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Electrolyte disorders related emergencies in children

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Abstract

This article provides a comprehensive overview of electrolyte and water homeostasis in pediatric patients, focusing on some of the common serum electrolyte abnormalities encountered in clinical practice. Understanding pathophysiology, taking a detailed history, performing comprehensive physical examinations, and ordering basic laboratory investigations are essential for the timely proper management of these conditions. We will discuss the pathophysiology, clinical manifestations, diagnostic approaches, and treatment strategies for each electrolyte disorder. This article aims to enhance the clinical approach to pediatric patients with electrolyte imbalance-related emergencies, ultimately improving patient outcomes.

Trial registration This manuscript does not include a clinical trial; instead, it provides an updated review of literature.

Keywords Electrolyte imbalances, Hyponatremia, Hypernatremia, Hypokalemia, Hyperkalemia, Hypocalcemia, Hypercalcemia, Pediatrics

Introduction

Homeostasis is a process by which an organism can preserve internal stability while adjusting to changing external conditions which involves complex interactions of multiple mechanisms and reactions in the body [1]. Electrolytes play a pivotal role in essential body functions. Electrolyte abnormalities are associated with prolonged hospital stays and higher in-hospital mortality among acutely ill children [2–5]. A comprehensive understanding of electrolyte pathophysiology is imperative for the effective management of these pediatric cases. Anticipating changes in plasma electrolyte concentration is crucial for preventing life-threatening emergencies. Anticipation can be achieved through continuous clinical assessment, recognizing symptoms of imbalance, understanding patient history, and appropriate laboratory tests. Additionally, cautious laboratory monitoring and early intervention can decrease the risk of severe complications. This article offers a comprehensive overview of electrolyte and water homeostasis, while also exploring the treatment strategies linked to electrolyte imbalance-related emergencies.

Sodium

Sodium (Na+) plays a crucial role as the primary extracellular cation, contributing to the maintenance of cellular homeostasis, regulation of ion and water metabolism, and the control of blood pressure. Plasma sodium concentration is maintained within narrow limits despite variable dietary intake and physical activity. Sodium and water balance are tightly linked. Children have higher total body water content compared to adults. In premature newborns, water makes up to 80% of body weight. Total body weight (TBW) decreases to 70% in term

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newborns, however, once children reach the age of 1 they have 60% of TBW which is similar to adults. About two-thirds of TBW is in the intracellular compartment and the remaining one-third is extracellular fluid, which consists of interstitial, intravascular, and transcellular fluid (cerebrospinal, ocular, synovial, and peritoneal fluid) [6]. These various fluid compartments are depicted in Fig. 1.

Abnormalities of plasma sodium are one of the most common electrolyte disorders. Complex neurohumoral mechanisms play a crucial role in maintaining sodium and water balance. Renin is released from juxtaglomerular cells in response to hypovolemia, sympathetic nerve activation, or decreased renal perfusion or delivery of sodium chloride to the distal tubule. Renin functions to enhance reabsorption of sodium and water in the proximal convoluted tubule (PCT) [7]. The synthesis of antidiuretic hormone (ADH) is conducted within the hypothalamus. ADH is secreted from the neurohypophysis and plays a role in water regulation. ADH acts on V2 receptors in the distal nephron to facilitate water reabsorption. Increased effective plasma osmolality stimulates cerebral osmoreceptors, leading to ADH release and inducing thirst. Hypotension is associated with a significant reduction of effective intravascular volume and is a strong stimulus for ADH release that may even supersede osmotic stimuli [8]. Additionally, hypotension decreases the baroreceptor firing rate leading to an increased heart rate, vasoconstriction, and activation of the renin–angiotensin–aldosterone system (RAAS) along with decreased production of natriuretic peptides. Collectively, these changes can enhance tubular sodium and water reabsorption [9]. Additionally, fluid and water intake can impact sodium concentration, therefore managing fluid intake is important in maintaining sodium balance.

Hyponatremia

Hyponatremia in children is defined as plasma sodium concentration < 135 mmol/L. In pediatric patients younger than 4 years of age, hyponatremia is considered the most common serum electrolyte abnormality (SEA). However, in patients older than 4 years, hypokalemia is the most common SEA. Gastrointestinal, renal, and endocrine diseases are the predominant causes of SEAs in children [10]. Hyponatremia is typically encountered in patients with excessive intake of free water paired with an inability of the kidney to excrete free water. The majority of cases of hyponatremia are associated with decreased osmolality. The various etiologies and differential diagnoses of hyponatremia are summarized in Table 1 and Fig. 2. Severe hyponatremia may lead to cerebral edema and hyponatremic encephalopathy. Early symptoms of hyponatremia include headache, nausea, vomiting, lethargy, and confusion. In more severe cases, altered consciousness, seizures, coma, respiratory arrest, and myocardial ischemia can develop [11]. Brain edema secondary to increased intracranial pressure may cause noncardiogenic pulmonary edema which can lead to hypoxia and impairment of brain volume regulation, known as Ayus-Arieff syndrome [12]. Children with cerebral edema are at an increased risk for developing

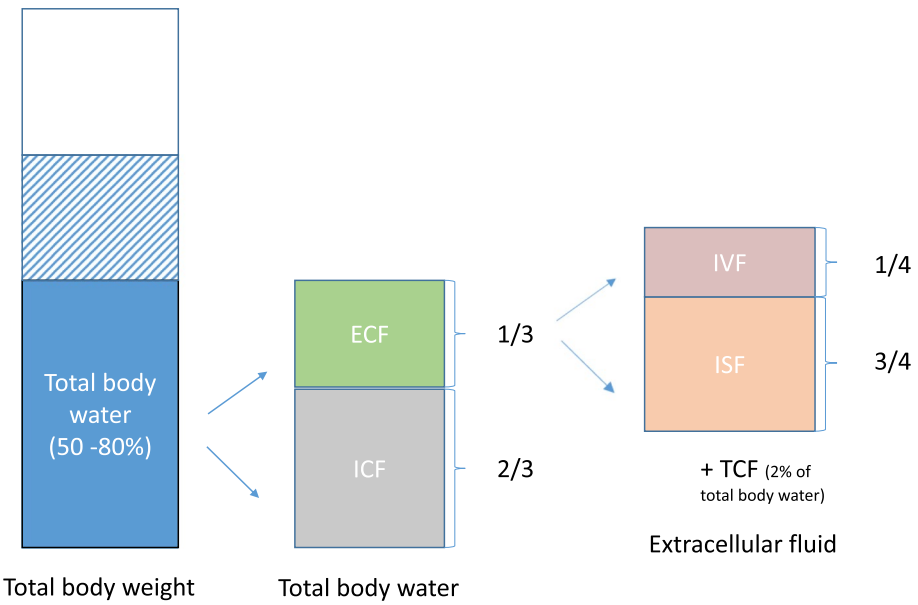

Fig. 1 Body fluid compartments. Illustration of the fluid compartments within the body. ECF-extracellular fluid, ICF-intracellular fluid, ISF-interstitial fluid, IVF-intravascular fluid, TCF-transcellular fluid

Table 1 Etiology of hyponatremia in children

Pseudohyponatremia	Lower sodium plasma concentrations in patients with hyperproteinemia or hypertriglyceridemia if measured by using indirect ion-selective electrode potentiometry
Extracellular fluid depletion- extrarenal Na loss	Dehydration (acute gastroenteritis, excess sweating, burns)
Renal sodium loss	Diuretics, mineralocorticoid deficiency, RSWS, salt losing nephropathy
Impaired water excretion in euvolemic patient	SIADH
Inability to excrete free water due to kidney dysfunction in hypervolemic patient	AKI, CKD
Excessive intake of free water	Psychogenic polydipsia
Conditions with low intravascular effective volume and ADH release	Nephrotic syndrome, cirrhosis, heart failure, hypothyroidism
Water retention in euvolemic patient	Glucocorticoid deficiency

ADH Antidiuretic hormone, *SIADH* Syndrome of inappropriate antidiuretic hormone secretion, *RSWS* Renal salt wasting syndrome, *AKI* Acute kidney injury, *CKD* Chronic kidney disease

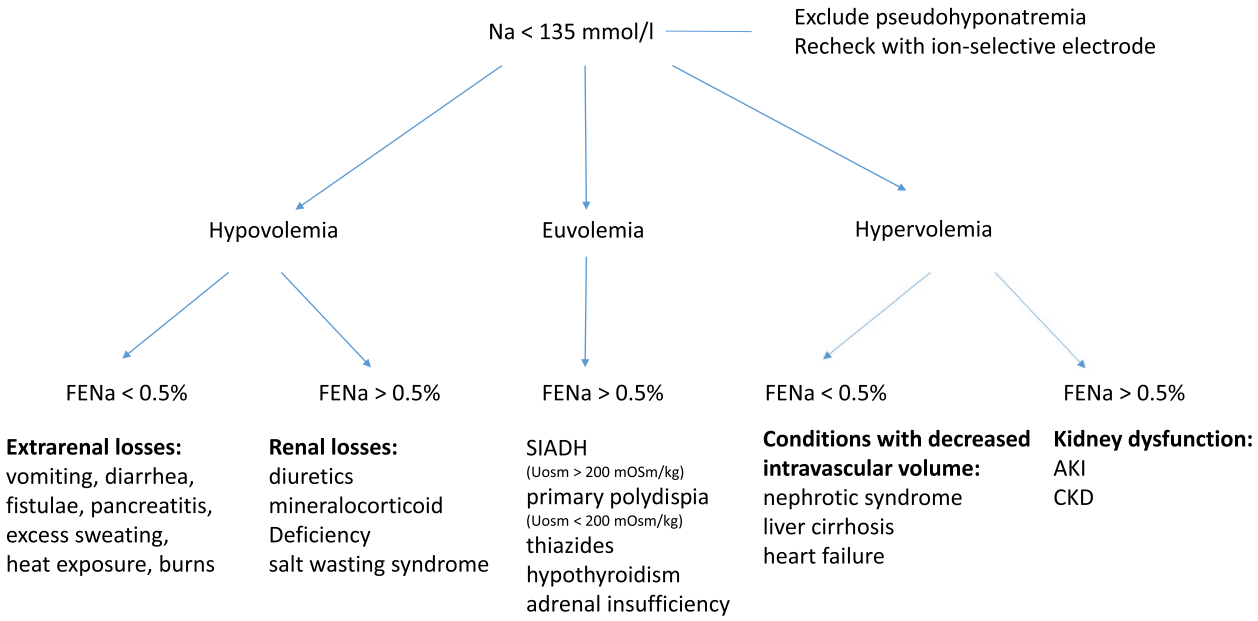

Fig. 2 Algorithm for differential diagnosis of hyponatremia, modified according to Zieg, J [13]. Low plasma osmolality is diagnostic for hypotonic hyponatremia, therefore pseudohyponatremia and translational hyponatremia must be excluded first. The next step is to assess the current volume status. The diagnostic workup should include basic measurement of plasma and urinary sodium and creatinine to calculate FENa. Both volume status and value of FENa are used to determine the cause of hyponatremia. SIADH- syndrome of inappropriate antidiuretic hormone, AKI- acute kidney injury, CKD- chronic kidney disease, FENa- fractional excretion of sodium (urinary sodium × serum creatinine)/(urinary creatinine × serum sodium) × 100

herniation given a higher ratio of brain volume to skull size compared to adults.

Hyponatremic encephalopathy is a medical emergency that requires early recognition and treatment with hypertonic saline 3% NaCl bolus 2 ml/kg with a maximum of 100 mL. If symptoms persist, the bolus should be repeated no more than two times [14]. Before pursuing additional diagnostic evaluations, it is essential to administer appropriate therapy to avoid potential harm to the patient due to treatment delays. In cases of symptomatic hyponatremia, it is recommended to aim for a safe increase of approximately 5–6 mmol/L in serum sodium concentration within the first one or two hours. However, it is crucial to avoid correcting serum sodium levels by more than 10 mmol/L within the first 24 h of therapy and by more than 20 mmol/L within 48 h to prevent potential complications [11]. Overcorrection of hyponatremia can lead to cerebral demyelination with severe neurologic symptoms. However, this complication primarily manifests in cases of chronic hyponatremia as there have

been no reported instances of cerebral demyelination in children treated with hypertonic saline for hyponatremia [11]. For patients with subacute or chronic hyponatremia, cerebral edema is prevented by the adaptive mechanism of the brain. Therefore, rapid correction of sodium is not necessary in chronic hyponatremia.

The approach for the management of hyponatremia depends on the patient's volume status. Hypervolemic hyponatremia is typically attributed to an excess of total body water due to conditions such as nephrotic syndrome or heart, liver, and kidney failure. Euvolemic hyponatremia is caused by various conditions including Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH), polydipsia, or hypothyroidism as there is a stable total body sodium level alongside an increase in total body water. Various risk factors for SIADH include central nervous system disturbances, lower respiratory tract infections, drugs, and certain malignancies [15]. Hypovolemic hyponatremia is due to a depletion of total body sodium, often caused by gastrointestinal losses, the use of diuretics, and mineralocorticoid insufficiencies. Patients experiencing hypovolemic hyponatremia with shock require fluid resuscitation using 0.9% saline, Ringers, Plasmalyte, or other isotonic solutions to restore hemodynamic stability. Treatment for hypervolemic hyponatremia varies depending on the etiology. For example, heart failure may be treated with diuretics whereas dialysis can be used to treat patients with end-stage kidney disease (ESKD) [16]. Patients presenting with euvolemic hyponatremia, such as in the instance of SIADH or psychogenic polydipsia must undergo fluid restriction. However, in cases of hypothyroidism, the underlying condition should be addressed for treatment. Iatrogenic hyponatremia is another concern in pediatric patients undergoing treatment with intravenous fluids. The 2018 American Academy of Pediatrics (AAP) guidelines recommend using isotonic fluids, such as 0.9% saline or Ringer's lactate, to maintain proper sodium levels and prevent the development of iatrogenic hyponatremia [17].

Hypernatremia

Hypernatremia is characterized by a plasma sodium concentration greater than 145 mmol/L. Hypernatremia is a less common SEA and generally affects children less than 4 years old [10]. This condition typically arises from decreased free water intake or increased loss of solute-free water and viral gastroenteritis is the leading cause. Additionally, a less common cause is salt poisoning. Importantly, hypernatremic dehydration can result from excessive water loss due to conditions including osmotic diuresis or urinary concentration defects. Determining the cause of the hypernatremic state is crucial for effective management and is depicted in Fig. 3. When the FENa is less than 1% and the patient demonstrates weight loss, this can be either attributed to free water loss or insufficient water intake. Free water loss in a hypernatremic state is attributed to extrarenal causes such as vomiting and diarrhea or renal losses such as antidiuretic hormone (ADH) resistance or osmotic diuresis. Furthermore, if a patient demonstrates a FENa of greater than 2% with weight gain, this is typically attributed to salt excess. Additionally, Table 2 demonstrates the various causes of hypernatremia in children.

Hypernatremia may lead to neurologic symptoms due to the shift of water from the intracellular compartment, resulting in cellular shrinkage. These symptoms include irritability, fever, and weakness. Severe cases may present with lethargy, focal neurologic deficits, altered mental status, coma, seizures, and death [20, 21]. Children with hypernatremic dehydration should first receive intravenous isotonic solutions to restore intravascular volume and tissue perfusion, followed by solutions containing higher free water content to correct hypernatremia. The free water deficit can be estimated using the formula: 4 ml x weight (kg) x desired change in serum sodium (mmol/L). This formula can be applied for patient management in situations where children are experiencing hypernatremia dehydration and require fluid supplements. It is essential to correct hypernatremia gradually with a recommended correction rate of below 1 mmol/L/h and 15 mmol/24 h to prevent the development of cerebral edema. Some experts recommend administering solutions with slightly higher sodium content (10–15 mmol/L lower) in children with severe hypernatremia (greater than 175 mmol/L) to avoid the risk of rapid decline in serum sodium due to excessive free water intake [22]. Regular monitoring of serum sodium is necessary to avoid a rapid drop in serum sodium levels [19]. Following fluid replacement for losses, hypotonic solutions with lower sodium content (Na 75 mmol/L) are recommended for severe hypernatremia and (Na 30 mmol/L) for mild cases to help control and gradually adjust the sodium concentration [22]. Rehydration strategies are different in children with renal concentration defects to control sodium levels according to specific needs. Individuals with nephrogenic diabetes insipidus should be given hypotonic solutions (dextrose), whereas those with central diabetes insipidus require replacement of water loss with hypotonic fluids alongside desmopressin administration. However, caution is exercised with these treatments as they potentially lead to hyponatremia in cases of renal impairment affecting electrolyte balance. Therefore, careful monitoring of electrolyte levels is essential when administering desmopressin and hypotonic fluids to prevent the development of hyponatremia.

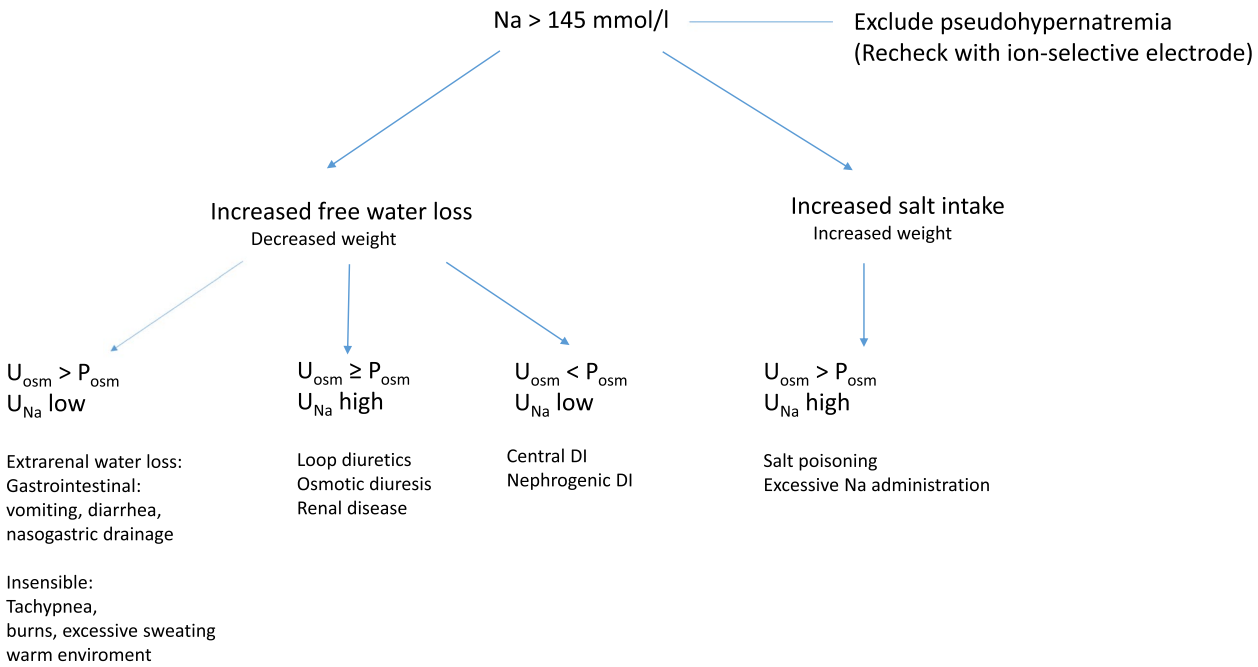

Fig. 3 Algorithm for differential diagnosis of hypernatremia, modified according to Bockenhauer et al. and Zieg, J [18, 19]. After excluding pseudohypernatremia, early management is tailored to the volume status and weight of the patient. While free water loss and insufficient water intake are associated with weight loss and low urine sodium, children with salt intoxication gain weight and their urine sodium is high. Measurement of plasma and urine osmolality is important in determining the cause of hypernatremia

Table 2 Etiology of hypernatremia in children

Excessive extrarenal water loss	Dehydration- acute gastroenteritis, excessive sweating, increased insensible water losses
Excessive renal water loss	Central and nephrogenic diabetes insipidus
Insufficient water intake	Infants, neurologically disabled children, and children with impaired thirst mechanism
Excessive salt intake	Iatrogenic, salt intoxication

In hemodynamically unstable patients, rapid correction of intravascular volume with isotonic saline should be initially used to stabilize the patient. Once stability is achieved, transitioning to hypotonic solutions may be considered [23, 24].

Potassium

Potassium (K) plays a pivotal role as the primary intracellular cation, contributing significantly to maintaining membrane voltage, nerve excitation, and acid–base balance. The normal plasma concentration is regulated within the range of 3.5 to 5 mmol/L. The potassium concentration gradient across cell membranes is essential for establishing resting cell potential and ensuring the normal function of excitable cells [25]. Potassium homeostasis is maintained by a balance between intake and excretion. Both excessively high and low potassium plasma concentrations increase the risk for life-threatening complications, including cardiac arrhythmias, cardiopulmonary arrest, and neuromuscular dysfunctions [26]. The kidney assumes a central role in regulating external potassium balance and is responsible for excreting almost 90% of this electrolyte into urine daily [27]. In individuals with significantly reduced kidney function, enhanced potassium elimination through the colon becomes a significant contributor to overall potassium elimination. Interestingly, increased plasma potassium concentrations can stimulate elevated potassium excretion which indicates the existence of direct gastrointestinal-renal kaliuretic signaling [28]. Evidence from animal models demonstrates the concept of feedforward mechanisms which suggest the presence of potassium receptors in the gastrointestinal tract [29]. Potassium excretion follows a cyclic pattern directed by the circadian oscillator in the hypothalamus. Internal potassium balance hinges on maintaining a functional Na/K ATP pump and a constant difference between intracellular and extracellular potassium levels. Additionally, hormones including

insulin, catecholamines, and mineralocorticoids, as well as drugs such as loop diuretics, thiazide diuretics, and beta-adrenergic agonists can stimulate tissue uptake of potassium, resulting in a decrease in plasma potassium levels [30]. Furthermore, the balance of potassium concentration is linked to acid–base equilibrium. For example, alkalosis results in hypokalemia due to increased potassium secretion and diminished potassium reabsorption in the collecting duct, whereas acidosis produces the opposite effect [31].

Hypokalemia

Hypokalemia in children may be categorized based on the severity: mild (3–3.5 mmol/L), moderate (2.5–3 mmol/L), and severe (< 2.5 mmol/L). In a retrospective study of pediatric patients with SEAs, hypokalemia was the most common in those older than 4 years old, accounting for 38.4% of patients [10]. The etiology of hypokalemia is diverse, with common causes stemming from extrarenal conditions such as diarrhea, malabsorption, protracted gastric suction, vomiting, refeeding syndrome, drug side effects, and excessive sweating. Other additional causes include endocrine disorders and tubulopathies which are demonstrated in Table 3. Comprehensive medical history and basic laboratory examinations play a crucial role in the differential diagnosis of hypokalemic states. The urinary K/creatinine ratio and transtubular potassium gradient (TTKG) are useful tools to assess potassium urinary wasting. Importantly, TTKG is valid only if urinary osmolality exceeds plasma osmolality [18]. Mild hypokalemia may manifest with nonspecific symptoms such as weakness, fatigue, nausea, vomiting, confusion, and diarrhea. Severe hypokalemia can lead to more serious consequences including paralysis, respiratory failure, and arrhythmias. ECG changes associated with hypokalemia include ST depression along with PR and QT prolongation. Prominent U waves recognized as positive deflections after T-wave and T-wave inversions are typical for severe hypokalemia. Both tachyarrhythmias and bradyarrhythmias- atrioventricular block or cardiac arrest may occur [32].

The primary goal of managing severe hypokalemia involves the reduction of further potassium wasting by addressing the identified cause (e.g. medication), treating the underlying disease, and administration of potassium to prevent further episodes of hypokalemia [34]. Administering oral potassium therapy is the safest approach and should be utilized when possible. The recommended dosage is 1–2 mEq/kg orally every few hours, with periodic serum potassium checks every 4 h. In situations where oral potassium therapy is not feasible due to patient status, in children with severe hypokalemia (< 2.5 mmol/L), and/or in the presence of arrhythmias, intravenous correction is a necessary option [18].

A recent study indicates that infusing 1 mmol/kg of potassium chloride over 1–2 h is likely safe for young children in intensive care units with mild to moderate hypokalemia, however, those with severe hypokalemia may require additional supplementation [35]. When administering potassium via peripheral veins, the concentration should not exceed 40 mmol/L to prevent phlebitis and pain. For higher concentrations, central venous lines are recommended, however, this does not apply to life-threatening conditions. Importantly, potassium dextrose-containing solutions must be avoided, as dextrose stimulates insulin secretion and can potentially worsen hypokalemia [26]. Additionally, it is important when removing dextrose from intravenous fluids in ill children not eating as this can also increase the risk of hypoglycemia. Regular monitoring of blood glucose levels is necessary to manage potential hypoglycemia in these patients. Potassium replacement should be scaled back when the serum potassium concentration exceeds 3.5 mmol/L. During this replacement approach, serum potassium checks are recommended every 1–2 h. Continuous ECG monitoring is essential, along with regular monitoring of blood gases and potassium levels. Additionally, concurrent hypomagnesemia in children with hypokalemia requires attention as it contributes to potassium wasting

Table 3 Etiology of hypokalemia in children [19, 26, 33].

Extrarenal losses	Gastrointestinal- prolonged diarrhea and vomiting, laxatives, nasogastric tube loss, ostomy, intestinal obstruction, decreased oral intake, congenital chloride diarrhea
	Skin- cystic fibrosis
Renal losses	Normotensive- Bartter syndrome, Gitelman syndrome, RTA, aminoglycosides, amphotericin B, diuretics
	Hypertensive- mineralocorticoid excess, primary hyperaldosteronism, licorice ingestion, AME, CAH, Cushing syndrome, Liddle syndrome, renovascular hypertension, mineralocorticoids, glucocorticoids, cisplatin, foscarnet, aminoglycosides, hypomagnesemia
Potassium transcellular redistribution	Beta 2 mimetics, insulin, xanthines, alkalosis, hyperthyroidism, familial hypokalemic periodic paralysis, hypothermia, barium, cesium intoxication

AME Apparent mineralocorticoid excess, *CAH* Congenital adrenal hyperplasia, *RTA* Renal tubular acidosis

and lowers tubular potassium reabsorption. Management should focus on correcting low magnesium levels since hypokalemia is refractory until magnesium levels are within the range of 0.7–1 mmol/L. In specific conditions such as correcting electrolyte imbalances or acid–base disorders, alternative forms of potassium supplementation may be considered. These scenarios include potassium phosphate in diabetic ketoacidosis or potassium citrate in renal tubular acidosis [36].

Hyperkalemia

Hyperkalemia in children is defined as plasma potassium greater than 5.5 mmol/L. A retrospective study demonstrated that hyperkalemia constitutes nearly 22.4% of SEA cases in children [10]. While plasma K > 7 mmol/L is found in severe hyperkalemia, children with moderate hyperkalemia have plasma potassium within a range of 6–7 mmol/L [32]. Notably, normal potassium levels are higher in newborns and infants due to their lower glomerular filtration rates and partial aldosterone resistance [37]. Pseudohyperkalemia arises from hemolysis and potassium leakage during or after capillary or venous blood collection. This phenomenon is more prevalent in small children, where the use of smaller needles and surrounding tissue squeezing during blood sample collection can contribute to its occurrence. Pseudohyperkalemia also occurs in patients with leukocytosis or blood clotting or may be a consequence of preanalytical errors including improper blood sample storage, delayed analysis, and specimen contamination [38]. It is recommended to repeat hemolyzed hyperkalemia samples to ensure accurate results [39].

Hyperkalemia most commonly occurs in children with acute kidney injury or ESKD. It can be attributed to various factors including excessive potassium intake, potassium redistribution, tissue injury (mainly skeletal and cardiac muscle), and massive cell lysis (as seen in tumor lysis syndrome). Additionally, it can be caused by decreased potassium excretion due to kidney dysfunction, mineralocorticoid deficiency, aldosterone resistance (such as in renal tubular acidosis type 4), or hyporeninemic hypoaldosteronism. The various etiologies of hyperkalemia are demonstrated in Table 4. Differential diagnosis of hyperkalemia is shown in Fig. 4 using a TTGK threshold of greater or less than 6, as evidenced by Choi et al. [40] While hyperkalemia is often asymptomatic, individuals may manifest symptoms such as weakness, muscular paralysis, and respiratory failure. Additional symptoms may be associated with the underlying disease, such as polydipsia and polyuria in diabetic ketoacidosis or failure to thrive in tubular disorders [32, 41]. Early ECG signs of hyperkalemia include peaked T waves, progressing to flattened broad P waves, and QRS complex prolongation with increasing potassium concentrations. In severe cases, hyperkalemia may lead to heart block, asystole, and ventricular tachycardia/fibrillation [42].

The treatment of hyperkalemia involves a stepwise approach to stabilize the myocardium, drive potassium into cells, and remove excess potassium from the patient. Initially, to stabilize the myocardium, calcium chloride or gluconate is administered slowly as an intravenous push in severe hyperkalemia. Monitoring serum calcium levels after each dose is crucial to avoid potential hypercalcemia, with preference given to assessing serum ionized calcium levels alongside cardiac monitoring. Due to the short-lived effect, repeated doses may be necessary. To drive potassium into cells, a combination of dextrose plus insulin infusion is utilized and is considered one of the most potent treatments for hyperkalemia short of hemodialysis. This approach facilitates the intracellular shift of potassium in exchange for sodium, and careful insulin dosing is essential to prevent hypoglycemia [44]. In the presence of acidosis, the pH is increased through methods such as hyperventilation, NaHCO3 administration, or a combination of both. However, caution is exercised and bicarbonate should not be administered to patients with a pH exceeding 7.4. Repeated sodium bicarbonate administration may be complicated by hypernatremia, volume overload, and hypocalcemia [41]. Additionally,

Table 4 Etiology of hyperkalemia in children

Pseudohyperkalemia	Leak of intracellular potassium to extracellular space
Endogenous increased potassium load	Tissue injury, rhabdomyolysis, hemolysis, tumor lysis syndrome
Increased exogenous potassium load	Diet, medication (penicillin G), massive transfusions, infusions with high potassium content
Shift of potassium from intracellular to extracellular space	Metabolic acidosis, hyperkalemic periodic paralysis
Decreased potassium excretion	AKI, CKD, adrenal insufficiency, RTA type 4, obstructive uropathy, drugs (potassium-sparing diuretics, RAAS inhibitors, calcineurin inhibitors, heparin, NSAID, ketokonazol, COX-2 inhibitors, pentamidine, trimethoprim), post renal transplant, RTA type 1, PHA type 1 and 2
Decreased activity of RAAS	Congenital adrenal hyperplasia

AKI Acute kidney injury, *CKD* Chronic kidney disease, *NSAID* Non-steroidal anti-inflammatory drugs, *RAAS* Renin–angiotensin–aldosterone system, *RTA* Renal tubular acidosis, *COX-2* Cyclooxygenase-2, *PHA* Pseudohypoaldosteronism

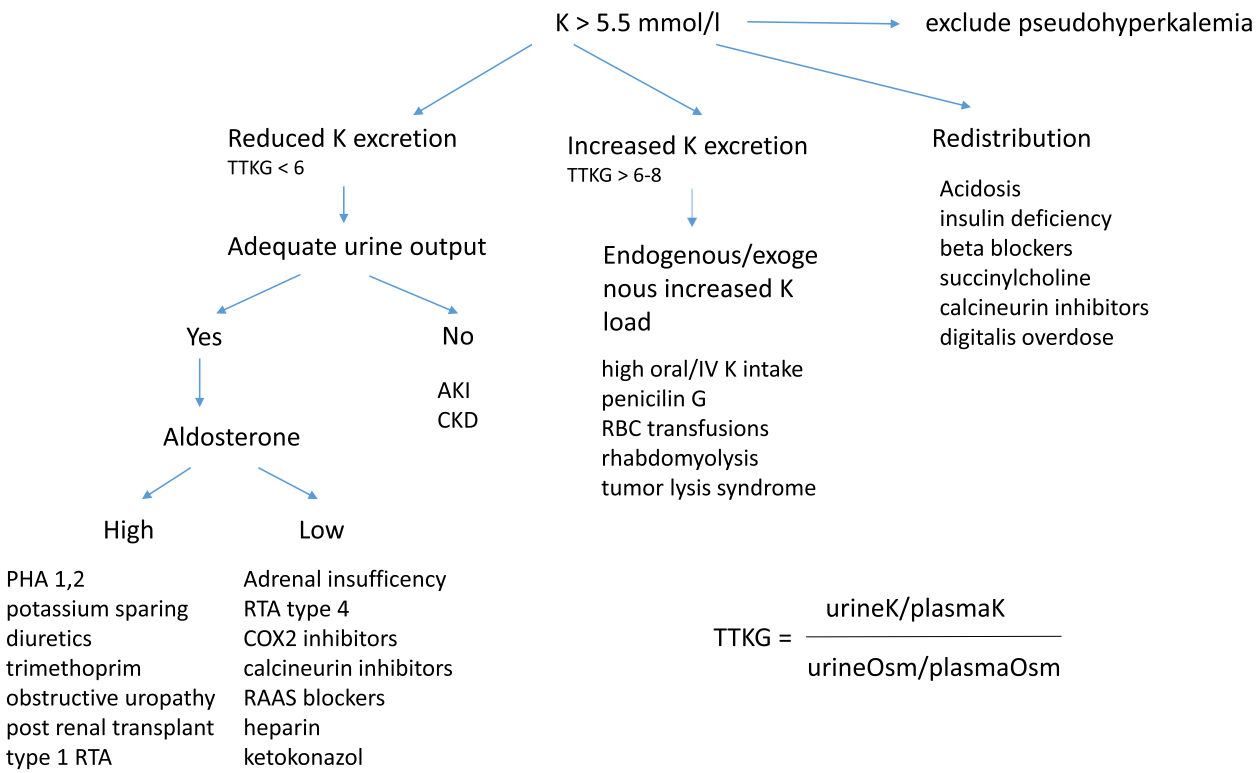

Fig. 4 Algorithm for differential diagnosis of hyperkalemia, modified according to Yang et al. [43]. After excluding pseudohyperkalemia, urinary potassium wasting using TTKG and urine output volume are assessed to divide hyperkalemic children into three groups. Plasma aldosterone level is used to further discriminate individuals with reduced potassium wasting and adequate urine output. K- potassium, AKI- acute kidney injury, CKD- chronic kidney disease, PHA- pseudohypoaldosteronism, RTA- renal tubular acidosis, COX- cyclooxygenase, RAAS- renin–angiotensin–aldosterone-system, RBC- red blood cells, IV-intravenous, Osm-osmolality, TTGK- trans-tubular potassium gradient

beta-2 agonists (salbutamol, albuterol) and sodium bicarbonate contribute to decreasing potassium levels by promoting the movement of potassium into cells [45, 46].

To reduce the potassium load within the patient, it is advised to discontinue all dietary sources of exogenous potassium in meals, drinks, formulas, and potassium-raising medications. For the elimination of excess potassium, diuretics can increase potassium urinary excretion in children with preserved diuresis. Loop diuretics have the highest kaliuretic effect. The utilization of sodium polystyrene sulfonate (SPS), a sodium/potassium exchange resin, is also recommended. This can be administered either as an enema in 20% sorbitol or orally as a powder mixed with liquid. Enema administration is preferred for its higher effectiveness in inducing potassium losses through diarrhea. The typical dose of SPS is approximately 1 g/kg, resulting in a reduction of serum potassium by around 0.8 meq/L. To ensure efficacy, it is essential to retain the resin in place for at least half an hour. Potential complications of SPS administration include hypocalcemia, hypomagnesemia, sodium overload, and hypokalemia [47]. Therefore, when administering SPS orally, it is important to avoid concurrent use of laxatives and antacids. An additional cation exchange resin that can be used to eliminate potassium includes sodium polystyrene sulfonate and calcium polystyrene sulfonate. These exchange sodium or calcium for potassium within the large intestine. These resins are administered orally or rectally and can be used preferentially for patients with chronic hyperkalemia. Although they can bind up to 1 mmol of potassium per 1 g of resin, their administration may lead to electrolyte abnormalities and gastrointestinal disturbances as side effects. Currently, their use in acute hyperkalemia cases is not supported by high-quality evidence [48]. Various medical therapies for acute hyperkalemia are shown in Table 5. In cases of persistent hyperkalemia despite conservative measures, renal replacement therapy is utilized, with hemodialysis being the preferred modality due to its rapid and immediate effectiveness.

Magnesium

Magnesium (Mg) is the second most prevalent intracellular cation within the human body. Nearly 60% of total magnesium is found in bones predominantly as surface substituents of hydroxyapatite. The majority of the

Table 5 Drugs for management of acute hyperkalemia. Adapted and modified from [18, 48]

Drug	Dose	Onset	Length of effect	Rule of thumb for fluid balance and administration
10% Calcium gluconate	0.5 - 1 ml/kg (max. 20 ml)	5 min	30 – 60 min	Ensure IV access and monitor ECG
10% Calcium chloride	0.2 ml/kg (max 10ml)	5 min	30 – 60 min	Ensure IV access and monitor ECG
8.4% Sodium bicarbonate	1 mmol/kg	within 60 min	120 min	Administer slowly to avoid fluid overload
glucose, insulin	10% glucose 5ml/kg with insulin 0.1 units/kg (max. 10 units)	10 – 20 min	depends on the therapy duration	Monitor blood glucose levels to prevent hypoglycemia
Intravenous salbutamol	5 µg/kg	within 30 min	120 min	Ensure proper dosing
Inhaled salbutamol	< 25 kg 2.5 mg > 25 kg 5 mg	within 30 min	120 min	Use apporpriate nebulizer dosage
Inhaled albuterol	neonates 0.4 mg < 25 kg 2.5 mg 25-50 kg 5 mg > 50 kg 10 mg (max. 20 mg)	5—10 min	4 – 8 h	Adjust dose per weight and monitor response
Furosemide	1 mg/kg, higher dosing in children with lower GFR	within 60 – 120 min	up to 6—8 h	Monitor urine output and electrolytes
SPS	1 g/kg	Oral: 1-2 h Rectal: 30 min	4—6 h	Ensure adequate hydration to prevent constipation

SPS Sodium polystyrene sulfonate (Kayexalate)

remaining magnesium is distributed in skeletal muscle and soft tissue, with only about 1% residing in the extracellular compartment. Magnesium is an essential cofactor for more than 300 enzymatic reactions, especially those involving energy metabolism (ATP generation), DNA, and protein synthesis. Additionally, magnesium also maintains neuromuscular excitability, cardiac function, and regulates potassium and calcium homeostasis While most of the magnesium (55–70%) is in ionized form, 20–30% of magnesium is protein bound and the remaining magnesium (5–15%) is complexed with anions [49]. Gut absorption and kidney reabsorption/excretion are the main determinants of serum magnesium levels. Due to the binding of extracellular magnesium to serum albumin, measuring magnesium levels does not accurately represent the total magnesium stores in the body. Magnesium is vital for facilitating the movement of potassium, sodium, and calcium in and out of cells. The normal range of plasma magnesium concentration is around 0.62 to 1.1 mmol/L. The interplay between these ions is significant and abnormalities in the levels of these ions, such as low potassium and magnesium, can cause severe arrhythmias. Maintaining a balance of magnesium is intricately linked to achieving a balance in levels of sodium, calcium, and potassium [50].

Hypomagnesemia

Hypomagnesemia is characterized by a serum magnesium concentration below 0.62 mmol/L and is typically more common than hypermagnesemia. The condition typically arises from diminished magnesium absorption or heightened loss via the kidneys or diarrhea. Changes in thyroid hormone activity and the use of specific medications such as pentamidine, diuretics, and alcohol can also contribute to the development of hypomagnesemia. Table 6shows the etiology of hypomagnesemia. Notably, hypomagnesemia can disrupt the impact of PTH and lead to hypocalcemia

Table 6 Etiology of hypomagnesemia in children [53]

Decreased dietary intake	Malnutrition, inappropriate parenteral nutrition, eating disorders
Increased gastrointestinal loss	Malabsorption, short bowel syndrome, prolonged diarrhea, gastric bypass
Congenital increased renal loss	FHHN, Bartter syndrome type III, IV, V, Gitelman syndrome, AD/AR hypomagnesemia, RCAD, intestinal hypomagnesemia with secondary hypocalcemia
Acquired increased renal loss	Cisplatin, aminoglycosides, loop diuretics, laxatives, calcineurin inhibitors, foscarnet, pentamidine, omeprazole, amphotericin B, ATN
Endocrine causes	Primary and secondary hyperaldosteronism, diabetes mellitus
Other	Refeeding syndrome, hungry bone syndrome, chronic alcohol abuse

ATN Acute tubular necrosis, *FHHN* Familial hypomagnesemia with hypercalciuria and nephrocalcinosis, *RCAD* Renal cysts and diabetes syndrome, *SIADH* Syndrome of inappropriate antidiuretic hormone secretion, *AD* Autosomal dominant, *AR* Autosomal recessive

and hypokalemia. The manifestations of hypomagnesemia include muscle tremors, tetany, changes in mental state, ocular nystagmus, and cardiac arrhythmias like torsades de pointes. Additional symptoms may encompass seizures, dysphagia, vertigo, and ataxia [51]. A very useful tool to aid in the differential diagnosis of hypomagnesemia is a calculation of the fraction excretion of magnesium (FEMg). The formula for FEMg is (urine Mg x serum creatinine)/(serum Mg x urine creatinine) × 100 [52]. While values of < 2% indicate extrarenal losses, FEMg of > 2% points to the renal cause of Mg wasting [53]. The interpretation of magnesium levels and corresponding clinical symptoms is demonstrated in Table 7. The management approach for hypomagnesemia depends on the severity and the patient's clinical condition. Mild cases can be treated with oral replacement therapy, starting with doses of 400–800 mg of elemental magnesium daily, divided into multiple doses to reduce adverse effects and improve tolerance. However, in instances of severe or symptomatic hypomagnesemia, or if malabsorption is suspected as the underlying cause, parenteral therapy or intravenous magnesium replacement can be indicated. Intravenous administration of magnesium sulfate is typically employed with a dosage range of 25–50 mg/kg/dose (max. 2 g) every 4–6 h (or every 8 h in neonates) over a 2–4 h period, ensuring that the rate does not exceed 125 mg/kg/hr [54]. Notably, 10 ml of 10% magnesium sulfate solution contains 1 g of magnesium sulfate and 98.6 mg of elemental magnesium equivalent to 4.06 mmol. In patients with torsades de pointes and cardiac arrest, 50 mg/kg/dose (max. 2 g/dose) of IV push magnesium sulfate should be given over 10 min [55]. The maximum concentration of elementary magnesium should not exceed 60 mg/ml for peripheral line administration and 200 mg/ml overall. Dosing should be reduced in children with renal impairment to avoid magnesium accumulation. Additionally, calcium supplementation is often necessary because individuals with hypomagnesemia often exhibit hypocalcemia as well [51, 53, 54].

Hypermagnesemia

Hypermagnesemia is characterized by a serum magnesium concentration exceeding 1.1 mmol/L with renal failure being the most common cause. Other etiologies are associated with excessive oral or parenteral magnesium intake in cases of post-magnesium infusion for hypomagnesemia and parenteral nutrition. Additional causes can include tumor lysis syndrome and magnesium containing medication such as antacids and magnesium supplements. Neurological manifestations of hypermagnesemia encompass paralysis, drowsiness, ataxia, muscle weakness, and confusion. A moderate increase in magnesium levels can lead to vasodilation, however severe hypermagnesemia may result in hypotension. Excessively elevated serum magnesium levels can manifest as lowered levels of consciousness, hypoventilation, cardiac arrhythmias, bradycardia, and ultimately cardiopulmonary arrest [56]. Addressing hypermagnesemia involves using calcium administration to counteract elevated magnesium levels in the bloodstream as it can remove magnesium from serum. Additionally, it is crucial to identify and decrease the sources of magnesium intake. In severe cases, cardiorespiratory support may be required until magnesium levels are under control. The administration of intravenous calcium, such as calcium gluconate (100 mg/kg/dose, max. 3 g) or calcium chloride (20 mg/kg/dose, max. 1 g), is recommended [54]. This dosage can be repeated as necessary to correct life-threatening arrhythmias. For severe cases of hypermagnesemia, dialysis is the preferred treatment. In situations where renal and cardiovascular functions are normal, intravenous saline diuresis involving the administration of normal saline and furosemide can enhance renal magnesium excretion until dialysis is feasible. However, it is important to note that diuresis may enhance the excretion of calcium which can lead to hypocalcemia and exacerbation of the signs and symptoms of hypermagnesemia [50].

Calcium

Calcium (Ca) is the most prevalent mineral in the body, playing crucial roles in various processes that rely on intracellular calcium concentration. These include

Table 7 Interpretation of magnesium levels

Magnesium levels	mmol/L	Manifestations
Severe hypomagnesemia	< 0.5	Nystagmus, seizures, psychosis, arrhythmia, tetany
Moderate hypomagnesemia	0.5 – 0.6	Hypokalemia, hypocalcemia, tremor, neuromuscular abnormalities
Moderate hypermagnesemia	2–5	Hyporeflexia, vomiting, bradycardia, nausea, confusion, lethargy
Severe hypermagnesemia	Greater than 5	Heart block, bradycardia, coma, delirium, respiratory dysfunction, muscle weakness

enzymatic reactions, the contraction of muscles, cardiac function, aggregation of platelets, and receptor activation. The normal serum calcium levels vary with age and are depicted in Table 8. Calcium is crucial for processes such as neuromuscular junction and bone strength. Most of the total calcium (99%) is in the bone tissue and the remaining less than 1% is in the extracellular fluid (ECF). Half of the ECF calcium is bound to albumin and the other half exists in its ionized, biologically active form. The regulation of calcium concentration is managed through vitamin D and PTH. A decrease in plasma calcium levels stimulates PTH secretion from the parathyroid glands, leading to increased bone resorption and subsequent release of calcium into the bloodstream. PTH additionally enhances calcium reabsorption in the kidneys by facilitating the production of 1,25-dihydroxyvitamin D. This active form of vitamin D enhances calcium and phosphate intestinal absorption and decreases renal excretion of these ions. Notably, 1,25-dihydroxyvitamin D also inhibits PTH synthesis. Calcitonin counteracts the action of vitamin D and PTH by inhibiting bone resorption and increasing renal calcium excretion, thus resulting in a reduction of calcium plasma levels. On the other hand, hypercalcemia causes decreased PTH secretion and inhibition of calcium release from bone tissue. Additionally, the total serum calcium level is directly linked to serum albumin concentration, with every 1 g/dL increase in serum albumin associated with a rise of 0.25 mmol/L in total serum calcium [57]. Conversely, with a decrease of 1 g/dL in serum albumin the total serum calcium will decrease by about 0.25 mmol/L. While total serum albumin is directly correlated to total serum calcium, there is an inverse relationship between ionized calcium and serum albumin. Clinically, a formula for adjusting total calcium for albumin is used: Adjusted Ca (mmol/L) = total Ca (mmol/L) + ({40—albumin (g/L)} × 0.02).

A decrease in serum albumin results in a higher proportion of total calcium existing in the ionized form. In instances of low albumin levels, despite a potential decrease in total calcium levels, the ionized calcium level may remain within the normal range. Additionally, calcium counteracts the actions of magnesium and potassium at the cell membrane. This ability allows it to be highly effective in addressing the consequences of both hypermagnesemia and hyperkalemia [50].

Table 8 Normal serum values of total calcium in children

Age	Total calcium (mmol/L)
Birth to 90 days	2—2.8
91—180 days	2.2—2.8
181—364 days	2.3 – 2.8
1—3 years	2.2—2.8
4—11 years	2.2—2.7
12 – 18 years	2.1 – 2.7

Hypocalcemia

Hypocalcemia is caused by decreased gastrointestinal absorption, decreased bone resorption, or increased kidney Ca excretion. It can occur in various conditions such as disturbances in serum magnesium levels, toxic shock syndrome, tumor lysis syndrome, post-thyroid surgery, and fluoride poisoning. Hypocalcemia can be divided into four main categories: neonatal, with high PTH, with low PTH, and miscellaneous. These various categories are demonstrated in Table 9. The main determinant of hypocalcemia is ionized calcium concentration. The onset of symptoms in hypocalcemia typically occurs when ionized levels drop to around a level of 0.63 mmol/L and present as tingling sensations in the extremities and face, carpopedal spasm, stridor, tetany, muscle cramps, and seizures. Patients may also exhibit hyperreflexia with positive Chvostek and Trousseau signs. Cardiac implications include reduced contractility and an increased risk of heart failure, while hypocalcemia can exacerbate digitalis toxicity. Prompt treatment of hypocalcemia involves administration of calcium, typically 10% calcium gluconate or calcium chloride. 1 ml of 10% calcium gluconate contains 100 mg of calcium gluconate, which is equivalent to 9.3 mg of elementary calcium [58]. Contrastingly, 1 ml of 10% calcium chloride contains 100 mg of calcium chloride which is equal to 27 mg of elementary calcium per milliliter. For acute symptomatic cases, give 20 mg/kg of elemental calcium IV over a 10–20 min period, which is approximately 2 ml/kg of 10% calcium gluconate or 0.7 ml/kg of 10% calcium chloride [58]. Follow this with an IV infusion of 200 mg/kg (or 500 mg/kg in neonates) of 10% calcium gluconate over 24 h [58]. Monitor serum calcium levels at intervals of 4 to 6 h to maintain a total serum calcium concentration within the range of 1.75 to 2.25 mmol/L. Any irregularities in magnesium, potassium, and pH should be addressed as well. One thing to note is that untreated hypomagnesemia can render hypocalcemia resistant to treatment. Hence, it is crucial to assess serum magnesium levels when dealing with hypocalcemia, especially if the condition does not respond adequately to the initial calcium therapy [50].

Table 9 Etiology of hypocalcemia in children

Neonatal	Early/late transient neonatal hypocalcemia	
Low PTH	Parathyroid gland dysgenesis	DiGeorge syndrome, Keny-Caffey syndrome
	Mitochondrial disorders	Kearns Sayre syndrome, MELAS syndrome
	Reduced PTH secretion	AD hypocalcemic hypercalciuria
	Autoimmune	Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy
	Acquired	Postsurgical, iron overload, copper deposition, amyloidosis, sarcoidosis
High PTH	Insufficient Ca intake	Malnutrition, malabsorption
	Hypovitaminosis D	Insufficient intake, decreased sun exposure, malabsorption, defect in vitamin D metabolism- liver disease, kidney dysfunction
	PTH insensitivity	Pseudohypoparathyroidism
Drugs	Bisphosphonates, bicarbonate, loop diuretics, denosumab, cinacalcet, citrated products	
Miscellaneous	Hypomagnesemia, hyperphosphatemia- tumor lysis syndrome, rhabdomyolysis, hungry bone syndrome, sepsis, acute pancreatitis, shock, alkalosis	

AD Autosomal dominant, *MELAS* Mitochondrial encephalopathy, lactic acidosis, stroke-like episodes

Hypercalcemia

Hypercalcemia can be divided based on severity (serum total Ca levels) to mild (< 3 mmol/L), moderate (3—3.5 mmol/L) and severe (> 3.5 mmol/L) [59]. It may be caused by increased bone resorption, increased gastrointestinal Ca absorption, or decreased renal Ca excretion. Approximately 90% of reported cases stem from primary hyperparathyroidism and malignancy. In these instances, there is an increased release of calcium from the bones and intestines, typically accompanied by potential impairment in renal clearance [60]. Generally, the causes of hypercalcemia may be divided into two categories- PTH-mediated and non-PTH-mediated. The various causes of hypercalcemia are depicted in Table 10. The onset of hypercalcemia related symptoms typically occurs when the total serum calcium concentration ranges from 3 to 3.75 mmol/L. At lower levels, individuals may experience neurologic symptoms such as depression, fatigue, and confusion. Higher levels can lead to more severe manifestations, including hallucinations, seizures, disorientation, and hypotonicity. Hypercalcemia also disrupts the kidney's ability to concentrate urine, potentially resulting in diuresis and subsequent dehydration [61]. The cardiovascular symptoms associated with hypercalcemia can be variable. Initially, there may be an increase in myocardial contractility until the calcium levels reach around 3.75 mmol/L. Beyond this threshold, myocardial depression occurs which can lead to decreased automaticity and shortened ventricular systole. Arrhythmias may result from a shortened refractory period. Additionally, hypercalcemia has the potential to exacerbate digitalis toxicity and contribute to hypertension.

Table 10 Etiology of hypercalcemia in children

PTH-mediated	Isolated primary hyperparathyroidism Syndromic primary hyperparathyroidism—(MEN) syndrome, hyperparathyroid jaw-tumor syndrome, tertiary hyperparathyroidism Familial hypocalciuric hypercalcemia, Jansen-type metaphyseal chondrodysplasia Neonatal hyperparathyreosis (inactivating CaSR mutations)	
Non-PTH-mediated	Malignancy	Local osteolysis (bone metastases), humoral hypercalcemia of malignancy, ectopic 1,25$(OH)_2$- vitamin D production, ectopic PTH production
	Granulomatous disease	TBC, sarcoidosis, cat-scratch disease
	Medications	Thiazides, antifungals, lithium, vitamins A and D, theophylline, PTH-related anabolic medicines- teriparatide, abaloparatide
	Endocrine disorders	Thyrotoxicosis, adrenal insufficiency, pheochromocytoma
	Inborn errors of metabolism	Congenital lactase deficiency, blue diaper syndrome, infantile hypophosphatasia
	Other	Immobilization, rhabdomyolysis in AKI, milk-alkali syndrome, Williams syndrome

AKI Acute kidney injury, *CaSR* calcium-sensing receptor, *MEN* Multiple endocrine neoplasia, *PTH* Parathormone

A significant number of individuals with hypercalcemia experience hypokalemia, and these conditions can collectively cause cardiac arrhythmias [62]. As the serum calcium surpasses 3.25 mmol/L, there is a typical shortening of the QT interval, accompanied by prolonged QRS and PR intervals as well. The progression of these abnormalities may lead to the development of atrioventricular block, which can lead to complete heart block. In severe instances, cardiac arrest can occur when the total serum calcium reaches 3.75 to 5 mmol/L. Additionally, hypercalcemia manifests gastrointestinal symptoms such as pancreatitis, constipation, dysphagia, and peptic ulcers. Renal effects involve a reduced capacity to concentrate urine which can result in diuresis and subsequent loss of crucial ions [60]. The clinical manifestations and interpretation of hypercalcemia levels are summarized in Table 11.

For symptomatic hypercalcemia, typically when the total serum concentration is around 3 mmol/L or when the calcium level exceeds 3.74 mmol/L, immediate treatment is necessary. The primary focus is on restoring intravascular volume and facilitating calcium urine excretion. In patients with sufficient renal and cardiovascular function, this is achieved by administering 0.9% saline allowing for serum calcium dilution and urinary calcium excretion [63]. The infusion continues until any fluid deficit is addressed and adequate diuresis is established. Throughout this treatment, closely monitor and sustain appropriate levels of potassium and magnesium due to the diuresis potentially causing deficiencies. Loop diuretics also increase calcium excretion, but should be used with caution because they may contribute to intravascular dehydration. Calcitonin may be used transiently (max. 48–72 h) due to the risk of tachyphylaxis [64]. Intravenous bisphosphonates are potent inhibitors of bone resorption, effectively lowering serum calcium levels. Denosumab can be used in patients with contraindications for bisphosphonates (e.g. chronic kidney disease). Glucocorticoids are also effective in reducing calcium levels, particularly in granulomatous disease [63]. In cases where there is a need for a rapid reduction in serum calcium, especially in patients with renal or cardiac dysfunction, hemodialysis is the preferred treatment. For severe conditions, chelating agents like 50 mmol of phosphate administered orally over 8 to 12 h or EDTA at a dose of 10 to 50 mg/kg over 4 h may be employed [63].

Phosphorous regulation

Following calcium, phosphorous is the most abundant essential mineral in the human body. Phosphate has various functions for the body including endochondral ossification, teeth, cellular functions, and bone mineralization. Nearly 80 to 90% of phosphorous is found in bones and teeth as hydroxyapatite and the rest is distributed across the extracellular fluid (ECF), soft tissues, and red blood cells [65]. Phosphate is freely filtered by the glomerulus at a rate of about 13 mg/kg/day in a healthy individual and approximately 60% to 70% of the filtered phosphate is reabsorbed in the proximal tubule [65]. This reabsorption process relies on a sodium-gradient dependent mechanism and involves various cotransporters. Serum phosphate levels are influenced by various factors such as the release of phosphate from bones, excretion by kidneys, and dietary intake. Three key hormones regulate phosphate homeostasis within the body: Vitamin D (1,25-dihydroxycholecalciferol), PTH, and fibroblast growth factor 23 (FGF-23) [66]. In the intestines, 1,25-dihyroxy vitamin D boosts phosphate uptake by increasing the expression of sodium phosphate cotransporters. On the other hand, FGF-23 is secreted by osteoblasts and osteocytes in response to elevated serum phosphate levels, ultimately reducing intestinal phosphate absorption by inhibiting the production of active vitamin D. In states of high serum phosphate levels, PTH is released to promote phosphate excretion by causing the internalization of various sodium phosphate cotransporters. Additionally, FGF-23 can reduce phosphate reabsorption within the proximal tubules by inhibiting transport proteins [66]. Hyperphosphatemia is defined as serum phosphate levels exceeding 1.45 mmol/L and can have various etiologies including external sources such as laxatives containing phosphate, vitamin D toxicity, endogenous sources including rhabdomyolysis and tumor lysis syndrome. Reduced phosphate excretion, most commonly due to

Table 11 Clinical manifestations of hypercalcemia levels

Body system	Mild (< 3 mmol/L)	Moderate (3—3.5 mmol/L)	Severe (> 3.5 mmol/L)
Musculoskeletal	Minimal	Weakness	Weakness
Neurological	Depression, fatigue, confusion	Depression, fatigue, confusion	Hallucinations, seizures, disorientation, and hypotonicity
Gastrointestinal	Constipation, nausea, anorexia	Constipation, nausea, anorexia	Pancreatitis
Renal	Polyuria	Dehydration	Renal dysfunction, dehydration
Cardiac	Decreased QT interval	Decreased QT interval, prolonged QRS, and PR intervals	Ventricular tachycardia, arrhythmias

kidney failure, or other conditions such as hypoparathyroidism and pseudohypoparathyroidism can also contribute to elevated phosphate levels [65]. Hyperphosphatemia can lead to symptoms associated with hypocalcemia due to the excessive binding of phosphate ions with calcium which results in decreased serum calcium levels. This can manifest as tetany, neurological symptoms, and muscle cramps [66]. Management of hyperphosphatemia focuses on identifying and treating the underlying cause. For patients with kidney failure, decreasing phosphate intake through phosphate binders is important to reduce the absorption of phosphate within the gastrointestinal tract. In patients with normal renal function, enhancing phosphate excretion can be accomplished by administering saline along with loop diuretics [67]. Hypophosphatemia is characterized by serum phosphate levels below 0.81 mmol/L and can arise from various causes such as reduced dietary intake due to malabsorption, malnutrition, and vitamin D deficiency. Additionally, it can be caused by increased phosphate excretion in cases of hyperparathyroidism, forced saline diuresis or genetic disorders affecting the proximal tubules [66]. Refeeding syndrome is another cause of hypophosphatemia that can lead to symptoms such as arrhythmias, muscle weakness, and seizures. Managing hypophosphatemia requires treating the root cause of the condition and providing phosphate supplementation [66].

Clinical considerations

Electrolyte abnormalities in children can present diverse challenges in clinical management and various factors must be understood for effective management. Distinguishing between acute and chronic electrolyte abnormalities is important in the approach for treatment. Acute imbalances may require immediate correction to prevent complications whereas chronic imbalances may need a more gradual correction, especially in cases to prevent osmotic demyelination syndrome [68]. Additionally, when a SEA is detected, physicians must be aware for potential errors in sampling or processing by considering the clinical context. This can be achieved through repeating tests to confirm the imbalance and once detected, the treatment should depend on the severity of the SEA. To ensure the detection of SEAs, physicians should have a high index of suspicion in cases involving high risk groups such as critically ill patients or those receiving intravenous fluids. Addressing these various factors can help improve overall patient management and outcomes.

Conclusion

Electrolyte imbalances are common in children and may cause life-threatening emergencies. Early identification of SEA and understanding of their pathophysiology is essential for adequate treatment. Adhering to safe correction limits and appropriate electrolyte monitoring is vital to prevent damage to the patient. The diagnosis is based on the history, physical examination, and laboratory tests. Medications are often responsible for changes in serum electrolytes. Therapy algorithms and treatment protocols should be available for clinicians to avoid inappropriate therapeutic measures.

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J.Z. and S.G. drafted and revised the main manuscript text, J.Z. and S.G. provided a literature review, J.Z. prepared the figures, and J.Z. and R.R. supervised the project. All authors reviewed the manuscript and approved the submitted version.

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