The Crucial Role of Electrolytes in Diabetic Patients: article Review.

Noor Thair Tahir*, Sahar Abdul Wahab ALShaban, Tawfeeq F. R. Al-Auqbi*****
National Diabetes Center, Mustansiriyah University, Baghdad, Iraq.
**** Department of Chemistry and Biochemistry, College of Medicine, Mustansiriyah University, Baghdad, Iraq.***
***** National Diabetes Center, Mustansiriyah University, Baghdad, Iraq.***

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Corresponding Author email:
dr.noorthair.ndc@uomustansiriyah.edu.iq
Orcid: https://orcid.org/0000-0001-9518-6634

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Abstract:

Patients with diabetes often experience a variety of electrolyte imbalances. These patients have significant disorders deficiencies in phosphate, magnesium, and potassium Both hypo- and hyper-natremia are associated with diabetes mellitus, which is indicative of the coexistence of processes related to hyperglycemia that tend to alter blood sodium in opposite ways.

Hyper tonicity, insulin insufficiency, potassium-sparing medications, and impaired renal function are other factors that contribute to the development of hyperkalemia. The electrolyte abnormalities that occur in diabetes mellitus are summarized in this article along with the fundamental mechanism. These strategies are designed to realization should open the door to pathophysiology directed treatment, which will help prevent the various negative consequences linked to electrolyte imbalances and their management. In people with diabetes, electrolyte imbalances are frequent and may be linked to higher rates of morbidity and death. Those with decompensated diabetes mellitus, the elderly, and those with renal impairment are more likely to have these disruptions. Doctors prescribe complex treatment regimens that work to regulate electrolyte imbalance in diabetics in order to control blood sugar levels. It is best to understand the physiological mechanism of patients suffering from electrolyte imbalance, which plays an important role in controlling sugar levels in diabetics.

Key word: Electrolytes imbalance, diabetes mellitus, Calcium, Sodium, Potassium, phosphorus, Magnesium.

الدور الحاسم للإلكتروليتات في مرضى السكري: مقال مراجعة

نور ثائر طاهر*، سحر عبد الوهاب الشعبان، توفيق فاخر العقبي*****
المركز الوطني لعلاج وبحوث السكري / الجامعة المستنصرية.
**** فرع الكيمياء والكيمياء الحياتية، كلية الطب، الجامعة المستنصرية.***
*****المركز الوطني لعلاج وبحوث السكري / الجامعة المستنصرية .***

الخلاصة:
غالبًا ما يعاني مرضى السكري من مجموعة متنوعة من اختلالات توازن الاملاح. يعاني هولاء المرضى من اضطرابات كبيرة ونقص في الفوسفات والمغنيسيوم والبوتاسيوم. يرتبط كل من نقص وارتفاع الصوديوم في الدم بمرض السكري، مما يدل على التعايش بين العمليات المرتبطة بفرط سكر الدم والتي تميل إلى تغيير صوديوم الدم بطرق متعاكسة. فرط التوتر، وقصور

الأنسولين، والأدوية الموفرة للبوتاسيوم، واختلال وظائف الكلى هي عوامل أخرى تساهم في تطور فرط بوتاسيوم الدم. يتم تلخيص اضطرابات الاملاح التي تحدث في مرض السكري في هذه المقالة جنبًا إلى جنب مع الآلية الأساسية. إن هذه الاستراتيجية مصممة بحيث يفتح تحقيقها الباب أمام العلاج الموجه إلى الفسيولوجيا المرضية، والذي سيساعد في منع العواقب السلبية المختلفة المرتبطة باختلال توازن الأملاح. اختلالات توازن الأملاح المتكررة لدى مرضى السكري تكون مرتبطة بمعدلات أعلى من الإصابة بالأمراض والوفاة. أولئك الذين يعانون من داء السكري غير المعرض، وكبار السن، وأولئك الذين يعانون من ضعف الكلى هم أكثر عرضة للإصابة بهذه الاضطرابات. يصف الاطباء انظمة علاجية معقدة يرتبط عملها بتنظيم اختلال التوازن الاملاح لدى مرضى السكري وذلك للتحكم في نسبة السكر بالدم ومن الافضل يتم فهم الالية الفسيولوجية لحالات المرضى اللذين يعانون من خلل توازن الالكترولايت والتي تلعب دورا مهم بضبط معدلات السكر لدى مرضى السكري.

الكلمات المفتاحية: توازن الاملاح، مرض السكري، كالسيوم، صوديوم، بوتاسيوم، فوسفات، مغنيسيوم.

Introduction:

Diabetes mellitus (DM) is one of the conditions that has a higher incidence of electrolyte abnormalities since diabetics frequently have the aforementioned conditions (particularly impaired renal function, malabsorption syndromes, acid-base disorders, and multidrug regimens) [1]. In clinical practice, electrolyte imbalances are frequent. They mostly affect hospital populations, affecting a wide range of patients from those who are asymptomatic to those who are in critical condition, and are linked to higher rates of morbidity and mortality [2]. Diabetes mellitus has extended epidemic scopes worldwide [3]. Blood glucose and electrolytes have a complicated relationship that is influenced by several other variables, including age and other disease. Since glucose has osmotically active properties, hyperglycemia raises serum osmolality, which causes water to leave cells and lower sodium levels through the dilution effect. Due to the movement of water from intracellular spaces, the osmotic impact of glucose also results in osmotic diuresis, which lowers the volume of blood in circulation and dehydrates cells.[4]

Numerous illnesses, such as diabetes mellitus, acute and chronic renal failure, rheumatoid arthritis, cardiovascular disease, and shock, can cause electrolyte imbalances [5]. Electrolyte abnormalities can be caused by a variety of mechanisms, such as changes in electrolyte distribution and absorption, changes in fluid status and shits, hormonal changes, insufficient or excessive fluid administration, and neurologic changes in excretion through gastrointestinal or renal losses [6]. In community subjects, electrolyte homeostasis disruptions are also commonly seen. Even modest and persistent community-acquired electrolyte abnormalities are associated with a poor prognosis [7]. The majority of electrolyte issues are complex. Numerous pathophysiological elements, either separately or in combination, are important, including acute sickness, pharmacological drugs, coexisting acid-base imbalances, nutritional condition, gastrointestinal absorption capacity, and other concomitant disorders (mostly renal diseases) [8-9].

Dysnatremia

Dysnatremia is a frequent electrolyte imbalance. Given the substantial morbidity and mortality rate associated with dysnatremia, age is a significant independent risk factor for the condition [10]. Dysnatremia can cause debilitating symptoms like nausea, lethargy, and seizures, and it has been repeatedly linked to a higher mortality rate in hospitalized patients, even though many dysnatremic patients remain

asymptomatic (especially if a change in the plasma sodium concentration is mild and the onset is gradual). Sodium is the most significant osmotically active particle because it is a dominant action in the extracellular space. Because of its tight relationship to the body's fluid balance, impaired or reduced sodium excretion causes the extracellular and intravascular volumes to expand, which raises blood pressure [11].

Diabetes mellitus is known to cause dysnatremias through a number of underlying processes [12] One osmotically active chemical is glucose. Increased blood osmolality from hyperglycemia results in the removal of water from cells, which dilutes serum sodium levels ([Na+]). The corrected [Na+], which is computed by adding (1.6 mmol/L) to measured [Na+] for each (5.55 mmol/L) increase in serum glucose above normal, should therefore be considered in hyperglycemic patients; a correction factor of (2.4 mmol/L) is applied when serum glucose concentrations exceed (22.2 mmol/L)[13-15]. Notably, one useful technique for the therapeutic monitoring of hyperglycemia is the adjusted [Na+] after the dilutional effect of hyperglycemia has been taken into consideration [16].

Hypovolemic-hyponatremia can also result from untreated diabetes mellitus osmotic diuresis-related[17]. Additionally, ketone molecules in diabetic ketoacidosis, specifically acetoacetate and b-hydroxybutyrate exacerbate renal salt depletion and necessitate electrolyte losses in the urine [17]. It should be mentioned, nevertheless, that if the water loss via osmotic diuresis is not sufficiently supplanted, Hypotonic renal losses—the loss of water in excess of sodium and potassium—may result from it. In an internal medicine clinic with poorly managed diabetes mellitus was associated with a third (34.5%) of instances of hypernatremia [18].

In these conditions, there is an artificial decrease in the sodium concentration in the blood (pseudohyponatremia), which is measured per liter of serum not water. A patient with hyperlipidemia who has normal serum sodium levels should also be suspected of having pseudonatremia, or hypernatremia. The reverse conditions of pseudohypernatremia and pseudonormonatremia, which are commonly observed in diabetics with nephrotic or malabsorption diseases, can also be caused by severe hypoproteinemia [19] . The direct ion-selective electrodes (ISE) method should be used for serum sodium detection in lipemic or hypoproteinemic samples since the indirect ISE approach is prone to misleading dysnatremias [19].

The balance between the water flow out of Osmotic diuresis brought on by glucoseuria, which tends to raise [Na+], and hyperglycemia-induced cells, which decrease [Na+], are reflected in the fluctuating serum levels of [Na+] in patients with uncontrolled diabetes mellitus[20]. An artificially lowered or raised serum sodium level that differs from the real systemic level is also linked to diabetes mellitus. In healthy people, water makes up around (93%) of the serum, with lipids and proteins making up the remaining (7.1%). Sodium is only present in the serum water phase [21]. Serum water percentage may drop (80%) in people with severe hyperlipidemia, much like lactescent serum in untreated diabetic mellitus[21].

Central pontinemyelinolysis orosmotic demyelination, a disorder characterized by central demyelinating lesions, especially in the pons, are known to result from rapid serum sodium correction. These lesions can cause severe disability or even death[22]. Since risk factors for osmotic demyelination syndrome , such as thiazide diuretics, malnutrition, hypokalemia, and hypoxia, are frequently present in diabetic patients, they may be at higher risk for developing osmotic

demyelination syndrome (ODS) after the correction of hyponatremia. In patients who acquire the condition, hypokalemia is also linked to a poor prognosis [23].
It is crucial to remember that ODS is mostly caused by premature remedy for persistent hyponatremia. But, among diabetics, ODS is infrequently linked to hypernatremia and hypokalemia (without hyponatremia or hyperosmolality). How these electrolyte abnormalities could cause ODS in diabetics is currently unknown [24]

Dyskalemia.
Serum potassium levels must be closely watched because dyskalemia, a common electrolyte disorder, can frequently result in cardiac arrest and deadly arrhythmia [25]. In order to maintain potassium homeostasis, intake and excretion must be balanced, and the extracellular and intracellular fluid compartments must be properly distributed. The resting plasma membrane potential of cells is determined by the fact that 98% of exchangeable potassium is found in the intracellular compartment, while only (2%) of the total potassium in the body is found in extracellular fluid [26]. .
One of the following factors can cause hypokalemia in people with diabetes: (a) potassium [K+] being redistributed from the extracellular to the intracellular fluid compartment (shift hypokalemia caused by insulin administration); (b) gastrointestinal K+ loss due to malabsorption syndromes (osmotic diuresis and/or coexisting hypomagnesemia, bacterial overgrowth, and chronic diarrheal states); and (c) renal K+ loss[27]. A low intracellular concentration of magnesium [Mg2+] stimulates the renal outer medullary K+ channel to generate more K+, which is why hypomagnesemia can result in hypokalemia. Exogenous insulin promotes the entry of K+ into skeletal muscles and hepatic cells by increasing the activity of the Na+-K+-ATPase pump, which may lead to mild hypokalemia [28].
Hyperosmolality and insulin insufficiency are thought to be the primary causes of the proportionate rise in serum potassium content in this case. As mentioned before, hyperglycemia causes water to leave cells by increasing serum osmolality[29]. When intracellular water is lost, a gradient for K+ to leave the cells is preferable since it increases the intracellular K+ concentration. Through the water pores in the cell membrane, K+ may be transported with water due to the friction forces between the solvent water and the solute [30]. Hyperkalemia is more common in diabetic individuals than in the general population [31].
Another factor could be the elevated epinephrine secretion brought on by insulin-induced hypoglycemia [32]. Treatment of severe hyperglycemia is the main situation where insulin therapy results in hypokalemia. Most patients with diabetic ketoacidosis (DKA) have a significant K+ deficiency. Although it can occasionally surpass (10 mEq/kg), the typical K+ deficiency is between (3 and 5 mEq/kg) [33]. Potassium depletion linked to DKA is caused by a variety of mechanisms, such as nausea, increased renal losses due to excretion of ketoacid anion and osmotic diuresis, and the loss of K+ from cells due to glycogenolysis [34]. Nevertheless, blood K+ levels are usually normal at admission or, in about one-third of patients, increased despite the K+ depletion [35].
Acidosis (potassium increases by about 0.45 mmol/L for every 0.15 drop in pH), insulin insufficiency, hypertonicity, cell lysis , and medications (beta blockers) are examples of shift hyperkalemia in diabetes mellitus[36]. Hyperkalemia is linked to decreased glomerular filtration of K+ (caused by acute renal injury and chronic kidney disease) and some medications that disrupt K+ excretion. Patients with additional risk factors that

further reduce the effectiveness of potassium excretion, such as renal failure, volume depletion, or the use of drugs that alter potassium handling, are more likely to have overt hyperkalemia [37]. It's interesting to note that individuals with moderate renal impairment brought on by osmotic diuresis may experience less hyperkalemia if they take dapagliflozin, a sodium-glucose transport protein 2 (SGLT2) inhibitor [38].
These drugs such as potassium diuretics, renin inhibitors, beta-blockers, angiotensin-converting enzyme inhibitors, and angiotensin II receptor blockers decrease tubular secretion of K+ as a result of the syndrome of hyporeninemic hypoaldosteronism which is the most common reason why diabetics experience chronic hyperkalemia. Notably, a normal, healthy diabetic diet tends to be low in sodium and high in K+, which might lead to hyperkalemia in vulnerable people [39]. Mild to severe renal impairment and asymptomatic hyperkalemia are common in diabetes patients [39].

Dysmagnesemia.

A magnesium level that is either hypomagnesemic or hypermagnesemic is referred to as dysmagnesemia[40] Both magnesium level extremes, however, present similarly in clinical settings. Muscle weakness, respiratory depression, cardiac arrhythmia, heart failure, and ultimately the possibility of cardiac arrest are examples of clinical manifestations.For many of the body's physiological processes, magnesium is essential. It is a cofactor in about 300 enzymatic activities that are necessary for proteins, nucleic acids, and mitochondria to function structurally. It is also a necessary mineral for muscle contraction, neuromuscular transmission, and the metabolism of energy molecules[41].
One common electrolyte imbalance in diabetic individuals is hypomagnesemia[42]. In community participants 55 years of age and older, diabetes mellitus has recently been found to be an independent risk factor for hypomagnesemia. A considerable fraction (40%) had DM. A recent prospective study found that 40% of hypomagnesemic individuals were hospitalized or admitted to an internal medicine clinic. mostly as a contributing factor. The primary cause of hypomagnesemia in these individuals with diabetes [43].
There are a number of alternative causes for hypomagnesemia in DM besides glucosuria. These consist of the use of diuretics, glomerular hyperfiltration, inadequate food intake, recurrent metabolic acidosis and altered insulin metabolism [44].
Low serum Mg2+ levels can also result from increased gastrointestinal Mg2+ losses from diarrhea brought on by diabetic autonomic neuropathy. Notably, metformin-induced diarrhea was linked to an instance of symptomatic hypomagnesemia [concentration of Mg2+] (0.35 mmol/L), range of references (0.73-0.95 mmol/L)] [45]. Moreover, insulin can cause hypomagnesemia by encouraging a net transfer of Mg2+ from the extracellular to intracellular area [46]. Another factor could be the elevated epinephrine secretion brought on by insulin-induced hypoglycemia [47] Because hyperglycemia causes greater renal Mg2+ loss by osmotic diuresis, poorly managed diabetic patients are more likely to experience hypomagnesemia associated with insulin therapy [47]. Hypokalemia, hypophosphatemia, and acidosis-related urine Mg2+ losses are the main causes of the high prevalence of hypomagnesemia when diabetic ketoacidosis is present [48]. Hypocalcemia may be linked to advanced chronic renal insufficiency because of concomitant low vitamin D levels and hyperphosphatemia. Even if the glomerular filtration rate is effectively maintained,

hypocalcemia may be present in patients with nephrotic syndrome[49]

Acute renal failure is more common in patients with diabetes mellitus due to volume depletion, sepsis, rhabdomyolysis, and medicines like Gentamicin, Rifampicin, Angiotensin Converting Enzyme inhibitors (ACEi), Angiotensin Renin Blockers (ARBs), ARB + hydrochlorothiazide, Furosemide, statin, fibrate, non-steroidal anti-inflammatory drugs (NSAIDs), and radiographic contrast medium [50]. When the failing kidney, with or without increased cell catabolism, is unable to remove phosphorous, severe hyperphosphatemia may ensue, leading to hypocalcemia. This is brought on by the decline in urine levels of 25-hydroxyvitamin D3 and the protein that binds it. Hypomagnesemia is another factor that may contribute to hypocalcemia in diabetics. The main causes of hypocalcemia caused by Mg2+ depletion are either Resistance of the renal tubules and skeleton to the action of parathyroid hormone (PTH) or poor PTH secretion [51]. Hypocalcemia may also result with the combination of furosemide and vitamin D insufficiency. There is proof that those with diabetes have comparatively low parathyroid levels [52].

Dyscalcemia .

Calcium is essential for many bodily processes, including blood coagulation, muscular contraction, signal transduction, nerve conduction, and skeletal mineralization. The metabolism of phosphate and magnesium is connected to that of Ca+2. Renal reabsorption, intestinal absorption, and bone turnover all affect Ca+2 homeostasis[53]. When the body's calcium levels diverge from normal, it can be categorized as either hypercalcemia or hypocalcemia, which are disorders of calcium metabolism. Ca is essential for both glucose control and insulin secretion. Pancreatic β-cells' intracellular calcium concentration determines the Ca-regulated process of glucose-dependent insulin production[54]. Furthermore, the myocyte's absorption of glucose is impacted by elevated cytosolic calcium. As a result, aberrant Ca homeostasis may contribute to the development of type 2 diabetes by causing problems with glucose homeostasis and insulin action abnormalities[55].

Long-term insulin resistance and relative insulin insufficiency are linked to hyperparathyroidism, which can result in overt diabetes mellitus or worsen the glycemic management of pre-existing diabetes mellitus [56]. It is believed that hyperparathyroidism-mediated insulin resistance is caused by an increased intracellular free calcium concentration, which raises the need for insulin by reducing normal insulin-stimulated glucose transport . Since untreated hyperparathyroidism is associated with hypertension, diabetic patients should be assessed for hypercalcemia [57]. A patient with type 1 diabetes should be suspected of having autoimmune hyperparathyroidism linked to anti-calcium-sensing receptor autoantibodies if elevated serum calcium levels are seen. Severe hypercalcemia (3.75 mmol/L) in DKA was recently documented in one case [58].

The main causes of hypocalcemia caused by Mg2+ depletion are either renal tubule resistance and skeletal to the activity of parathyroid hormone (PTH) or poor PTH secretion [59]. Hypocalcemia may also result with the use of furosemide and vitamin D insufficiency [60]. There is proof that those with diabetes have comparatively low parathyroid levels. Indeed, it has been noted that patient with insulin-dependent diabetes show a slight shift lower in the PTH set-point secretion, but those with uremic diabetes have a decreased sensitivity of the parathyroid gland to hypocalcemia [61-62].

The most significant contributing cause to the development of hypercalcemia in this instance may be dehydration[63]. There may also be a function for metabolic acidosis-induced decreased bone production and severe insulin deficiency-induced enhanced bone mineral breakdown and resorption.[64]

Dysphosphatemia

Abnormal serum phosphate levels are the cause of illnesses related to phosphorus metabolism. Defects in phosphate intake, excretion, and cellular usage are the cause of these aberrant levels [65]. Low blood phosphate levels are known as hypophosphataemia, whereas excessive blood phosphate levels are known as hyperphosphataemia. It is unclear exactly what causes hypophosphatemia in diabetic people. Reduced high energy phosphate and tissue hypoxia may result from a paradoxical metabolic imbalance in inorganic phosphate that is hypothesized to start early in the course of diabetes. These alterations occur in cells and tissues when insulin does not limit glucose entry, especially in poorly managed diabetes [66].

Hypophosphatemia is more likely to develop in diabetic patients due to underlying medical issues. Among these is the use of diuretics, such as furosemide and thiazides. malabsorption, vitamin D insufficiency, and primary hyperthyroidism [67]. It is well known that elevated insulin level facilitates the uptake of phosphate and glucose by the liver cells and skeletal muscle. Insulin treatment, however, only slightly lowers serum phosphate levels in healthy patients. When there is underlying phosphate deficiency, the risk of severe hypophosphatemia is elevated [68]. osmotic diuresis-induced increased phosphate loss in decompensated diabetes mellitus with ketoacidosis. Because phosphate is shifted out of cells by both insulin insufficiency and metabolic acidosis, the serum of phosphate content upon presentation is typically normal or even elevated despite phosphate depletion [69]. Phosphate deficiency may be discovered by administering insulin and water, correcting ketoacidosis, and causing an intracellular shift that lowers plasma phosphate concentrations sharply [70].

Since randomized trials have not demonstrated any clinical advantage from phosphate administration, it is not advised to routinely administer phosphate throughout the treatment of DKA [70-71]. Furthermore, hypophosphatemia treatment may result in negative side effects such hypocalcemia and hypomagnesemia. Individuals with severe hypophosphatemia of less than 1.0 mg/dL (0.32 mmol/L), respiratory depression, hemolytic anemia, or heart failure must get careful phosphate replacement [72].

Conclusion:

In people with diabetes, electrolytes imbalance are frequent and may be linked to higher rates of morbidity and death. Those with decompensated diabetes mellitus, the elderly, and those with renal impairment are more likely to have these disruptions. DM patients may be prescribed complicated medication regimens, some of which may be linked to electrolytes imbalance. Preventing electrolytes imbalance in diabetic patients requires rigorous glycemic control, if feasible, and the cessation of these drugs like chlorpropamide, tolbutamide, insulin or other medications like diuretics, amitriptyline for the treatment of diabetic neuropathy. Understanding the pathophysiologic mechanisms is the only way to handle these conditions effectively.

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