Journal of Chemistry Studies
ISSN: 2753-4634
DOI: 10.32996/jcs
Journal Homepage: www.al-kindipublisher.com/index.php/jcs

JCS
AL-KINDI CENTER FOR RESEARCH AND DEVELOPMENT

| RESEARCH ARTICLE

Effects of decreasing and increasing group IA cations in the body

Sayed Rafiullah Sadat[1] ✉, and Mohammad Arif Abed[2]
[12] *Department of Chemistry, Faculty of Education, University of Takhar, Takhar, Afghanistan*
Corresponding Author: Sayed Rafiullah Sadat, **E-mail**: ssayedrafiullah@gmail.com

| ABSTRACT
Sodium (Na+) and potassium (K+) are essential electrolytes that play critical roles in maintaining fluid balance, nerve conduction, muscle contraction, and enzymatic function. Alterations in their serum concentrations, manifesting as hypo- or hypernatremia and hypokalemia or hyperkalemia, can lead to serious clinical outcomes, including cardiac arrhythmias, neuromuscular disturbances, and renal dysfunction. This review provides an in-depth analysis of the normal physiological roles of these ions, the clinical features and causes of their imbalances, and the intricate regulatory mechanisms that govern their homeostasis. Special attention is given to conditions where multiple electrolyte disorders co-exist, such as in renal insufficiency, gastrointestinal fluid losses, and adverse drug reactions. By focusing on sodium and potassium, this article underscores the foundational role these cations play in electrolyte regulation and highlights their central importance to maintaining human health.

| KEYWORDS

Electrolyte imbalance, Hypernatremia, Hyperkalemia, Hypokalemia, Multi-electrolyte disorders, Ion regulation

| ARTICLE INFORMATION

ACCEPTED: 01 October 2025 **PUBLISHED:** 09 October 2025 **DOI:** 10.32996/jcs.2025.4.1.1

1. Introduction

Living organisms are intricately composed of an immense variety of both inorganic and organic molecules, each playing vital roles in maintaining biological processes. Among these, water stands out as a critical inorganic molecule, often comprising between 50% and 95% of a cell's total weight. Additionally, inorganic ions such as sodium (Na^+), potassium (K^+), magnesium (Mg^{2+}), and calcium (Ca^{2+}) typically form around 1% of the cellular content, further underscoring their importance in physiological functions. However, the majority of the diverse molecular composition within living organisms consists of organic molecules, which are fundamental to the complexity and functionality of life (McKee & McKee, 2014).

Sodium and potassium are the two most vital cations in the human body. As the primary electrolyte, sodium plays a key role in conjunction with chloride and bicarbonate ions as an extracellular electrolyte. In contrast, potassium functions predominantly as an intracellular ion (Khan Chamani, 2007).

As primary electrolytes, they are crucial for maintaining fluid and acid-base balance, transmitting nerve impulses, and ensuring proper muscle contraction (Emsley, 2011; Fijorek *et al*., 2014; Neligan, 2021; Clausen & Nielsen, 1994). Their precise regulation is vital for generating membrane potentials and facilitating rapid signaling within neural, muscular, and cardiac tissues, thereby supporting essential cardiovascular, neurological, and endocrine functions (McCormick, 2014; Elliott & Cooper, 2024; Shattock *et al*., 2015).

Disturbances in the concentration of these ions (termed hyponatremia/hypernatremia for sodium and hypokalemia/hyperkalemia for potassium) can lead to significant clinical consequences such as cardiac arrhythmias, muscle weakness or paralysis, confusion,

and even seizures or coma in severe cases. These imbalances are often the result of conditions such as acute or chronic kidney failure, severe dehydration, gastrointestinal fluid loss, or adverse drug effects (Agrawal *et al*., 2008).

Given the critical roles of sodium and potassium in sustaining homeostasis and the potential severity of their dysregulation, a comprehensive understanding of these cations is essential. This review focuses on the normal physiological functions, etiologies, and clinical manifestations of both hypo- and hyperstates of sodium and potassium. Additionally, the review highlights the interconnected nature of their regulation and implications for medical management. By synthesizing current evidence, the aim is to support improved clinical recognition, diagnosis, and treatment of disorders related to Group I cation imbalances.

2. Sodium (Na^+)

2.1. Normal Role and Homeostasis

Sodium (Na^+) is introduced into the body through dietary intake, absorbed into the bloodstream, and distributed throughout the system. Its primary route of elimination is via urine, with a minor portion expelled through sweat. As the principal cation in extracellular fluid, sodium is essential for sustaining the body's physiological and biochemical equilibrium (Salehi Khishki, 2017).

Its significance stems from its ability to regulate osmotic equilibrium, which ensures the proper distribution of water across cellular compartments, thereby maintaining overall hydration and cellular function. Additionally, sodium is integral to managing the volume of extracellular fluid, preventing imbalances that could lead to issues such as edema or dehydration. Furthermore, it contributes to stabilizing the membrane potential across cellular structures, a critical function that facilitates intercellular communication and the proper functioning of cells (Palmer and Clegg, 2015; Mohamed *et al*., 2025).

Beyond these fundamental roles, sodium is indispensable for various physiological mechanisms that sustain life. It enables the transmission of nerve impulses by facilitating the rapid movement of ions across neuronal membranes, ensuring efficient communication within the nervous system. Moreover, sodium is vital for enabling muscle contraction by triggering electrical changes necessary for muscle fibers to respond effectively. Lastly, it also plays a key part in maintaining acid-base homeostasis, helping to regulate pH levels, which are crucial for enzymatic activity and overall metabolic stability within the body (Mohamed *et al*., 2025).

Sodium reabsorption in the kidneys is primarily controlled by adrenal hormones, with aldosterone playing a key role in the process. Additionally, bones serve as a major reservoir of sodium, releasing stored amounts to support the body when sodium levels become insufficient (Shahbazi & Maleknia, 2005).

The regulation of sodium levels within the body is an intricate process overseen by sophisticated hormonal mechanisms that ensure precise balance and stability. Two key systems play a central role in this regulation: the renin-angiotensin-aldosterone system (RAAS) and antidiuretic hormone (ADH), each contributing through distinct yet interconnected pathways. RAAS primarily governs the renal reabsorption of sodium by signaling the kidneys to retain or release sodium based on the body's needs, thereby influencing blood pressure and fluid equilibrium. Complementing this function, ADH manages water retention and balance, adjusting kidney function to maintain optimal hydration levels and prevent drastic shifts in sodium concentration. Together, these systems work symbiotically to preserve homeostasis and support essential physiological processes (Bernal *et al*., 2023; Mohamed *et al*., 2025).

The typical concentration of sodium in the blood serum is considered to be within the range of 135 to 145 millimoles per liter. Maintaining this balance is crucial for the body's proper functioning, as deviations from these established levels even marginal ones can give rise to a variety of noticeable and potentially serious clinical symptoms. These symptoms often stem from the disruption of essential physiological processes that rely on precise sodium regulation (Fijorek *et al.,* 2014; Mohamed *et al*., 2025).

Dehydration, diabetes insipidus, elevated sodium consumption, and steroid therapy contribute to a rise in blood sodium levels, leading to hypernatremia. Conversely, factors such as diuretic use, excessive sweating, kidney disorders, congestive heart failure, and sodium loss through the digestive system, including diarrhea, result in lowered blood sodium levels, causing hyponatremia (Zahrayi *et al*., 2012).

2.2. Hyponatremia (Low Sodium)-Causes and Effects

Hyponatremia, characterized by a serum sodium concentration falling below the threshold of 135 mmol/L, holds the distinction of being the most prevalent electrolyte imbalance encountered in clinical settings. This condition reflects either an excess of total body water compared to sodium or an actual sodium deficiency. It is categorized based on the individual's volume status into hypovolemic, euvolemic, and hypervolemic forms. Hypovolemic hyponatremia occurs when both sodium and water are lost, but the loss of sodium surpasses that of water. Common triggers for this subtype include excessive use of diuretics (particularly

thiazides), gastrointestinal losses such as vomiting and diarrhea, and adrenal insufficiency (Verbalis et al., 2013; Mohamed *et al*., 2025).

Euvolemic hyponatremia, on the other hand, is typically linked to impaired water excretion caused by heightened antidiuretic hormone (ADH) activity. This mechanism is frequently associated with the syndrome of inappropriate antidiuretic hormone secretion (SIADH), which may stem from malignancies, pulmonary conditions, or central nervous system disorders. Lastly, hypervolemic hyponatremia occurs in settings of fluid overload, such as congestive heart failure, nephrotic syndrome, or liver cirrhosis. In these cases, water retention surpasses sodium retention due to reduced renal perfusion and subsequent secondary neurohormonal activation (Verbalis et al., 2013; Bernal *et al*., 2023; Mohamed *et al*., 2025).

Hyponatremia, from a pathophysiological standpoint, triggers a decrease in plasma osmolality, which prompts water to shift into brain cells. This influx may cause cerebral edema, especially in cases of rapid sodium depletion, ultimately paving the way for neurological symptoms. The clinical presentation varies widely, spanning mild issues such as nausea, headache, and fatigue to severe complications like confusion, seizures, coma, and potentially fatal outcomes. Both the severity and the speed of sodium reduction significantly influence the progression of these manifestations (Verbalis et al., 2013; Palmer and Clegg, 2015; Mohamed *et al*., 2025).

Chronic hyponatremia has been associated with a heightened risk of several serious health complications, particularly within elderly populations. Among these risks are an increased likelihood of experiencing falls due to impaired balance and physical instability, the development or worsening of osteoporosis resulting from weakened bone density, and the onset of cognitive deficits, which may manifest as memory impairments, diminished reasoning abilities, or reduced overall mental acuity. These potential outcomes underscore the importance of timely recognition and management of hyponatremia to safeguard the health and well-being of individuals in older age groups (Verbalis et al., 2013; Mohamed *et al*., 2025).

Treatment approaches are tailored to address the specific underlying cause as well as the patient's overall volume status. In cases where correction is needed, especially for chronic conditions, it is vital to proceed with caution. Rapidly reversing imbalances in serum osmolality can trigger osmotic demyelination syndrome (ODS), a severe neurological disorder stemming from abrupt changes in osmolality levels. This potential complication highlights the importance of vigilant monitoring and developing a treatment plan that is carefully tailored to meet the unique needs of each patient (Hwang, 2023).

2.3. Hypernatremia (High Sodium)-Causes and Effects

Hypernatremia refers to a condition in which the concentration of sodium in the blood rises above 145 mmol/L, signifying an imbalance that primarily stems from insufficient water in the body as opposed to an excessive accumulation of sodium. This state highlights a disruption in fluid homeostasis, often caused by dehydration, impaired water intake, or increased fluid loss, resulting in a relative deficit of water needed to maintain balanced sodium levels within the bloodstream. Although less prevalent than hyponatremia, it poses a greater risk for complications, often leading to higher rates of morbidity and mortality, particularly among hospitalized individuals and the elderly (Yun *et al*., 2022).

Hypernatremia, a condition characterized by elevated levels of sodium in the blood, most commonly arises from one of three primary factors: insufficient water intake, excessive loss of water, or, in rare instances, an overload of sodium. This imbalance can be further categorized according to the patient's overall fluid volume status into hypovolemic, euvolemic, or hypervolemic subtypes, each with distinct underlying mechanisms and clinical implications (Yun *et al*., 2022).

Hypovolemic hypernatremia, the most prevalent form of the condition, occurs when the loss of water surpasses the loss of sodium. This typically manifests in scenarios such as severe diarrhea, persistent vomiting, osmotic diuresis often associated with uncontrolled diabetes mellitus, or profuse sweating due to extreme physical exertion or environmental heat. This type of hypernatremia is especially common in vulnerable populations like infants and elderly individuals who may have limited ability or access to adequate hydration when fluid losses occur (Yun *et al*., 2022).

Euvolemic hypernatremia develops primarily as a consequence of pure water loss, where sodium levels remain largely unchanged relative to total body fluid volume. Its most notable cause is diabetes insipidus, a condition wherein the kidneys prove unresponsive to antidiuretic hormone (ADH), a hormone critical for regulating water balance, whether due to central origins from impaired hormone secretion or nephrogenic causes stemming from renal dysfunction (Muhsin and Mount, 2016; Yun *et al*., 2022).

Hypervolemic hypernatremia represents a rarer classification and is typically attributable to the introduction of hypertonic sodium-containing solutions into the body. These include infusions such as sodium bicarbonate or hypertonic saline administered for therapeutic uses or conditions requiring extreme measures. Alternatively, it may occur due to exceptionally high dietary sodium

intake paired with compromised renal function that prevents effective sodium excretion, a scenario most often observed in critically ill patients whose systems are already under significant physiological stress (Muhsin and Mount, 2016; Yun *et al*., 2022).

Hypernatremia, from a pathophysiological standpoint, triggers cellular dehydration, especially within the brain, as water shifts osmotically from intracellular to extracellular spaces. This process can provoke neurological manifestations such as irritability, lethargy, muscle twitching, seizures, and even coma. When hypernatremia occurs abruptly, the sharp rise in serum osmolality can induce intracranial hemorrhage due to vascular rupture driven by cell shrinkage (Muhsin and Mount, 2016; Yun *et al*., 2022).

In cases of chronic hypernatremia, brain cells mitigate dehydration by synthesizing osmolytes, a natural adaptive mechanism. Despite this, the adjustment introduces a heightened risk of cerebral edema if serum sodium levels are normalized abruptly. As a result, treatment protocols emphasize a gradual reduction of sodium levels through hypotonic fluids, ensuring the decrease does not exceed 10–12 mmol/L within a 24-hour period to avoid adverse outcomes (Al-Absi et al., 2012; Yun *et al*., 2022).

Thirst serves as the body's primary safeguard against hypernatremia, so its absence or diminished presence often points to issues such as a compromised thirst mechanism, neurological conditions, or restricted access to water. This is especially common among vulnerable groups like newborns, the elderly, and individuals with cognitive impairments or physical disabilities (Muhsin and Mount, 2016; Yun *et al*., 2022).

3. Potassium (K^+)

3.1. Normal Role and Regulation

Potassium plays a vital role as the predominant intracellular cation, constituting around 98% of the total potassium content within the human body. This mineral is predominantly localized within skeletal muscle tissues, the liver, and red blood cells, highlighting its significance in maintaining cellular function across various organ systems. The concentration gradient of potassium across the cellular membrane is fundamental to sustaining the resting membrane potential in excitable cells such as those found in cardiac tissues, neurons, and skeletal muscle fibers. This finely regulated ionic balance is indispensable for a range of physiological activities, enabling actions such as the transmission of nerve impulses, the regulation of cardiac rhythm, and the facilitation of smooth muscle contractions in numerous functional systems (Palmer and Clegg, 2016; Udensi *et al*., 2017; Mohamed *et al*., 2025).

Beyond its contributions to electrical excitability, potassium also influences several key biochemical and metabolic processes. It acts as a cofactor for enzymatic activities, supports the synthesis of proteins, and contributes to maintaining metabolic equilibrium within cells. Its broad impact demonstrates potassium's versatility in sustaining both structural and functional integrity across a vast array of physiological contexts (Mohamed *et al*., 2025).

Potassium homeostasis is meticulously maintained through a dynamic interplay among dietary intake, intracellular redistribution, and the regulation of renal excretion. Central to this process are the kidneys, which serve as the primary organs responsible for managing potassium balance. They possess the remarkable ability to excrete substantial amounts of potassium when serum concentrations rise above normal thresholds, thereby safeguarding physiological stability. Integral to this regulatory mechanism is the hormone aldosterone, which exerts its influence by stimulating the activity of epithelial sodium channels (ENaC) and renal outer medullary potassium (ROMK) channels within the distal segments of the nephron. This hormonally driven activation promotes efficient potassium secretion, ensuring proper electrolyte equilibrium and supporting overall homeostatic function (Palmer and Clegg, 2016; Udensi *et al*., 2017).

Beyond renal excretion, the regulation of potassium distribution within the body is significantly influenced by transcellular shifts facilitated through mechanisms involving insulin and β_2-adrenergic stimulation. These physiological processes act by triggering the activation of Na^+/K^+-ATPase, an enzyme crucial for maintaining cellular ionic balance. Upon activation, Na^+/K^+-ATPase effectively promotes the uptake of potassium into cells, thereby contributing to the precise management of potassium concentrations and preventing potentially harmful imbalances in extracellular potassium levels (Udensi *et al*., 2017; Fijorek *et al*., 2014).

The normal range for serum potassium is carefully regulated between 3.5 and 5.0 mmol/L, as even slight fluctuations can lead to significant clinical effects, particularly in individuals with preexisting health conditions (Fijorek *et al*., 2014).

3.2. Hypokalemia (Low Potassium)- Symptoms, ECG changes

Hypokalemia, characterized by a serum potassium concentration under 3.5 mmol/L, is among the most common electrolyte imbalances observed in hospitalized individuals. Its causes can be traced to reduced potassium intake, excessive losses through the gastrointestinal system due to vomiting or diarrhea, renal excretion linked to conditions like diuretic use or hyperaldosteronism,

or transcellular shifts triggered by factors such as insulin, β_2-agonists, or metabolic alkalosis (Udensi *et al*., 2017; Mohamed *et al*., 2025).

Clinically, symptoms of hypokalemia are often nonspecific in mild cases, and making it somewhat challenging to diagnose at initial stages. However, as the severity of the condition escalates, affected individuals may experience a broad spectrum of manifestations, including muscle cramps, generalized weakness, and constipation. In more critical situations, hypokalemia can lead to respiratory failure, highlighting the urgency of proper intervention. Among the ramifications of this electrolyte imbalance, issues affecting the cardiovascular system are especially concerning and warrant significant attention due to their potential to cause life-threatening complications (Udensi *et al*., 2017; Kardalas *et al*., 2018).

Hypokalemia profoundly influences cardiac function, with its effects often detectable through characteristic abnormalities on an electrocardiogram (ECG). These deviations from normal cardiac electrical activity frequently present as ST-segment depression, flattening or inversion of T waves, the emergence of pronounced U waves, and an elongation of the QT interval. Each of these changes reflects a disruption in the heart's delicate electrical equilibrium, significantly heightening the likelihood of developing arrhythmias. Such arrhythmias may include both atrial and ventricular tachycardia, posing a considerable threat to overall cardiac stability. The danger associated with these rhythm disturbances becomes even more severe in individuals with preexisting cardiovascular conditions or those receiving digitalis therapy, as these factors can exacerbate the heart's vulnerability and amplify the potential seriousness of hypokalemia-related complications (Udensi *et al*., 2017; Mohamed *et al*., 2025).

When potassium concentrations fall below 2.5 mmol/L, a level indicative of severe hypokalemia, the clinical scenario transforms into a highly critical state. At this point, patients are at significantly heightened risk of life-threatening complications, including ventricular fibrillation or cardiac arrest, should timely interventions not be administered. Recognizing hypokalemia swiftly and accurately becomes pivotal in minimizing these dire consequences. Integrated treatment strategies often emphasize continuous electrocardiogram (ECG) monitoring to track cardiac activity and the implementation of tailored potassium replacement protocols to remediate the deficiency. For those presenting with pronounced symptoms or in critical condition, intravenous potassium supplementation emerges as the preferred approach, given its ability to achieve rapid correction and stabilization of electrolyte imbalances. This method not only mitigates the risk of critical adverse events but also serves as a key intervention for preserving cardiovascular health and preventing further deterioration (Udensi *et al*., 2017; Piner and Spangler, 2023).

3.3. Hyperkalemia (High Potassium)-Effects on heart, muscles, etc.

Hyperkalemia refers to a serum potassium level higher than 5.5 mmol/L, becoming a critical medical emergency when concentrations surpass 6.5 mmol/L because of its potential to adversely affect heart function (Palmer and Clegg, 2017).

The primary causes of this condition can be grouped into distinct mechanisms, with reduced renal excretion being one of the most prevalent. This is commonly observed in situations like acute or chronic kidney disease, as well as in hypoaldosteronism, where the body's ability to eliminate potassium through the kidneys is compromised (An *et al*., 2012; Udensi *et al*., 2017).

Another contributing factor involves the use of medications known to spare potassium, including ACE inhibitors, angiotensin receptor blockers (ARBs), nonsteroidal anti-inflammatory drugs (NSAIDs), and spironolactone, which can hinder the natural excretion process. Furthermore, a range of circumstances that promote abnormal redistribution of potassium from intracellular compartments to the extracellular space play a significant role. Such conditions include metabolic acidosis, where the shift is driven by disrupted ionic gradients, tumor lysis syndrome caused by rapid destruction of cancer cells, hemolysis involving red blood cell breakdown, rhabdomyolysis from muscle tissue injury, or burns that lead to extensive cell damage. Collectively, these factors highlight the complexity of mechanisms underlying potassium irregularities (Schepkens *et al*., 2001; Burns *et al*., 2014; Ben Salem *et al*., 2014; Kovesdy, 2014; Udensi *et al*., 2017).

Symptoms of hyperkalemia may be vague in mild cases but can rapidly progress to profound muscle weakness, ascending paralysis, and sensory disturbances in severe cases. In more critical cases, hyperkalemia poses the greatest threat to the cardiovascular system due to its direct impact on cardiac function. Potassium plays an integral role in regulating cardiac myocyte membrane excitability, and elevated serum levels can reduce the resting membrane potential, resulting in compromised depolarization and conduction processes (Udensi *et al*., 2017; Hunter and Bailey, 2019).

As hyperkalemia progresses, its cardiac effects become evident through distinct electrocardiogram (ECG) alterations. These typically include pronounced and peaked T waves, progressive widening of QRS complexes, prolongation of the PR interval, and, in extreme cases, sine-wave patterns an ominous precursor to life-threatening arrhythmias such as ventricular fibrillation or asystole. While ECG changes are considered critical diagnostic signs, their appearance can sometimes be inconsistent or delayed, particularly in individuals with underlying conditions such as chronic kidney disease or diabetes mellitus. In these patients, reliance

on laboratory testing becomes indispensable to confirm hyperkalemia and guide timely interventions aimed at stabilizing potassium levels and preventing potentially fatal complications (Udensi *et al*., 2017; Kovesdy, 2014).

Approaches to treating hyperkalemia are designed with multiple objectives to ensure comprehensive management of the condition. The first priority is to stabilize the cardiac membranes, which is commonly achieved through intravenous administration of calcium gluconate. This step reduces the immediate risk of arrhythmias associated with elevated potassium levels. The next phase involves facilitating the movement of potassium from the extracellular space into the intracellular compartment to lower serum potassium concentrations effectively. Several methods can be employed here, including the administration of insulin combined with glucose to prevent hypoglycemia, the use of β_2-adrenergic agonists to stimulate potassium uptake into cells, and, in specific cases, sodium bicarbonate to counteract acidosis and promote intracellular potassium shifts (Palmer and Clegg, 2017; Moussavi *et al*., 2019; Palmer and Clegg, 2024).

In addition to these urgent measures, enhancing potassium clearance represents a critical component of managing hyperkalemia. This can be accomplished by increasing renal excretion through pharmacological interventions or resorting to dialysis in severe or refractory cases. For the longer-term management of hyperkalemia in individuals with chronic conditions, there has been growing acceptance of potassium-binding agents such as sodium zirconium cyclosilicate and patiromer. These medications help regulate serum potassium levels more sustainably by binding potassium in the gastrointestinal tract and aiding in its elimination via feces. Together, these strategies provide a layered response to both acute and chronic presentations of hyperkalemia, addressing immediate risks while offering options for ongoing control (Hunter and Bailey, 2019; Palmer and Clegg, 2017).

5. Interactions Between Sodium and Potassium

5.1. Integrated Electrolyte Regulation in Health and Disease

Electrolytes such as sodium (Na^+) and potassium (K^+) play an indispensable role in supporting various physiological functions, including maintaining osmotic balance, regulating acid-base homeostasis, facilitating nerve signaling, enabling muscle contractions, and modulating enzyme activity. While each cation serves unique purposes and is governed by distinct regulatory systems, their actions are intricately connected, creating a dynamic interplay where an imbalance in one can disrupt the equilibrium and functionality of others. A thorough grasp of these interdependencies is vital for accurate clinical assessment and management, particularly in conditions such as renal failure, endocrine disorders, and critical illnesses where multielectrolyte imbalances are prevalent (Page and Di Cera, 2006; Fijorek *et al*., 2014; Neligan, 2021; Alabi *et al*., 2020).

Sodium and potassium exhibit a dynamic interplay that extends well beyond their isolated functions, playing crucial roles in vital systems. Their interdependence is essential for regulating acid-base balance, sustaining cardiac function, ensuring neuromuscular responsiveness, facilitating nerve signal transmission, supporting enzymatic processes as cofactors, and enabling proper muscle activity (Zahrayi *et al*., 2012).

Their homeostasis is meticulously governed by hormonal regulatory networks, including the renin-angiotensin-aldosterone system (RAAS), antidiuretic hormone (ADH), and parathyroid hormone (PTH). These pathways orchestrate the transport of ions across kidney tubules and cellular membranes to preserve physiological equilibrium (Cappuccio, 2000; Morris *et al*., 2006; Fijorek *et al*., 2014; Mohamed *et al*., 2025).

When one electrolyte deviates from its normal range, it often initiates a cascade of compensatory mechanisms that can destabilize others. For instance, in hypokalemia, increased renal ammoniagenesis leads to intracellular shifts in hydrogen and potassium ions, which can further disturb sodium handling and acid–base balance. Such interconnected dynamics underscore the complexity of electrolyte regulation and emphasize the necessity of a comprehensive clinical approach when addressing these imbalances (Han, 2011; Fijorek *et al*., 2014; Mohamed *et al*., 2025).

5.2. Concurrent Electrolyte Disturbances in Kidney Failure

Chronic kidney disease (CKD) and acute kidney injury (AKI) serve as classic examples of medical conditions characterized by the simultaneous occurrence of multiple electrolyte imbalances. In these scenarios, reduced kidney function hinders potassium excretion, often causing hyperkalemia, while the retention of sodium promotes fluid overload and hypertension. These coexisting disturbances in sodium and potassium homeostasis not only complicate treatment strategies but also significantly elevate the risk of cardiovascular complications and arrhythmias (Slatopolsky, 1998; Block *et al*., 2004; Erfurt *et al*., 2023).

5.3. Electrolyte Losses in Severe Gastrointestinal Conditions

Excessive diarrhea and vomiting result in significant depletion of sodium, potassium, and bicarbonate, triggering hypovolemia, metabolic acidosis, and impaired muscle function. In both children and older adults, these disturbances can rapidly escalate to life-

threatening conditions due to their limited physiological compensatory capacity. Persistent vomiting frequently leads to hypokalemia, which is often accompanied by metabolic alkalosis and further neuromuscular complications (Kardalas *et al*., 2018; Tayab and Hoq, 2020).

5.4. Drug-Induced Multielectrolyte Disturbances

A wide range of pharmacological agents are known to simultaneously influence multiple electrolytes, often producing complex and interconnected effects on the body's electrolyte balance. For instance, loop and thiazide diuretics are commonly associated with increased urinary excretion of sodium and potassium, which can result in significant electrolyte disturbances. These changes may further lead to secondary imbalances such as hypocalcemia or hypercalcemia, depending on the mechanisms of renal compensation activated in response to the initial loss (Nanji, 1983; Liamis *et al*., 2009). Similarly, angiotensin-converting enzyme (ACE) inhibitors and potassium-sparing diuretics pose a risk of inducing severe hyperkalemia, particularly when used in combination or administered to individuals with underlying conditions such as chronic kidney disease (CKD). Such risks highlight the importance of cautious monitoring in vulnerable patients. Moreover, certain chemotherapeutic agents and the antifungal medication amphotericin B exert their effects by disrupting cellular membrane integrity. This disruption compromises ion gradients across cellular membranes, initiating a cascade of imbalances known as combined dyselectrolytemia, which can be clinically challenging to manage (Perazella, 2000; Burke *et al*., 2006; Raebel, 2012).

5.5. Clinical Management of Mixed Electrolyte Imbalances

Managing patients with multiple electrolyte disorders demands a meticulous and methodical approach to correction. For example, treating hypokalemia without simultaneously addressing hypomagnesemia often proves ineffective because magnesium plays a critical role in the kidneys' ability to conserve potassium. Additionally, correcting chronic hyponatremia too rapidly can lead to osmotic demyelination syndrome, especially when underlying hypokalemia goes unnoticed. As such, a thorough grasp of ionic interplay is crucial for informed and effective clinical intervention (Whang *et al*., 1992; Verbalis *et al*., 2013; Gagnon, 2021).

6. Conclusion

Electrolyte balance, particularly concerning the key cations sodium (Na^+) and potassium (K^+), plays a central role in maintaining physiological homeostasis. This review highlights the essential functions of each ion: sodium in fluid balance and neuronal signaling, and potassium in membrane potential and muscle function. Disruptions in the levels of these ions, manifesting as hyponatremia, hypernatremia, hypokalemia, or hyperkalemia, can have profound and often life-threatening effects on multiple organ systems, particularly the brain, heart, kidneys, and muscles. Importantly, these cations do not function in isolation. Their physiological regulation is intricately interdependent, involving shared transport mechanisms (such as the Na^+/K^+-ATPase pump) and hormonal regulators (including aldosterone). Combined disturbances, as seen in conditions such as renal failure, heart failure, severe gastrointestinal losses, and certain pharmacologic toxicities, further complicate diagnosis and treatment, demanding a holistic and dynamic clinical approach.

Given the complexity of these interactions, clinical management requires careful monitoring and correction of all affected electrolytes, not just isolated abnormalities. Overcorrection, particularly of sodium, can lead to irreversible neurological damage such as osmotic demyelination syndrome, while neglecting concurrent hypokalemia may exacerbate arrhythmias or neuromuscular symptoms. Therefore, an integrated therapeutic strategy is vital.

From a research perspective, further studies are warranted to refine our understanding of the cellular and molecular mechanisms underlying multi-electrolyte imbalances, particularly in the context of emerging diseases, critical care, and polypharmacy. In addition, the development of predictive models and clinical decision-support tools for anticipating combined electrolyte disturbances could enhance patient safety and outcomes. Exploring the genomic and epigenetic factors influencing individual susceptibility to electrolyte disorders also represents a promising future direction.

In conclusion, maintaining precise regulation of sodium and potassium is fundamental to human health. Awareness of their dynamic interactions and early recognition of imbalances are essential for effective prevention and management of a wide array of clinical conditions. A continued focus on research, education, and interdisciplinary collaboration will be key to improving outcomes in patients affected by these vital electrolyte disturbances.

References

[1] Agrawal, V., Agarwal, M., Joshi, S. R., & Ghosh, A. K. (2008). Hyponatremia and hypernatremia: disorders of water balance. *JAPI 56,* 956-64.

[2] Alabi, F.O., Alabi, C.O., Basso, R.G., Lakhdar, N., & Oderinde, A.O. (2020). Multiple electrolyte imbalances and mixed acid-base disorder posing a diagnostic dilemma: a case report. *Journal of Medical Case Reports,* 14(1), 15.

[3] Al-Absi, A., Gosmanova, E.O., & Wall, B.M. (2012). A clinical approach to the treatment of chronic hypernatremia. *American Journal of Kidney Diseases,* 60(6), 1032-1038. http://dx.doi.org/10.1053/j.ajkd.2012.06.025.

[4] An, J.N., Lee, J.P., Jeon, H.J., Kim, D.H., Oh, Y.K., Kim, Y.S., & Lim, C.S. (2012). Severe hyperkalemia requiring hospitalization: predictors of mortality. *Critical Care,* 16(6) R225.

[5] Ben Salem, C., Badreddine, A., Fathallah, N., Slim, R., & Hmouda, H. (2014). Drug-induced hyperkalemia. *Drug safety,* 37(9), 677-692.

[6] Bernal, A., Zafra, M.A., Simón, M.J., & Mahía, J. (2023). Sodium homeostasis, a balance necessary for life. *Nutrients,* 15(2), 395. https://doi.org/10.3390/nu15020395.

[7] Block, G.A., Klassen, P.S., Lazarus, J.M., Ofsthun, N., Lowrie, E.G., & Chertow, G.M. (2004). Mineral metabolism, mortality, and morbidity in maintenance hemodialysis. *Journal of the American Society of Nephrology,* 15(8), 2208-2218.

[8] Buckley, M.S., LeBlanc, J.M., & Cawley, M.J. (2010). Electrolyte disturbances associated with commonly prescribed medications in the intensive care unit. *Critical Care Medicine,* 38, S253-S264. https://doi.org/10.1097/ccm.0b013e3181dda0be.

[9] Burke, D., Lal, R., Finkel, K.W., Samuels, J., & Foringer, J.R. (2006). Acute amphotericin B overdose. *Annals of Pharmacotherapy,* 40(12), 2254-2259. https://doi.org/10.1345/aph.1h157.

[10] Burns, R.A., Topoz, I., & Reynolds, S.L. (2014). Tumor lysis syndrome: risk factors, diagnosis, and management. *Pediatric Emergency Care,* 30(8), 571-576.

[11] Cappuccio, F.P. ed. (2000). Sodium, potassium, calcium and magnesium and cardiovascular risk. *Journal of Cardiovascular Risk* 7(1), 1-3.

[12] Clausen, T., & Nielsen, O.B. (1994). The Na^+, K^+-pump and muscle contractility. *Acta physiologica scandinavica,* 152(4), 365-373.

[13] Elliott, E.R., & Cooper, R.L. (2024). The Effect of Calcium Ions on Resting Membrane Potential. *Biology,* 13(9), 750. https://doi.org/10.3390/biology13090750.

[14] Emsley, J. *Nature's building blocks: an AZ guide to the elements*. Oxford University Press, 2011.

[15] Erfurt, S., Lehmann, R., Matyukhin, I., Marahrens, B., Patschan, S., & Patschan, D. (2023). Stratification of acute kidney injury risk, disease severity, and outcomes by electrolyte disturbances. *Journal of Clinical Medicine Research,* 15(2), 59. https://doi.org/10.14740/jocmr4832.

[16] Fijorek, K., Püsküllüoglu, M., Tomaszewska, D., Tomaszewski, R., Glinka, A., & Polak, S. (2014). Serum potassium, sodium and calcium levels in healthy individuals: literature review and data analysis. *Folia Medica Cracoviensia,* 1,53-70.

[17] Gagnon, D. (2021). Hyponatremia, osmotic demyelination syndrome, and the importance of the patient's history. *The Southwest Respiratory and Critical Care Chronicles.* 9(37), 45-53. https://doi.org/10.12746/swrccc.v9i37.797.

[18] Han, K.H. (2011). Mechanisms of the effects of acidosis and hypokalemia on renal ammonia metabolism. *Electrolyte & Blood Pressure: E & BP,* 9(2), 45-49. https://doi.org/10.5049/ebp.2011.9.2.45.

[19] Hunter, R.W., & Bailey, M.A. (2019). Hyperkalemia: pathophysiology, risk factors and consequences. *Nephrology Dialysis Transplantation,* 34(3), iii2-iii11. https://doi.org/10.1093/ndt/gfz206.

[20] Hwang, C. (2023). Osmotic demyelination syndrome in a high-risk patient despite cautious correction of hyponatremia. *Electrolytes & Blood Pressure: E & BP,* 21(2), 61. https://doi.org/10.5049/ebp.2023.21.2.61.

[21] Kardalas, E., Paschou, S.A., Anagnostis, P., Muscogiuri, G., Siasos, G., & Vryonidou, A. (2018). Hypokalemia: a clinical update. *Endocrine Connections,* 7(4), R135-R146. https://doi.org/10.1530/ec-18-0109.

[22] Khan Chamani, J. (2007). Laboratory Biochemistry. Mashhad: Jahan Farda.

[23] Kodintsev, V. V., Lenda, I. V., Ponomarev, A. V., Naumov, N. A., & Salatov Ya, S. (2022). Sodium as one of the basic elements in human life. *European Journal of Natural History 5*, 4-7.

[24] Kovesdy, C.P. (2014). Management of hyperkalaemia in chronic kidney disease. *Nature Reviews Nephrology,* 10(11), 653-662. https://doi.org/10.1038/nrneph.2014.168.

[25] Liamis, G., Milionis, H.J., & Elisaf, M. (2009). A review of drug-induced hypocalcemia. *Journal of Bone and Mineral Metabolism,* 27(6), 635-642.

[26] McCormick, D. A. (2014). Membrane potential and action potential. In *From molecules to networks*, 351-376. Academic Press.

[27] McKee, T., & McKee, J.R. (2014). Biochemistry: the molecular basis of life. (Vol. 3). Oxford, United Kingdom: Oxford University Press.

[28] Mohamed, E.T., Mahmood, F.N., Merie, G.M.S., & Saadi, A.M. (2025). The Medical Importance of Sodium and Potassium. *International Journal of Pharma Growth Research Review,* 2(2), 01-10. https://doi.org/10.54660/ijpgrr.2025.2.2.01-10.

[29] Morris Jr, R.C., Schmidlin, O., Frassetto, L.A., & Sebastian, A. (2006). Relationship and interaction between sodium and potassium. *Journal of the American College of Nutrition,* 25(3), 262S-270S. https://doi.org/10.1080/07315724.2006.10719576.

[30] Moussavi, K., Fitter, S., Gabrielson, S.W., Koyfman, A., & Long, B. (2019). Management of hyperkalemia with insulin and glucose: pearls for the emergency clinician. *The Journal of Emergency Medicine,* 57(1), 36-42. https://doi.org/10.1016/j.jemermed.2019.03.043.

[31] Muhsin, S.A., & Mount, D.B. (2016). Diagnosis and treatment of hypernatremia. *Best Practice & Research Clinical Endocrinology & Metabolism,* 30(2), 189-203.

[32] Nanji, A.A. (1983). Drug-induced electrolyte disorders. *Drug Intelligence & Clinical Pharmacy,* 17(3), 175-185.

[33] Neligan, P.J. (2021). Fluid and electrolyte balance. *Anaesthesia & Intensive Care Medicine,* 22(3), 169-173. https://doi.org/10.1016/j.mpaic.2021.01.011.

[34] Page, M.J., & Di Cera, E. (2006). Role of Na^+ and K^+ in enzyme function. *Physiological Reviews,* 86(4), 1049-1092. https://doi.org/10.1152/physrev.00008.2006.

[35] Palmer, B.F., & Clegg, D.J. (2015). Electrolyte and acid–base disturbances in patients with diabetes mellitus. *New England Journal of Medicine,* 373(6), 548-559. https://doi.org/10.1056/nejmra1503102.

[36] Palmer, B.F., & Clegg, D.J. (2016). Physiology and pathophysiology of potassium homeostasis. *Advances in Physiology Education*, 40(4), 480-490. https://doi.org/10.1152/advan.00121.2016.

[37] Palmer, B.F., & Clegg, D.J. (2017). Diagnosis and treatment of hyperkalemia. *Cleve Clin J Med,* 84(12), 934-942. https://doi.org/10.3949/ccjm.84a.17056.
[38] Palmer, B.F., & Clegg, D.J. (2024). Hyperkalemia treatment standard. *Nephrology Dialysis Transplantation,* 39(7), 1097-1104. https://doi.org/10.1093/ndt/gfae056.
[39] Perazella, M.A. (2000). Drug-induced hyperkalemia: old culprits and new offenders. *The American Journal of Medicine,* 109(4), 307-314.
[40] Piner, A., & Spangler, R. (2023). Disorders of potassium. *Emergency Medicine Clinics,* 41(4), 711-728.
[41] Raebel, M.A. (2012). Hyperkalemia associated with use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers. *Cardiovascular Therapeutics,* 30(3), e156-e166.
[42] Salehi Khishki, S. (2017). Urine Biochemistry. *Department of Medical Technology*, Kabul University of Medicine, Kabul, Afghanistan.
[43] Schepkens, H., Vanholder, R., Billiouw, J.M., & Lameire, N. (2001). Life-threatening hyperkalemia during combined therapy with angiotensin-converting enzyme inhibitors and spironolactone: an analysis of 25 cases. *The American Journal of Medicine,* 110(6), 438-441.
[44] Shahbazi, V. Maleknia, N. (2005). General Biochemistry. Volumes 1 and 2. University of Tehran. Tehran, Iran.
[45] Shattock, M. J., Ottolia, M., Bers, D. M., Blaustein, M. P., Boguslavskyi, A., Bossuyt, J., Bridge, J.H., Chen-Izu, Y., Clancy, C.E., Edwards, A., Goldhaber, J., ... & Xie, Z. J. (2015). Na^+/Ca^{2+} exchange and Na^+/K^+-ATPase in the heart. *The Journal of Physiology,* 593(6), 1361-1382. https://doi.org/10.1113/jphysiol.2014.282319.
[46] Slatopolsky, E. (1998). The role of calcium, phosphorus and vitamin D metabolism in the development of secondary hyperparathyroidism. *Nephrology Dialysis Transplantation* 13. https://doi.org/10.1093/ndt/13.suppl_3.3.
[47] Tayab, M.A., & Hoq, M.A. (2020). Acid-base and electrolyte disturbances in children presenting with acute watery diarrhoea in emergency observation and referral unit of Dhaka Shishu (Children) hospital. *Dhaka Shishu (Children) Hospital Journal,* 36(2), 120-124. https://doi.org/10.3329/dshj.v36i2.54390.
[48] Udensi, U.K., & Tchounwou, P.B. (2017). Potassium homeostasis, oxidative stress, and human disease. *International Journal of Clinical and Experimental Physiology,* 4(3), 111. https://doi.org/10.4103/ijcep.ijcep_43_17.
[49] Verbalis, J.G., Goldsmith, S.R., Greenberg, A., Korzelius, C., Schrier, R.W., Sterns, R.H., & Thompson, C.J. (2013). Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. *The American Journal of Medicine,* 126(10), S1-S42. https://doi.org/10.1016/j.amjmed.2013.07.006.
[50] Whang, R., Whang, D.D., & Ryan, M.P. (1992). Refractory potassium repletion: a consequence of magnesium deficiency. *Archives of Internal Medicine,* 152(1), 40-45.
[51] Yun, G., Baek, S.H., & Kim, S. (2022). Evaluation and management of hypernatremia in adults: clinical perspectives. *The Korean journal of internal medicine,* 38(3), 290. https://doi.org/10.3904/kjim.2022.346.
[52] Zahrai, Mihan et al. (2012). Medical Biochemistry. Volume 2, Tehran: Ayer