4%. Hyponatremia was a common SEA in pediatric patients aged <4 years, while the most common electrolyte disorder in those >4 years old was hypokalemia. GI, renal, and endocrine diseases were the most common clinical conditions associated with SEAs in pediatric patients in the PED in this study. Children <4 years old with SEAs had longer PICU stays than the other age groups. These results will increase awareness of the need for early identification and appropriate interventions for SEAs in seriously ill children to prevent adverse outcomes.

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## Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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## Abbreviations

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| SEAs | serum electrolyte abnormalities |
| PICU | pediatric intensive care unit |
| PED | pediatric emergency department |
| eGFR | estimated glomerular filtration rate |
| LOS | length of stay |
| IQR | interquartile range |
| GI | gastrointestinal |
| OHCA | out-of-hospital cardiac arrest |
| NSAID | nonsteroidal anti-inflammatory drug |