Egypt. J. Chem. Vol. 67, SI: M. R. Mahran, pp. 925-943 (2024)

Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

Hyperglycemic Crises in Diabetic Patients-Overview, Role of Health Informatics and Neurological Findings-Magnetic Resonance Neuroimaging-Review Article

Nahlah Salah A.Albari Burayk[1], Renad Abduallah Mohammed Saigh[1], Megren Bander Ageeb Almutiri[2], Raheem Mohammed Abod Balkhtab[1], Mohammed Ali Yahya Asiri[3], Alaa Hussain Yahya Moafa[1], Bader Nasser Abdulaziz Alhamidi[4], Ahlam Ahmad Adwan[5], Aisha Ahmed Yahya Al Majrashi[6], Salha Abdu Joshan[7], Fatimah Ali Hakami[8], Fatimah Jameel Al/Qobaii[9], Ibtisam Hamdan Refaei Almutairi[10], and Ahlam Awied Alanezi[11]

[1]Jazan University Hospital, Jazan, Saudi Arabia [2]Majmaah University, Saudi Arabia
[3]Ministry of Health Branch in Riyadh Region, Saudi Arabia [4]Tumair general hospital, Saudi Arabia
[5]Nursing technician, Shared services management, Ministry of health, Saudi Arabia
[6]Nursing technician, Al Mansoura Health Center, Ministry of health, Saudi Arabia
[7]Nursing technician, Al Aziziyah Health Center II, Ministry of health, Saudi Arabia
[8]Nursing technician, Ministry of health, Saudi Arabia
[9]Health information Health Informatics Technician, Al Wadi Health Center, Ministry of health, Saudi Arabia
[10]health informatics technician, the first health cluster, Human resources, community health
[11] Ministry of Health, Saudi Arabia

In Loving Memory of Late Professor Doctor ""Mohamed Refaat Hussein Mahran""

Abstract

Background: Diabetic crises, including diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS), are acute, life-threatening conditions requiring prompt and effective management. Both conditions are associated with significant electrolyte disturbances, including hypokalemia, hypophosphatemia, and acidosis, which can lead to severe complications if not managed quickly. These complications may cause significant damage to the brain.

Objective: This study aims to evaluate management strategies for electrolyte disturbances and complications associated with diabetic crises, focusing on the role of standard and advanced diagnostic imaging in assessing brain conditions and examining the impact of ketoacidosis brain damage through case studies. Additionally, it assesses the role of health informatics and artificial intelligence in improving diagnosis and treatment.

Methods: A comprehensive review was conducted of current clinical guidelines and management practices for diabetic ketoacidosis and hyperosmolar hyperglycemic state. Data was collected from recent literature on electrolyte replacement, bicarbonate therapy, and complications associated with diabetic crises. The review also included an analysis of the role of health informatics in managing these conditions, with emphasis on data integration, decision support systems, and remote monitoring. Furthermore, several diagnostic cases were examined using MRI and imaging to study the anatomical and functional brain changes in patients with ketoacidosis conditions.

Results: Effective management of diabetic crises requires careful monitoring and electrolyte replacement, with potassium and phosphate being critical. Bicarbonate therapy should be used selectively due to its potential negative effects. Common complications include seizures, organ failure, and brain edema, which require vigilant monitoring. Health informatics enhances patient care through data management, decision support, and remote monitoring, while artificial intelligence techniques show promise in improving diagnostic accuracy and efficiency.

Conclusion: Comprehensive management of diabetic crises involves addressing electrolyte imbalances and preventing complications. Data reveals changes in brain structure and function in affected individuals, with health informatics and artificial intelligence serving as valuable tools that enhance the management and outcomes of these critical conditions by facilitating accurate diagnosis, real-time monitoring, and data-driven decision-making.

Keywords: Diabetic crises, diabetic ketoacidosis, hyperosmolar hyperglycemic state, electrolyte disturbances, health informatics, artificial intelligence, machine learning, diabetes management.

Introduction:

Diabetes mellitus (DM) is a chronic metabolic disorder that impairs the metabolism of essential macronutrients, including proteins, fats, and carbohydrates (1, 2). It is a well-documented risk factor for cardiovascular disease, leading to a 2- to 4-

*Corresponding author e-mail: Nahlabreak@hotmail.com (Nahlah Salah A.Albari Burayk).
Receive Date: 14 September 2024, Revise Date: 19 October 2024, Accept Date: 23 october 2024
DOI: 10.21608/ejchem.2024.320857.10430

fold increase in mortality rates (1, 3). DM is a major global health issue, being the leading cause of kidney failure, lower-limb amputations, and adult blindness (1, 3, 4). As of 2019, the global prevalence of DM was approximately 9.3%, affecting around 463 million individuals, with projections indicating that this prevalence could rise to 10.9% (700 million) by 2045 (3). Consequently, emergency admissions due to hyperglycemic crises, such as Diabetic Ketoacidosis (DKA) and Hyperglycemic Hyperosmolar State (HHS), remain frequent and challenging (1–3). Both conditions are associated with significant mortality if not promptly treated, with the mortality rate for DKA being less than 1% and approximately 15% for HHS (1). Notably, elevated mortality rates have been observed among elderly patients diagnosed with DKA (1).

Diabetic Ketoacidosis (DKA) and Hyperglycemic Hyperosmolar State (HHS) are two distinct, yet related metabolic crises encountered in emergency settings. While both conditions are characterized by hyperglycemia, the severity of hyperglycemia is generally more pronounced in HHS. DKA, primarily associated with Type 1 Diabetes (T1D) due to absolute insulin deficiency, is distinguished by the presence of ketoacidosis. In contrast, HHS usually does not exhibit ketoacidosis unless it is a mixed variant, due to residual insulin levels sufficient to inhibit ketosis. Previously, DKA was considered specific to T1D and HHS to Type 2 Diabetes (T2D), but this distinction is becoming increasingly obsolete as more cases of DKA are observed in T2D and HHS in T1D. Moreover, the age distribution traditionally associated with acute hyperglycemic emergencies no longer holds true, and it is not uncommon to encounter patients presenting with features of both conditions simultaneously.

Both DKA and HHS necessitate urgent hospitalization, which adversely affects national healthcare economies. DKA predominantly impacts T1D and can be the initial presentation in up to 25% of cases. Recently, EDKA (Euglycemic Diabetic Ketoacidosis) has been observed in patients with T1D and T2D receiving SGLT2 inhibitors. Consequently, a high index of suspicion is required for diabetic patients on SGLT2 inhibitors presenting with symptoms without overt hyperglycemia, and EDKA should be considered. Approximately 42% of DKA hospitalizations are due to readmissions within a year. Fortunately, DKA mortality rates have decreased significantly over the past two decades, from 7.96% to under 1%. However, mortality remains elevated in patients over 60 years old with comorbidities, those in low-income countries, and among non-hospitalized patients. Current global mortality rates for HHS are estimated between 5% and 16%, highlighting the need for early diagnosis and effective prevention strategies. Access to affordable insulin globally is crucial. In children and young adults, cerebral edema is the most common cause of mortality, whereas in adults and the elderly with HHS, mortality is attributed to a range of factors including severe hypokalemia, cardiac dysrhythmia, severe hypoglycemia, ARDS, pneumonia, acute coronary syndrome (ACS), and sepsis.

To reduce hospitalization rates and acute metabolic crises in diabetes, efforts should focus on enhancing diabetes education and improving healthcare access in underdeveloped regions. Differences in management protocols for DKA, EDKA, and HHS warrant attention. This review aims to present current insights into the epidemiology, pathophysiology, management, and prevention of acute metabolic emergencies in diabetes.

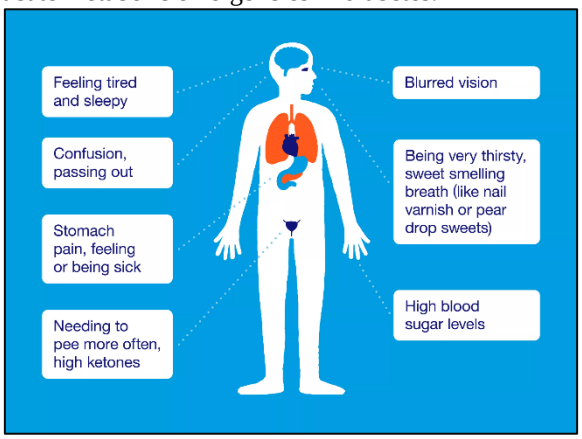

Figure 1: Diabetic Ketoacidosis (DKA).

Pathophysiology:

Diabetic Ketoacidosis (DKA) and Hyperglycemic Hyperosmolar State (HHS) share similarities in their pathophysiology, though there are notable differences. The underlying mechanisms of HHS are less well understood compared to DKA (2, 5). DKA is a complex metabolic disorder resulting from a reduction in effective insulin levels, whether absolute or relative, and an increase in counterregulatory hormones such as catecholamines, cortisol, glucagon, and growth hormones (5, 6). Hyperglycemia in DKA is driven by three primary mechanisms: enhanced gluconeogenesis, accelerated glycogenolysis, and decreased glucose utilization by peripheral tissues (7). The reduction in insulin and the rise in counterregulatory hormones exacerbate lipolysis, leading to elevated free fatty acids in the bloodstream. This, in turn, stimulates the liver to convert fatty acids into ketones through oxidation (7, 8). The increase in free fatty acids and ketones exacerbates hyperglycemia by inducing insulin resistance, ultimately causing ketonemia and metabolic acidosis (7, 8). Studies have indicated that elevated glucose and fatty acid levels contribute to a pro-inflammatory and oxidative state in DKA patients (9, 10). Oxidative stress, characterized by an

increase in reactive oxygen species (ROS), leads to cellular damage affecting lipids, membranes, and proteins (9). This oxidative state also heightens the risk of chronic diabetic complications following a DKA episode (9). Elevated levels of inflammatory cytokines such as IL-6, IL-1β, IL-8, and TNF-α further diminish the efficacy of insulin therapy. Therefore, insulin treatment and hydration are crucial for normalizing these parameters (9).

In contrast, HHS is marked by relatively preserved insulin production, which prevents significant ketogenesis and lipolysis (4). Consequently, patients with HHS exhibit mild to moderate ketonemia and acidemia. HHS is primarily characterized by severe hyperglycemia and hyperosmolality (4, 5). The extreme hyperosmolality in HHS leads to osmotic diuresis, causing substantial dehydration and greater fluid loss compared to DKA (4, 5). This extensive loss of intracellular fluids results in markedly elevated blood glucose levels in HHS compared to DKA (4, 5). Euglycemic DKA, a relatively recent and unique presentation of DKA, is characterized by a blood glucose level below 250 mg/dl while still presenting symptoms of DKA (6, 11). The precise pathophysiology of euglycemic DKA remains unclear, but it has been associated with various factors including diabetes treatment regimens, carbohydrate restriction, high alcohol consumption, and inhibition of gluconeogenesis (6, 11). Additionally, it can be induced by certain medications, most notably sodium-glucose cotransporter 2 (SGLT-2) inhibitors and insulin (6, 11).

Diagnosis:

Signs and Symptoms:

Diabetic Ketoacidosis (DKA) typically progresses more rapidly than Hyperglycemic Hyperosmolar State (HHS). In some instances, DKA can develop within a few hours following the precipitating factor (12). Both conditions present with common symptoms of hyperglycemia, including polyuria, polydipsia, weakness, and alterations in mental status (6, 12). Additionally, a fruity odor on the patient's breath may be noticeable in DKA cases. Both DKA and HHS are also associated with signs of dehydration such as dry mucous membranes, poor skin turgor, tachycardia, hypotension, and delayed capillary refill, especially in severe dehydration (8, 12). In advanced stages of DKA, untreated cases can lead to unconsciousness (6).

Laboratory Findings:

The initial laboratory evaluation for patients suspected of DKA or HHS should encompass measurements of blood glucose (BG), blood urea nitrogen, serum creatinine, serum ketones, electrolytes, anion gap, osmolality, urine ketones, and arterial blood gases (6, 8). To differentiate chronic hyperglycemia from acute metabolic decompensation in a previously well-controlled diabetic patient, assessment of HbA1c is crucial (6). DKA severity is classified as mild, moderate, or severe based on the level of acidosis and the patient's mental status. A key diagnostic criterion for DKA is elevated circulating blood ketones and high anion gap metabolic acidosis, defined as an anion gap >12 (4, 6). Other causes of high anion gap metabolic acidosis, such as ethylene glycol toxicity, isoniazid overdose, lactic acidosis, methanol toxicity, propylene glycol ingestion, salicylate toxicity, and uremia, must be excluded (13). Most patients with DKA exhibit blood glucose levels >2 mg/dL, bicarbonate levels between 10-15 mEq/L, and elevated anion gap metabolic acidosis 12 (4, 6). Occasionally, HHS patients may present with mild acidosis (pH >7.30 and bicarbonate level >20 mEq/L) and negative plasma and urine ketone tests (4). HHS patients with higher levels of osmolarity and pH often experience more severe dehydration and impaired mental status (4). A distinguishing diagnostic criterion for HHS is the severe elevation in serum osmolality (>320 mOsm/kg) (4, 6).

DKA Onset:

Diabetic Ketoacidosis (DKA) is primarily triggered by a shortage of insulin in the body, which leads to a series of metabolic disturbances. The main causes of DKA onset include:

1. **Infection**: Infections, such as pneumonia or urinary tract infections, are common precipitating factors. They can cause increased insulin resistance and elevated stress hormone levels, which exacerbate hyperglycemia and ketogenesis (1).
2. **Inadequate Insulin Therapy**: Missing insulin doses or insufficient insulin administration can lead to DKA. This might occur in individuals with Type 1 Diabetes (T1D) who are not managing their insulin regimen properly or in patients who have transitioned from hospital to home care and are not adhering to their prescribed insulin therapy (2).
3. **New-Onset Diabetes**: DKA can be the initial presentation of undiagnosed diabetes, particularly in individuals who have had undetected Type 1 Diabetes (T1D) (3).
4. **Severe Stress or Trauma**: Physical or emotional stress, such as surgery, trauma, or severe illness, can trigger DKA by increasing the production of stress hormones that counteract insulin and promote ketogenesis (4).
5. **Dehydration**: Significant fluid loss, often from gastrointestinal issues like vomiting or diarrhea, can worsen DKA by concentrating blood glucose and ketones and reducing insulin effectiveness (5).
6. **Poor Diabetes Management**: Factors such as non-compliance with dietary recommendations, missed insulin doses, or

incorrect insulin administration can precipitate DKA (6).

7. **Medications**: Certain medications, such as corticosteroids or SGLT2 inhibitors, can contribute to DKA by increasing blood glucose levels or affecting insulin action (7).
8. **Alcohol or Drug Abuse**: Excessive alcohol intake or the use of recreational drugs can disrupt glucose metabolism and insulin regulation, leading to DKA (8).
9. **Other Medical Conditions**: Conditions such as pancreatitis or severe illness unrelated to diabetes can also precipitate DKA by affecting insulin production or metabolism (9).

These triggers lead to a deficiency of insulin, which in turn causes hyperglycemia, increased lipolysis, and ketogenesis, ultimately resulting in the clinical manifestation of DKA.

Treatment and Therapeutics

The resolution of Diabetic Ketoacidosis (DKA) involves correcting dehydration, hyperglycemia, and electrolyte imbalances. The target parameters for DKA resolution are: blood glucose (BG) < 200 mg/dL, along with at least two of the following: a serum bicarbonate level ≥ 15 mEq/L, a venous pH > 7.3, and a calculated anion gap ≤ 12 mEq/L (6, 8). For Hyperglycemic Hyperosmolar State (HHS) resolution, normal osmolality must also be achieved (6, 8). It is essential to review the patient's history to identify and address any modifiable precipitating factors to prevent recurrence (6). Many cases of DKA and HHS can be avoided through effective patient education and access to chronic diabetes medications (6). **Figure 2** outlines a suggested management pathway for DKA and HHS according to the American Diabetes Association (ADA) 2009 guidelines and the Joint British Diabetes Societies for Inpatient Care (JBDS-IP) 2021 revised guidelines (1, 14).

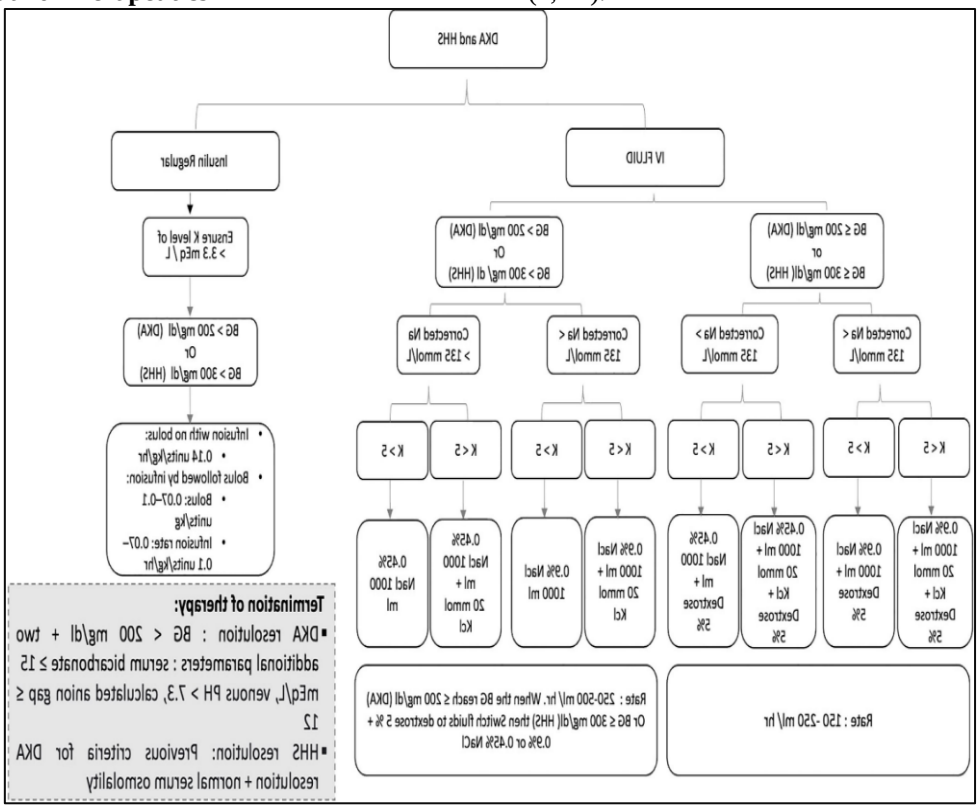

Figure 2: Management pathway for DKA and HHS according to the American Diabetes Association (ADA).

Fluid Management and Stewardship:

Fluid therapy is critical in managing DKA and HHS. Aggressive repletion with isotonic saline is fundamental for expanding extracellular volume and stabilizing cardiovascular function (15). This approach also helps to reduce BG levels by up to 80% in the initial hours of rehydration, reverses ketosis, and decreases serum osmolality, thereby increasing insulin sensitivity (16). Initial fluid management practices follow the ADA guidelines 2009 for hyperglycemic crises in adults with diabetes. The recommended approach involves administering a 0.9% sodium chloride intravenous (IV) bolus at a rate of 15-20 mL/kg per hour, approximately 1 to 1.5 L/hour, to address hypovolemia and facilitate hemodynamic resuscitation (1). After two to three hours of initial fluid replacement, the choice of fluid type and infusion rate should be adjusted based on corrected sodium concentration (corrected sodium = measured sodium + [1.6 (glucose – 100) / 100]), serum glucose

levels, and the patient's volume status. Subsequent fluid choices, such as 0.45% sodium chloride or 0.9% sodium chloride, should be administered at a rate of 250 to 500 mL/hour, depending on the corrected serum sodium level (1, 17).

During fluid replacement, hyperglycemia is expected to be corrected more rapidly than ketoacidosis and DKA resolution (1). Once serum glucose falls to approximately 200 mg/dL, intravenous fluid should be switched to a mixture of 5% dextrose with 0.45% sodium chloride (1). Ongoing assessment of serum osmolality, urine output, and cardiac function is necessary to guide fluid administration and avoid iatrogenic overload (1). These recommendations are based on expert opinion and tracer studies evaluating fluid repletion in DKA patients, though clinical trials on the efficacy and safety of different crystalloid solutions are lacking (1). The use of 0.9% sodium chloride for fluid resuscitation is known to cause hyperchloremic acidosis (HA) due to its high chloride ion content (18). As an alternative, some practitioners use balanced fluids, which may offer a more physiologically appropriate composition and potentially expedite the resolution of acidosis (18-19).

Fluid Management:

Recent trials have compared the effects of balanced crystalloids and 0.9% sodium chloride (normal saline) in managing DKA. Small trials suggested that balanced fluids might improve insulin sensitivity or expedite bicarbonate correction and acidosis resolution (20, 21). A post-hoc analysis of the SALT-ED and SMART trials revealed that balanced crystalloids resulted in a shorter median time to DKA resolution compared to saline (13.0 vs. 16.9 hours; 95% CI, 1.18-2.38; P = .004) and a shorter median time for insulin discontinuation (9.8 vs. 13.4 hours; 95% CI, 1.03-2.03; P = 0.03) (22). The SCOPE-DKA trial found no significant difference in DKA resolution at 48 hours or length of ICU and hospital stay between balanced fluids (Plasmalyte-148) and saline, but the Plasmalyte-148 group reached DKA resolution more quickly at 24 hours (69% vs. 36%; 95% CI 1.68–10.72, p = 0.002) (23).

Insulin Dosing:

Insulin is a critical component of DKA and HHS management, acting to reduce hepatic glucose production, enhance peripheral glucose uptake, and inhibit lipolysis, ketogenesis, and glucagon secretion (2, 6, 24). Insulin should be administered immediately after initial fluid resuscitation (2, 6, 24). The primary goal of insulin therapy is to close the anion gap caused by ketone body production, rather than solely achieving euglycemia (6, 24). Intravenous insulin can be given as a continuous infusion of regular insulin in 0.9% NaCl or D5W, or as intravenous glulisine insulin (2, 25, 26). Standard dilution is 1 unit/mL, though more concentrated solutions (16 units/mL) can be used if necessary (25). Frequent subcutaneous or intramuscular injections are also options for mild to moderate DKA, but continuous intravenous infusion is preferred for its rapid onset and easy titration (6, 24).

Current recommendations suggest a continuous infusion rate of 0.14 units/kg/hr without an initial loading dose (27, 28). Loading doses can increase the risk of cerebral edema and worsening shock and are thus avoided at the start of treatment (29). However, an insulin loading dose of 0.07–0.1 units/kg over 5 minutes, with a low-dose continuous infusion, may be utilized to achieve target BG and anion gap (27, 28). Factors such as blood glucose reduction rate, insulin sensitivity, and nutritional status should be considered when titrating insulin infusion (2). Rapid BG reduction is associated with cerebral edema risk (2). High insulin sensitivity is seen in the elderly, those with renal dysfunction, and patients with low daily insulin requirements (2). Insulin infusion rates may be adjusted around mealtimes and continued at a higher rate post-meal (2). For NPO patients, BG should be closely monitored, and maintenance fluids should include 5% dextrose once BG drops below 250 mg/dL (2).

Comparative trials found no significant differences between insulin dosing strategies (27, 28). The use of an insulin loading dose has been linked to an increased risk of cerebral edema (27, 28). For mild to moderate DKA, a subcutaneous bolus of 0.2 units/kg of rapid-acting insulin, followed by 0.1–0.2 units/kg every 1–3 hours until BG falls below 250 mg/dL, is an alternative approach (30, 31). Recommended BG reduction rates are 50-75 mg/dL/hr for patients with normal renal function, with a 50% reduction in insulin dosing for those with kidney disease to reduce hypoglycemia risk while maintaining euglycemia (BG: 140–180 mg/dL) (30, 31). Patients with end-stage renal disease (ESRD) and acute kidney injury (AKI) require cautious management to avoid rapid osmolality changes and hypoglycemia; initial infusion rates should be 0.05–0.07 units/kg/hr with close BG monitoring, adjusting as needed (32, 33).

Transition from Intravenous to Subcutaneous Insulin in DKA Management:

Transitioning from intravenous to subcutaneous insulin is crucial once DKA resolution is achieved, defined as a blood glucose (BG) level <200 mg/dL and meeting at least two of the following criteria: serum bicarbonate level ≥15 mEq/L, venous pH >7.3, and a calculated anion gap ≤12 mEq/L, along with the ability to accept oral dietary intake (6, 24). To ensure a smooth transition, subcutaneous insulin should overlap with intravenous insulin for at least 30-60 minutes before discontinuation (6, 24).

The Joint British Diabetes Societies guidelines recommend continuing long-acting insulin

analogs during the initial management of DKA, as these provide basal insulin coverage when intravenous insulin is discontinued (6, 24). After DKA resolution, transitioning to subcutaneous long-acting insulin, combined with ultra-short acting insulins such as glargine or glulisine, can help reduce hypoglycemic events compared to other regimens like NPH insulin and regular insulin (24, 25). For newly diagnosed insulin-dependent diabetes patients, subcutaneous insulin is generally started at a dose of 0.5-0.7 units/kg/day (24, 25). For patients who were using insulin or antidiabetic agents prior to DKA admission, the transition process remains less well-defined (24, 25). In ICU settings, clinicians often discontinue all oral antidiabetic agents and rely on insulin regimens due to insulin's shorter half-life and predictable action (24, 25). This area may benefit from further investigation to determine the optimal transition strategies and their impact on patient outcomes (24, 25). Additionally, insulin sequestration in plastic IV tubing can lead to insulin wastage and dosing inaccuracies. Flushing the IV tube with 20 mL of priming fluid is recommended to minimize insulin losses (34, 35).

Electrolytes Management in Hyperglycemic Crises

Potassium Therapy:

Patients with hyperglycemic crises are at increased risk of hypokalemia due to several factors, including insulin therapy, correction of acidosis, and hydration (1, 29). Additionally, volume depletion can lead to secondary hyperaldosteronism, exacerbating hypokalemia by increasing urinary potassium excretion (1, 29).

- **Initial Serum Potassium Assessment:** Measure serum potassium upon presentation and before starting insulin therapy (1, 29).
- **Replacement Strategy:** Potassium replacement is generally required, regardless of initial serum potassium levels, due to hydration and insulin therapy, except in cases of renal failure (1, 29). A common approach is to administer 20–30 mEq of potassium per liter of intravenous fluid to maintain normal serum potassium levels (1, 29).
- **Thresholds for Replacement:** If baseline serum potassium is > 5.2 mEq/L, potassium replacement may not be immediately necessary (1). If baseline potassium is < 3.3 mEq/L, insulin therapy should be delayed until potassium is replaced and levels are > 3.3 mEq/L (1, 29).

Phosphate Therapy

Hypophosphatemia is another potential electrolyte disturbance during hyperglycemic crises, due to osmotic diuresis and the intracellular shift of phosphate (1, 29).

- **Indications for Replacement:** Phosphate replacement is not routinely required unless severe hypophosphatemia is present (serum phosphate < 1 mg/dL) to avoid symptoms like muscle weakness, respiratory depression, and seizures (1, 29).
- **Replacement Dosage:** If needed, 20–30 mEq/L of potassium phosphate may be administered (1, 29). Caution is advised due to the risk of secondary hypocalcemia (1, 29, 36).

Bicarbonate Therapy

Acidemia in DKA is due to the overproduction of ketoacids, leading to various physiological disturbances including impaired myocardial contractility and systemic vasodilation (37, 38). Sodium bicarbonate therapy is controversial and should be used selectively:

- **Clinical Benefit:** Evidence shows a lack of consistent benefit from bicarbonate therapy in DKA management. Its use is generally limited to severe cases with a pH < 6.9 and life-threatening hyperkalemia (37–42).
- **Adverse Effects:** Sodium bicarbonate can cause hypernatremia, hypocalcemia, hypokalemia, and metabolic alkalosis, and may increase the risk of side effects like impaired myocardial contractility and altered hemoglobin-oxygen affinity (39, 40).
- **Administration:** If bicarbonate therapy is deemed necessary due to severe acidosis or hyperkalemia, administer 1 mL/kg of 8.4% sodium bicarbonate solution or 50-100 mEq in 1 liter of IV fluid. This should be given until pH rises above 6.9 (42).

In summary, effective management of electrolyte disturbances in hyperglycemic crises involves careful monitoring and appropriate replacement strategies for potassium, phosphate, and bicarbonate, tailored to the patient's clinical condition and response to treatment.

Complications of Hyperglycemic Crisis

Prompt and effective therapy for hyperglycemic crises is critical to minimize complications and reduce morbidity and mortality (6, 43). If left untreated or managed inadequately, hyperglycemic crises can lead to severe complications, including:

- **Seizures, Organ Failures, Coma, and Death:** Mortality rates are notably high in the first 48–72 hours, often due to precipitating causes, electrolyte imbalances (e.g., hypo- or hyperkalemia), and cerebral edema (43). Mortality from Hyperosmolar Hyperglycemic State (HHS) tends to be higher than that of Diabetic Ketoacidosis (DKA), particularly in older patients. When

adjusted for age, this prognosis difference is still significant (43).

- **DKA Complications:**
  - **Prolonged Hypotension:** Can lead to acute myocardial infarction and bowel infarction (6, 44).
  - **Kidney Dysfunction:** The kidney's role in correcting pH and electrolyte imbalances is crucial. Pre-existing kidney dysfunction or end-stage chronic kidney disease can significantly worsen prognosis (6, 44).
- **HHS Complications:**
  - **Severe Dehydration:** Increases the risk of myocardial infarction, stroke, pulmonary embolism, mesenteric vein thrombosis, and disseminated intravascular coagulation (6, 44).
  - **Venous Thromboembolism (VTE):** Data indicates that hospitalized HHS patients have a comparable risk of VTE to sepsis (HR = 16.3; 95% CI: 10-25), which is higher than in diabetic patients without hyperglycemic crises (45).

Management-Associated Complications:

- **Electrolyte Abnormalities:** Includes hypo- or hyperkalemia, often exacerbated by insulin and fluid replacement therapies. Hypoglycemia also occurs in about 25% of treated patients, necessitating frequent monitoring of electrolytes and blood glucose levels (4, 5).
- **Cerebral Edema:** Though rare in adults, cerebral edema is a severe complication in children and adolescents. It is hypothesized to result from rapid hydration and severe acidosis. Preventive measures include maintaining blood glucose concentrations above 250-300 mg/dL and avoiding rapid drops in serum osmolality (>3 mOsm/kg/hour) (7, 48). Treatment with mannitol or hypertonic saline can be effective in preventing neurological deterioration (7, 48). Risk factors include elevated blood urea nitrogen (BUN) and sodium concentrations (46).

Other Serious Complications:

- **Transient Acute Kidney Injury (AKI):** Occurs as a complication of hyperglycemic crises (7).
- **Pulmonary Edema:** Particularly in patients with pre-existing congestive heart failure (7).
- **Myocardial Infarction:** Risk is elevated due to severe dehydration and other factors (7).
- **Pancreatitis:** An increase in pancreatic enzymes can occur with or without acute pancreatitis (7, 24).
- **Cardiomyopathy and Rhabdomyolysis:** Seen in patients with severe dehydration (7, 24).

Summary: Effective management of hyperglycemic crises requires vigilant monitoring and proactive management of potential complications. Ensuring rapid and appropriate therapy while closely monitoring for electrolyte imbalances, cerebral edema, and other serious conditions is essential to improving patient outcomes.

Neurological Findings:

Case-1:

A 9-year-old male with persistently inadequately managed type 1 diabetes mellitus (DM1) was admitted to our pediatric neuro-intensive care unit presenting with diabetic ketoacidosis (DKA) and a Glasgow Coma Scale (GCS) score of 6. During his stay, the child exhibited spastic quadriplegia with decorticate posturing and retraction of all four limbs in response to painful stimuli. Baclofen was initiated to address the spasticity. Due to an autonomic crisis, Midazolam and Diazepam were initially administered, later being gradually phased out in favor of Clobazam. After 7 days, a tracheostomy was performed, and the patient maintained eupnea. We encountered significant challenges in glycemic management, necessitating ad hoc insulin boluses to keep blood glucose levels below 300 mg/dl. Transitioning to enteral nutrition through percutaneous endoscopic gastrostomy (PEG), combined with subcutaneous insulin, proved effective in managing blood glucose levels. A ventricular-peritoneal shunt was inserted to manage elevated intracranial pressure (ICP), recorded at 23 mmHg over a continuous 1-hour period [4]. Both brain computed tomography (CT) and brain magnetic resonance imaging (MRI) were conducted at admission and throughout hospitalization. Alongside conventional imaging techniques, advanced imaging sequences were utilized to more precisely delineate the neural substrates associated with potentially residual sensorimotor functions [49].

The brain CT scan revealed indications of intracranial hypertension, including diffuse sulcal effacement, diminished visibility of the basal cisterns, a narrowed third ventricle, subtle hypodensity, and edema in the thalami and occipital lobes, attributed to ischemia in the posterior cerebral artery (PCA) territories resulting from prior central brain herniation and arterial insufficiency. The brain MRI demonstrated diffuse cerebral edema, with extensive confluent areas of T2-FLAIR hyperintensity and restricted diffusion affecting the thalami, hypothalamus, optic chiasm, anterior perforated substance, fornix, subfrontal regions, cerebral peduncles, periaqueductal gray matter, globus pallidi, caudate nuclei, hippocampi/parahippocampal gyri, posterior cingulate gyri, occipital lobes, and the splenium of

the corpus callosum (**Figure 3**). Additionally, mild bilateral uncal herniation was observed, causing effacement of the perimesencephalic cisterns, sagging of the brainstem, and descent of the midbrain through the incisura, accompanied by signs of Duret's hemorrhage (**Figure 3**). Three-dimensional time-of-flight magnetic resonance angiography (3D-TOF MRA) and phase-contrast magnetic resonance venography (PC-MRV) did not reveal any abnormalities (**Figure 3**). Follow-up brain MRIs indicated ongoing malacic changes in the parenchymal lesions and progressive dilation of the supratentorial ventricular system (**Figure 3**) [49].

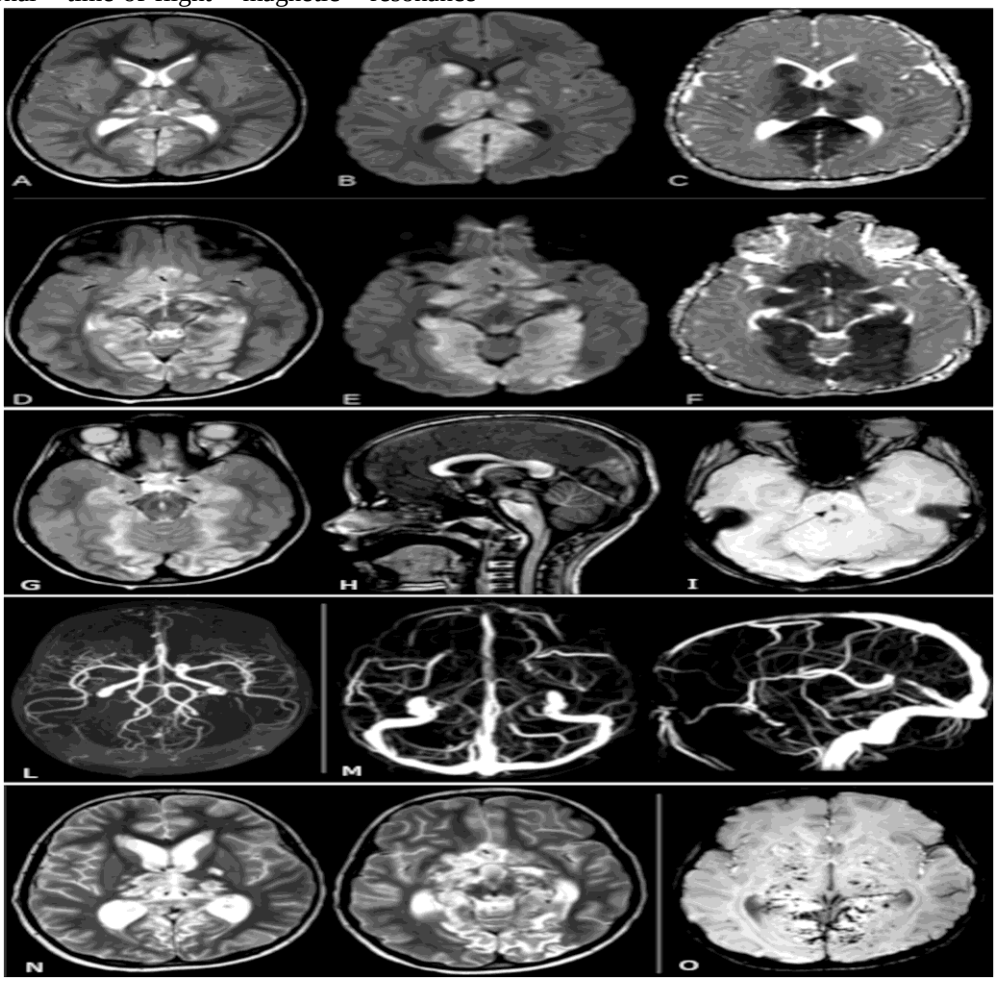

Figure 3: ADC sequences showing the presence of large areas of T2 hyperintensity and restricted diffusion consistent with striking parenchymal ischemia.

Advanced MRI Imaging: Techniques and Findings (DTI and fMRI)

The examination of white matter sensory pathways was conducted using diffusion tensor imaging (DTI), while cortical sensory processing was evaluated through functional MRI (fMRI). Imaging was performed on a 3 T scanner (Achieva, Philips Healthcare, Best, the Netherlands). The protocol included a DTI sequence with 64 diffusion encoding directions and three fMRI sequences involving tactile stimulation of the patient's hands and feet using a block design with 15-second on/off intervals. The DTI data were processed using Tortoise (Pierpaoli et al., 2010), Diffusion Toolkit, and Trackvis (Wang et al., 2007) software. This involved realignment, anatomical T1 volume registration, correction for motion and eddy current distortions, and upsampling of diffusion images to a final voxel size of 1.5 mm. Virtual dissection was performed on the bilateral corticospinal tract (CST) and the arcuate fasciculus (AF) in its three segments (frontoparietal, frontotemporal, and temporoparietal, as described in Catani, 2005). The fMRI data were imported into Brain Voyager software (Brain Innovation, Maastricht, the Netherlands) and underwent preprocessing, including 3D motion correction and spatial smoothing. Activation maps for each stimulation area on the left and right sides were generated [49].

The DTI analysis indicated that the thalamic lesion impacted the thalamic-cortical projections of the somatosensory white matter pathways. In the tractographic representation, these projections appeared disrupted, while the spinal-thalamic pathway remained intact. There was a slight left/right asymmetry, with thinner right cortical projections

compared to the left, which was consistent with conventional MRI findings showing more severe lesions in the right thalamus. On the left side, there was also increased directional coherence between higher and lower projections, potentially indicating residual white matter integrity supporting cortical activity. For fMRI, only the sensory activations from foot stimulation were considered due to significant involuntary head motion during hand stimulation. Stimulation of the right foot elicited robust activation in the left sensorimotor cortex. Notably, stimulation of the left foot also produced overlapping activation in the same left, ipsilateral region, though to a lesser extent. This ipsilateral activation for the left foot reached statistical significance at the threshold (<0.001) after Bonferroni correction for multiple comparisons. These findings suggest selective damage to the right subcortical sensory pathways and a possible contralateral cortical reorganization for processing tactile information (**Figure 4**).

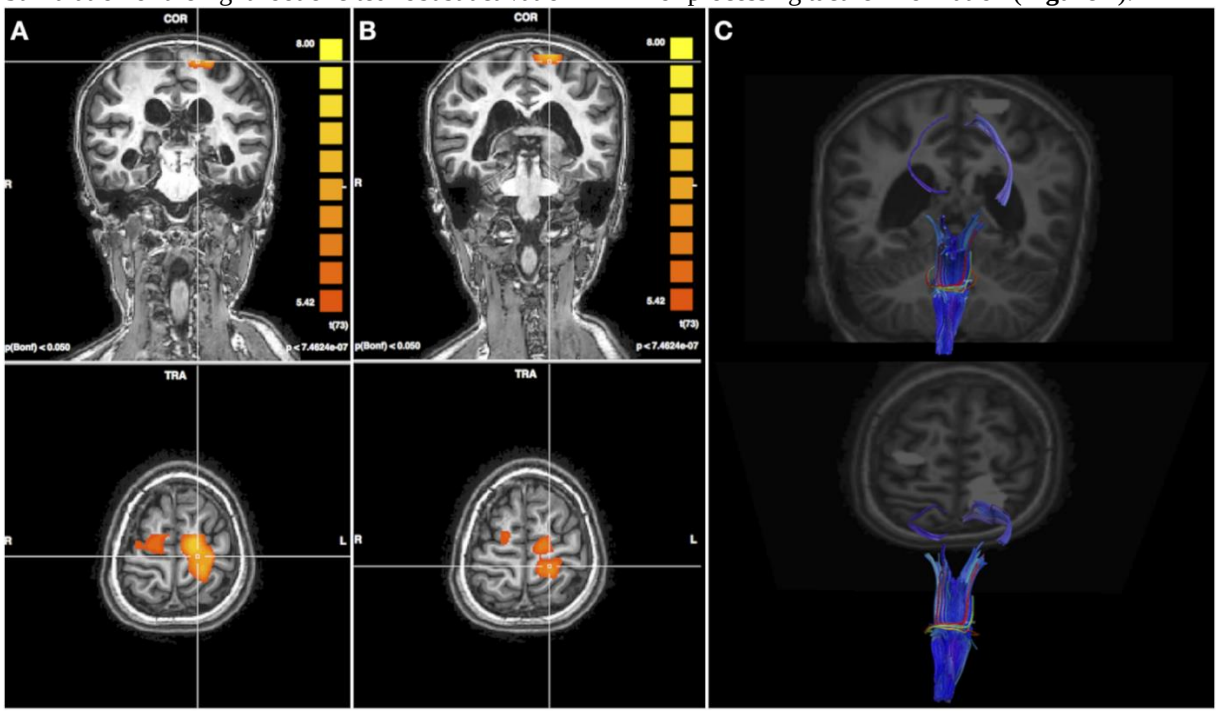

Figure-4: (a) fMRI activation maps for right foot tactile stimulation displayed on T1 axial and coronal views. (b) fMRI activation maps for left foot tactile stimulation shown in the same projections. (c) Tractographic reconstruction demonstrated partial disruption of sensory white matter pathways, with more pronounced impairment observed in the right pathway, aligning with the greater involvement of the ipsilateral thalamus as indicated by conventional MRI. Functional activation clusters are also overlaid in light grey.

Diabetic ketoacidosis (DKA) is a well-recognized complication of type 1 diabetes mellitus (DM1) that affects approximately one-third of children with DM1 under the age of 5 [49]. In rare instances, DKA can result in significant central nervous system (CNS) injury, leading to adverse long-term neurocognitive and sensorimotor outcomes. Notable feared complications include cerebral edema, central brain herniation, and diffuse ischemic-hemorrhagic damage [49]. Literature suggests that the mechanisms underlying brain injury in DKA may involve a combination of intracranial hypertension and a metabolically induced proinflammatory state accompanied by vascular endothelial dysfunction. The metabolic disturbances contribute to hyperosmolarity and increased blood viscosity, endothelial damage, acidemia-induced stiffness of red blood cells, and hyperglycemia-related vasoconstriction. These factors collectively lead to brain edema and intracranial hypertension, resulting in mechanical compression and stretching of major vessels [49]. A comprehensive description of brain manifestations in DKA through conventional imaging is limited in the literature [49]. Barrot described two cases of DKA with acute CNS involvement, where neuroimaging revealed brain edema causing secondary signs of intracranial hypertension, such as sulcal effacement, effacement of the basilar cisternal spaces, reduced cerebral ventricular size, and ischemic changes in the PCA territories [49]. In the current case, elevated intracranial pressure due to cerebral edema resulted in uncal herniation, midbrain sagging, and severe central brain herniation, leading to extensive ischemic areas. Advanced imaging techniques were employed to further characterize the neural substrates of potentially residual sensorimotor function. Diffusion tensor imaging (DTI) and tractography reconstruction were utilized to assess the integrity of white matter somatosensory pathways, while functional MRI (fMRI) evaluated cortical sensory processing. Notably, tactile

stimulation of both feet produced robust activation in the left sensorimotor cortex. It is hypothesized that the predominant damage to the right subcortical sensory pathways, consistent with conventional MRI findings showing more severe involvement of the right thalamus, may have prompted early cortical reorganization in the left hemisphere, where subcortical projection fibers appeared more preserved. Figure 2 illustrates the spatial congruity between the left corticothalamic tract and the cortical activations in the left sensorimotor cortex, triggered by stimulation of both lower limbs. This imaging representation may reflect the anatomical substrate underlying functional plasticity. The advanced MRI findings, which document residual somatosensory function and signs of initiated neural plasticity, facilitated the referral of the patient to a specialized rehabilitation center.

Case-2:

The first patient is a girl who was initially diagnosed with type 1 diabetes mellitus (DM1) at age 11. Despite initiating medication and dietary management, her blood glucose levels remained poorly controlled, leading to two episodes of diabetic ketoacidosis (DKA) and brief admissions to our tertiary pediatric hospital. Several months later, she presented to the emergency department (ED) with acute abdominal pain, headaches, vomiting, and altered mental status. A diagnosis of a new episode of DKA was confirmed. Her mental status rapidly deteriorated, with a Glasgow Coma Scale (GCS) score dropping from 11 to 3, necessitating intubation and transfer to the pediatric intensive care unit (PICU). Acute head computed tomography (CT) revealed diffuse hypodensity of the cerebral white matter, sulcal effacement, compression of the third ventricle and basal cisterns, and crowding of the foramen magnum, indicative of severe diffuse brain edema and early tonsillar herniation (**Figure 5**). An intracranial pressure monitoring device was placed, and conservative management for acute intracranial hypertension was initiated. The GCS improved to 8–9 [50].

One week later, brain magnetic resonance imaging (MRI) showed focal areas of hyperintensity on T2-weighted and fluid-attenuated inversion recovery (FLAIR) images, with corresponding bright signals on trace diffusion maps and low apparent diffusion coefficient (ADC) values in the left posterior lateral pons, left posterior limb of the internal capsule, bilateral anterior medial thalami, and body of the corpus callosum (**Figure 6**). Additionally, focal areas of hyperintensity on T2-weighted and FLAIR images with high ADC values were observed in the left inferior olivary nucleus, left paracentral posterior pons, left posterior lateral thalamus, right posterior limb of the internal capsule, right genu of the internal capsule, and bilateral medial thalamus (**Figure 6**). These findings were consistent with multiple areas of acute and subacute to early chronic ischemic injury, likely secondary to increased intracranial hypertension. After two weeks in the PICU, she was extubated and transferred to the general ward, where she was partially responsive to verbal or painful stimuli and exhibited extensor posturing in her limbs. Rehabilitation therapy was initiated on the ward, leading to continued neurological improvement. Six months post-admission, she could speak, albeit with dysarthria, and was wheelchair-dependent. She also presented with bilateral dysmetria, left facial nerve palsy, spasticity in both arms and legs, and dysphagia requiring gastrostomy tube feeding [50].

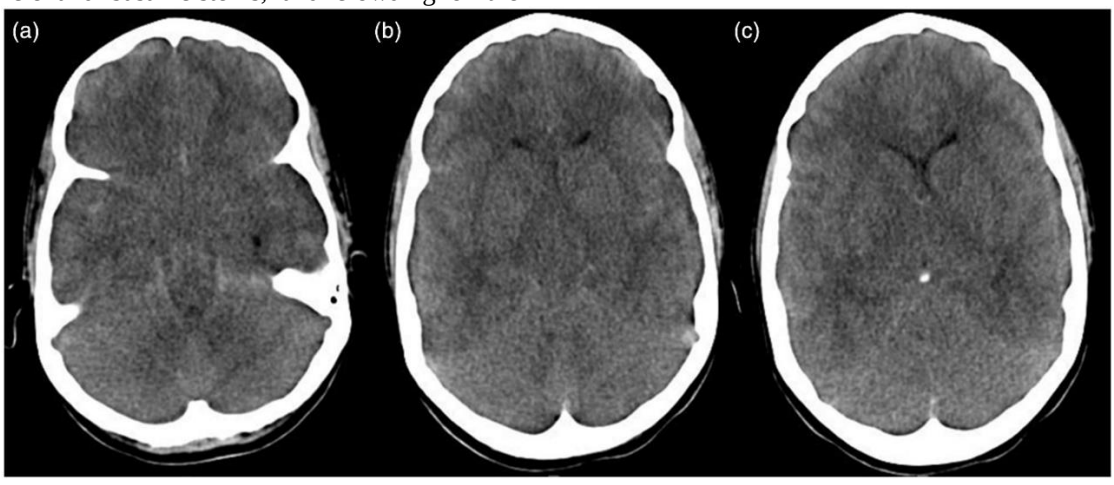

Figure-5: Acute axial computed tomography (CT) images of Patient 1 reveal diffuse cerebral edema characterized by hypodense brain parenchyma and the effacement of sulci and basal cisterns .

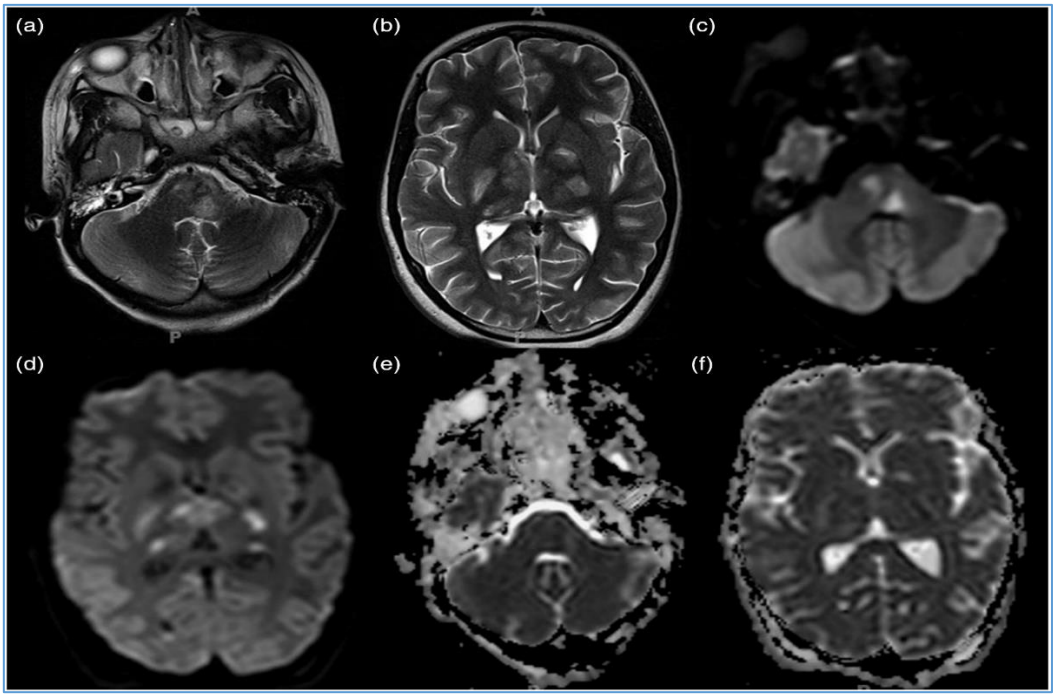

Figure 6: Follow-up axial T2-weighted MR images (Figures (c), (d)), trace of diffusion images, and ADC maps (Figures (e), (f)) of Patient 1, conducted one week after the CT (Figure 5), reveal T2-hyperintense signals corresponding with bright signals on trace diffusion images and low ADC values in the left posterior lateral aspect of the pons, left posterior limb of the internal capsule, bilateral anterior medial thalami, and the genu of the corpus callosum. Additionally, focal areas of T2-hyperintense signals with high ADC values are observed in the left inferior olivary nucleus, left paracentral posterior pons, left posterior lateral thalamus, right posterior limb of the internal capsule, right genu of the internal capsule, and bilateral medial thalami. MR: magnetic resonance; ADC: apparent diffusion coefficient; CT: computed tomography.

Case-3:

The third patient is a 5.8-year-old girl who was initially diagnosed with type 1 diabetes mellitus (DM1) at age 3.5. Despite starting medicamentous therapy and dietary management, her blood glucose levels remained poorly controlled, as evidenced by elevated glycated hemoglobin. She presented to the emergency department (ED) of our tertiary pediatric hospital with acute onset of vomiting, diarrhea, and altered mental status, leading to a diagnosis of diabetic ketoacidosis (DKA). Clinical examination revealed absent pupillary reactions bilaterally, no spontaneous movement in the extremities, and lack of response to stimuli. She was intubated and transferred to the pediatric intensive care unit (PICU). Head computed tomography (CT) indicated diffuse effacement of the sulci and basal and suprasellar cisterns, suggestive of global cerebral edema with impending transtentorial herniation (**Figure 7**). Additionally, hypodensity in the left posterior cerebral artery (PCA) territory raised concerns of an acute/subacute ischemic stroke (Figure 3). Conservative management for cerebral edema was initiated. A brain magnetic resonance imaging (MRI) conducted the following day revealed bright signals on trace diffusion maps with corresponding reduced apparent diffusion coefficient (ADC) values in the left PCA distribution, confirming the ischemic stroke (**Figure 8**). Small areas of restricted diffusion were also observed in the bilateral medial thalami, midbrain, bilateral amygdala, posterior inferior aspects of the bilateral frontal lobes, and right medial temporal lobes (**Figure 8**). The distribution of these predominant midline ischemic lesions is likely attributable to transtentorial herniation. Susceptibility-weighted imaging (SWI) showed multiple small areas of susceptibility artifact within the left PCA infarct, indicating partial hemorrhagic transformation. The patient's neurological status gradually improved, and she was extubated and transferred to the clinical ward after approximately two weeks in the PICU. Rehabilitation therapy was initiated on the ward, leading to further neurological improvement. Five months post-admission, she was alert and cooperative, with fluent speech and normal sensory and motor exams of all extremities. Her neurological examination did reveal right anisocoria, homonymous hemianopsia, and reduced short-term memory. Follow-up MRI at this stage showed chronic encephalomalacic changes in the left PCA territory, bilateral medial thalami, midbrain, bilateral amygdala, posterior inferior aspects of the bilateral frontal lobes, and right medial temporal lobes (not shown). At the final follow-up two years post-admission, her neurological status remained stable [50].

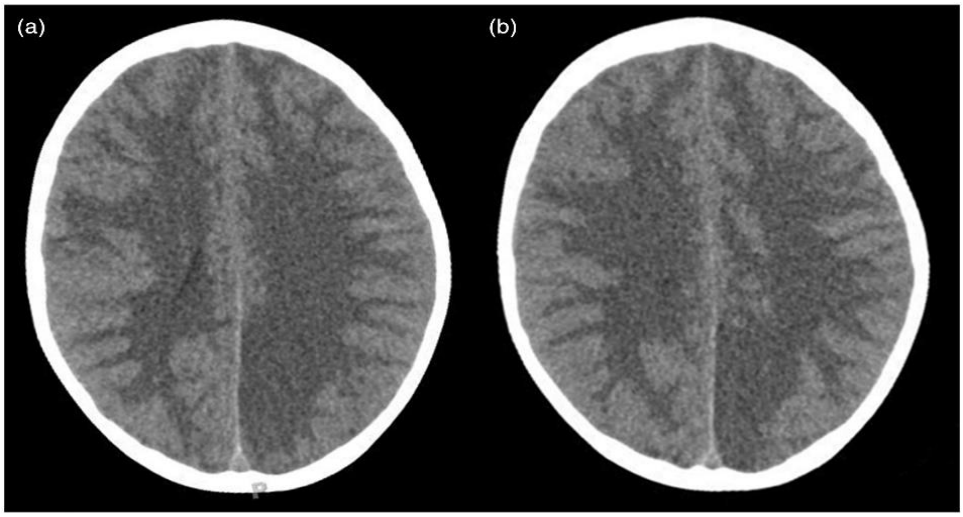

Figure 7: Acute axial CT images of patient 2 show diffuse effacement of the sulci and basal and suprasellar cisterns suggestive of global cerebral edema.

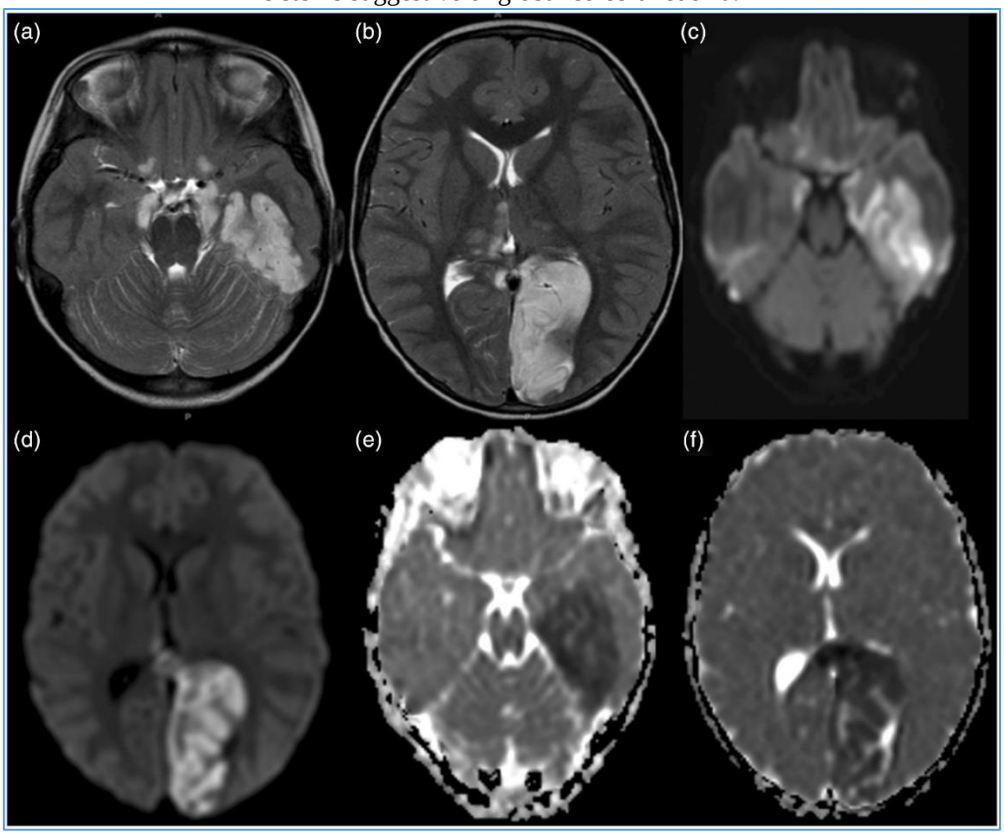

Figure 8: Axial T2-weighted MR images (Figures (c), (d)), trace of diffusion images, and ADC maps (Figures (e), (f)) of Patient 2, performed the day after the CT (Figure 7), demonstrate T2-hyperintense signals with corresponding bright signals on trace diffusion images and reduced ADC values within the vascular territory of the left posterior cerebral artery, confirming the presence of an acute/subacute arterial ischemic stroke. Additionally, T2-hyperintense foci with restricted diffusion are observed in the bilateral medial thalami, midbrain, bilateral amygdala, posterior inferior aspects of the bilateral frontal lobes, and left medial temporal lobe. These latter findings are likely secondary to transtentorial herniation. MR: magnetic resonance; ADC: apparent diffusion coefficient; CT: computed tomography.

Diabetic Ketoacidosis (DKA) and Neuroimaging Findings in Pediatric Patients

DKA is a common complication in pediatric patients with Type 1 Diabetes Mellitus (DM1), affecting approximately 36% of children under 5 years and 16% of teenagers over 14 years. While most cases have a favorable prognosis, about 1% of children with DKA experience severe neurological

outcomes, such as acute brain changes associated with poor long-term neurocognitive function. Accurate neuroimaging is crucial for diagnosing and managing DKA with acute central nervous system (CNS) involvement. Here is an overview of neuroimaging findings and their implications:

1. **Cerebral Edema:**
   - Cerebral edema is the most common neuroimaging finding in pediatric DKA, occurring in 0.5%–1% of cases. It is associated with increased morbidity and mortality, particularly in children with severe acidosis, hypocapnia, and dehydration.
   - The exact mechanisms behind cerebral edema in DKA are multifactorial. Potential contributors include:
     - Osmotic gradients drawing fluid into hypertonic astrocytes during intravenous therapy.
     - Intracellular sodium and water accumulation due to the correction of intracellular acidosis.
     - Vasodilatation and reperfusion following initial cerebral vasoconstriction.
2. **Neuroimaging Characteristics:**
   - On CT, cerebral edema is characterized by the effacement of sulci and cisterns, compression of cerebral ventricles, and reduced gray-white matter differentiation.
   - MRI, particularly diffusion-weighted and diffusion-tensor imaging, can further delineate cerebral edema and differentiate between vasogenic and cytotoxic types. Increased ADC values typically indicate vasogenic edema, often found in the basal ganglia, thalamus, and white matter.
3. **Severe Complications:**
   - Focal Stroke: Occurs in up to 20% of DKA cases, affecting areas like the mesial basal ganglia and thalamus. It may be secondary to cerebral edema or other factors such as hyperosmolality and systemic inflammatory responses.
   - Brain Herniation: An uncommon but serious complication of cerebral edema, presenting with sudden deterioration of consciousness and brainstem responses. It usually happens 6–13 hours after symptom onset.
   - Ischemic and Hemorrhagic Stroke: Can result from increased blood viscosity, thrombosis, and endothelial damage. Hemorrhagic strokes may occur secondary to sinovenous thrombosis or hemorrhagic transformation of ischemic strokes.
   - Extrapontine Myelinolysis: A rare complication characterized by T2-/FLAIR-hyperintense signals and restricted diffusion in specific brain regions, likely due to rapid electrolyte correction.
4. **Clinical Management:**
   - In patients with DKA and neurological symptoms, early neuroimaging (preferably MRI) is recommended to identify cerebral edema and other complications. Despite CT being commonly used, it may not always reveal acute abnormalities, making MRI a better tool for detailed assessment.

Case-4:

A 35-year-old man with Type 1 Diabetes Mellitus (T1DM) presented to the emergency department in an acutely confused state after being discovered in a disheveled and unresponsive condition at home. He had been isolated in his bedroom for two days prior to intervention, which led to emergency services forcibly entering the premises. Upon examination, the patient was found to be agitated, disoriented, and uncommunicative. His medical history, provided primarily by his family, revealed that he had been in good health until the recent presentation. They noted that he had a history of poor engagement with medical services, particularly concerning his diabetes and multiple sclerosis. Information regarding his social and recreational activities indicated occasional illicit drug use, excessive alcohol consumption, and smoking. His previous medical treatments and interventions were documented in his medical records. The patient's medical history was significant for T1DM, diagnosed at the age of nine. He was managing his diabetes with basal/bolus insulin, but had a history of inadequate glycemic control, with HbA1c levels fluctuating between 67 and 99 mmol/mol (8.3 to 11.2%) over the past decade. He had a prior episode of diabetic ketoacidosis (DKA) attributed to alcohol use and insulin omission and a hypoglycemic seizure due to incorrect insulin administration. Additionally, he had been diagnosed with Relapsing Remitting Multiple Sclerosis (RRMS) at age 26 and had previously been prescribed interferon beta, which he discontinued five years prior. His MS had remained stable clinically and radiographically, with the most recent MRI of the brain performed two months before his current presentation. He had also been managing mild to moderate depression with escitalopram for the past four years. A suspected seizure six months before admission had not been investigated due to his failure to attend follow-up. This presentation underscores the complexity of managing chronic conditions such as T1DM and MS, particularly in patients with poor adherence to treatment and lifestyle modifications. The patient's acute confusion could potentially be linked to his poorly controlled diabetes, possible complications from his MS, substance abuse, or a combination of these factors. Comprehensive diagnostic assessments, including blood glucose measurements, neuroimaging, toxicology screening, and neurological evaluation, are essential to determine the precise etiology of his

acute condition and guide appropriate treatment strategies. There was no notable family history of relevance. The patient was employed as a caretaker at a school and lived independently. His lifestyle included smoking ten cigarettes daily, excessive alcohol consumption, and cannabis use twice a week. Upon examination, the patient's vital signs were within normal ranges; however, his Glasgow Coma Scale (GCS) score was 9, with eye opening at 3, verbal response at 1, and motor response at 5. Cardiovascular, respiratory, and abdominal examinations were unremarkable. A focused neurological assessment, including evaluations of cranial nerves, fundoscopy, gait, tone, and reflexes, did not reveal any focal deficits. However, the assessment was constrained by the patient's inability to cooperate fully, particularly with evaluations of higher cortical functions [50].

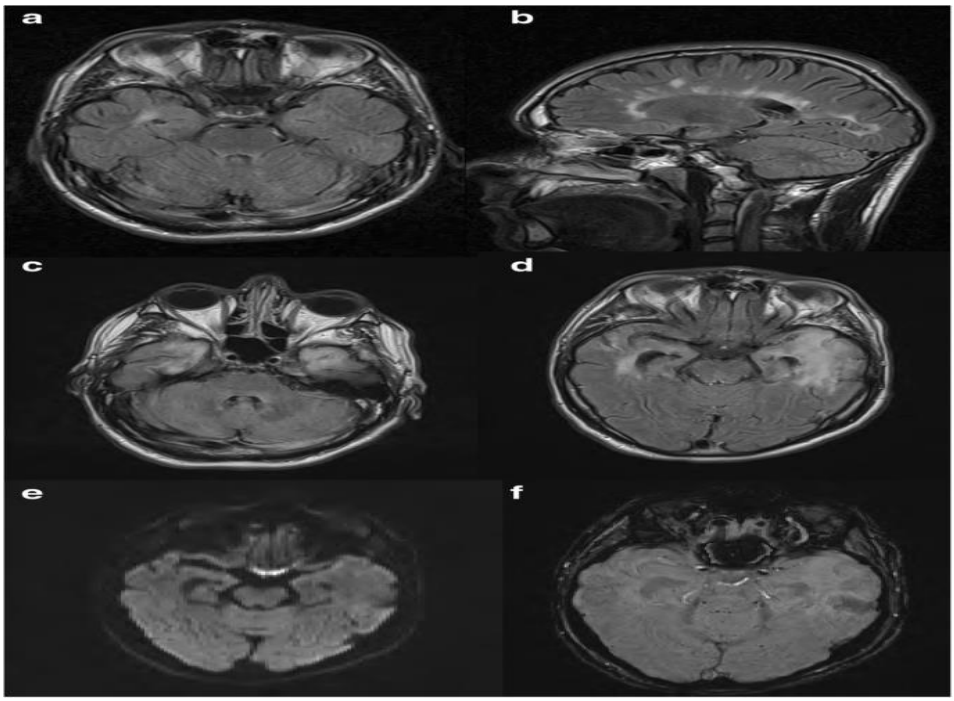

Figure 9: Axial FLAIR (a) and sagittal FLAIR (b) sequences from the most recent MRI performed two months prior to presentation reveal stable periventricular white matter lesions, with a notable isolated demyelinating plaque located in the right temporal horn. At presentation, axial FLAIR sequences (c and d) display high signal abnormalities in both temporal lobes, extending into the insular cortex. Axial diffusion-weighted imaging (e) shows no evidence of restricted diffusion, and susceptibility-weighted imaging (f) reveals no focal hemorrhage.

Case-5:

A 52-year-old male with poorly controlled diabetes mellitus experienced recurrent episodes of abnormal movements in the left upper and lower limbs over a two-month period. Clinically, these movements were diagnosed as chorea. Upon admission, his glycated hemoglobin (HbA1c) was elevated at 9.4% (normal range: 4–5.6%). Blood tests were negative for ketone bodies. Non-contrast computed tomography (NCCT) of the brain (**Figure. 10**) revealed hyperdensity in the right putamen and right caudate nucleus, along with age-related diffuse cerebral atrophy. An incidental finding was a chronic lacunar infarct in the left external capsule. The diagnosis of hyperglycemia-induced hemichorea–hemiballismus (HCHB) syndrome was established based on the imaging and clinical findings [51].

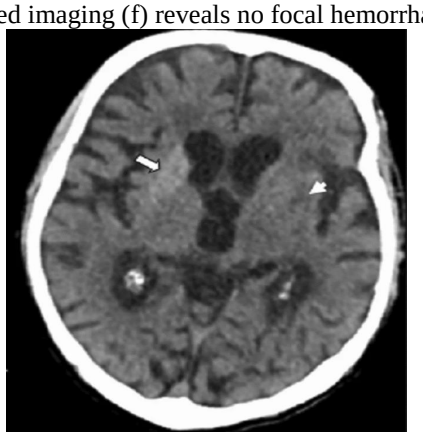

Figure 10: Axial non-contrast computed tomography (NCCT) image of the brain in a 52-year-old male with hyperglycemia-induced hemichorea–hemiballismus (HCHB) syndrome demonstrates hyperdensity in the right putamen and caudate nucleus (long arrow). Additionally, a lacunar infarct in the left external capsule is noted (short arrow).

Case-6:

A 78-year-old male with diabetes mellitus presented with left upper-limb ballism. Despite being on oral hypoglycemic agents, his blood glucose level was markedly elevated at 450 mg/dl (normal range 70–140 mg/dl) upon admission. Both urine and blood ketones were negative, and his HbA1c was elevated at 9.5% (normal range 4–5.6%). Serum osmolality was within normal limits at 295 mOsm/kg (normal range 275 to 295 mOsm/kg). MRI (**Figure. 11**) showed distinctive T1 hyperintensity in the contralateral (right) putamen. Despite achieving glycemic control over a three-month follow-up, the ballism movements persisted. The final diagnosis of hyperglycemia-induced hemichorea–hemiballismus (HCHB) syndrome was made based on these findings [51].

Case-7:

A 69-year-old male with diabetes mellitus presented with bilateral chorea persisting for two weeks. On admission, his HbA1c was elevated at 9.0% (normal range 4–5.6%), and his blood glucose level was significantly high at 390 mg/dl (normal range 70–140 mg/dl). Urine ketones were absent. MRI of the brain (**Figure. 12**) displayed distinctive T1 hyperintensity in the bilateral putamen. The diagnosis of hyperglycemia-induced hemichorea–hemiballismus (HCHB) syndrome was established based on the clinical presentation and imaging findings [51].

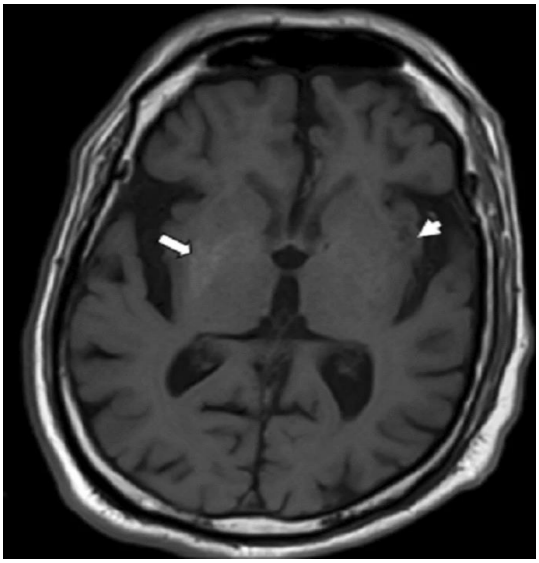

Figure 11: Axial fast spin echo T1-weighted (T1W) MR image of the brain in a 78-year-old male with hyperglycemia-induced hemichorea–hemiballismus (HCHB) syndrome reveals hyperintensity in the right putamen (long arrow). The image also shows a chronic insular infarct on the left (short arrow).

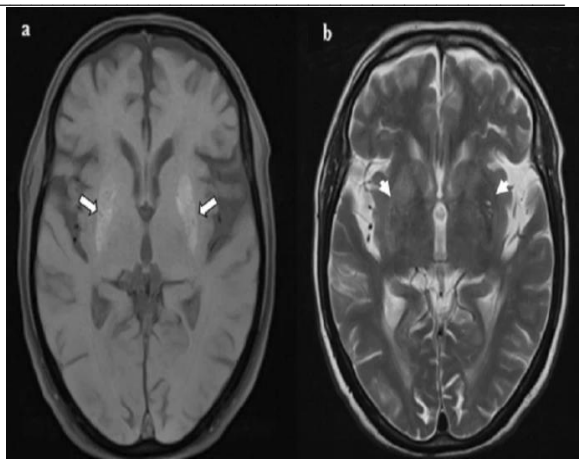

Figure 12: Axial fast spin echo T1-weighted (T1W) MR image (a) and axial T2-weighted (T2W) MR image (b) of the brain in a 69-year-old male with hyperglycemia-induced hemichorea–hemiballismus (HCHB) syndrome. Image (a) shows bilateral putaminal T1 hyperintensity (long arrows), while image (b) reveals peripheral T2 hyperintensity with central T2 hypointensity (short arrows) involving the bilateral putamen.

Previous literature has documented the disappearance of signal abnormalities in imaging with adequate glycemic control in many patients. Consistent with this clinical observation, complete resolution of chorea symptoms was noted in two patients (**cases 5 and 7**). Unfortunately, follow-up imaging was not available for the reported cases of hyperglycemia-induced hemichorea–hemiballismus (HCHB) syndrome. The most frequently affected sites include the putamen, caudate nucleus, globus pallidus, and anterior limb of the internal capsule. However, T1 hyperintensity in the basal ganglia is not exclusive to HCHB syndrome and can be seen in other conditions such as chronic hepatic encephalopathy, post-cardiac arrest encephalopathy, hypoglycemic coma, and mild focal ischemia. Given the resolution of symptoms following treatment, petechial hemorrhages rather than post-ischemic calcifications are hypothesized to underlie the observed signal abnormalities. Additionally, manganese and iron deposition have been associated with other conditions like chronic hepatic encephalopathy and various neurodegenerative disorders. Literature has described cases with bilateral putaminal lesions, presenting with bilateral, unilateral, or no movement disorders in different patients. Consistent with these findings, bilateral movement disorders and bilateral putaminal lesions were observed in **case 7** [51-53].

Diabetes, Diabetic Keto Acidosis, and Health informatics:

Role of Health Informatics in Managing Hyperglycemic Crises

Health informatics plays a transformative role in the management of hyperglycemic crises, such as Diabetic Ketoacidosis (DKA) and

Hyperosmolar Hyperglycemic State (HHS), by leveraging data and technology to enhance patient care, streamline processes, and improve outcomes. The integration of health informatics into clinical practice helps address the complexities of managing these critical conditions through various key functions.

Data Management and Integration

Health informatics systems facilitate the collection, integration, and analysis of patient data from various sources, including electronic health records (EHRs), laboratory results, and monitoring devices. For patients experiencing hyperglycemic crises, accurate and timely data on blood glucose levels, electrolyte balances, and vital signs are crucial. Health informatics tools ensure that this information is readily accessible to healthcare providers, enabling informed decision-making and prompt interventions. By integrating data from multiple sources, informatics systems help create a comprehensive view of the patient's condition, which is essential for effective management.

Decision Support Systems

Decision support systems (DSS) are a critical component of health informatics that aid in the clinical decision-making process. In the context of hyperglycemic crises, DSS can provide evidence-based guidelines and alerts to clinicians about recommended treatment protocols, such as insulin dosing and electrolyte replacement. These systems can also offer real-time alerts for abnormal lab values or potential complications, helping healthcare providers to act quickly and appropriately. By reducing the risk of human error and ensuring adherence to best practices, decision support systems enhance the quality of care provided.

Monitoring and Remote Care

Health informatics enables continuous monitoring of patients, especially in critical care settings. Advanced monitoring systems can track glucose levels, electrolytes, and other vital parameters in real time, allowing for immediate adjustments to treatment plans. Remote monitoring technologies, such as wearable devices and telemedicine platforms, also support the management of hyperglycemic crises by providing ongoing oversight and facilitating virtual consultations. This capability is particularly beneficial for patients in rural or underserved areas, where access to specialized care may be limited.

Data Analytics and Outcome Improvement

Data analytics, a key aspect of health informatics, plays a significant role in identifying trends, evaluating treatment outcomes, and improving clinical practices. By analyzing data from past cases of hyperglycemic crises, healthcare organizations can gain insights into treatment efficacy, complication rates, and patient outcomes. This information can be used to refine treatment protocols, enhance training for healthcare providers, and implement quality improvement initiatives. Data-driven approaches ensure that care strategies are continually updated based on the latest evidence and best practices.

Patient Education and Engagement

Health informatics also contributes to patient education and engagement, which are crucial for managing chronic conditions like diabetes. Informatic systems can provide patients with access to educational materials, self-management tools, and personalized feedback on their condition. Patient portals and mobile health applications offer resources for monitoring blood glucose levels, tracking medication adherence, and receiving alerts for potential issues. Engaging patients in their care through technology enhances their ability to manage their diabetes effectively and reduce the risk of future hyperglycemic crises.

Coordination of Care

Effective coordination of care is essential for managing hyperglycemic crises, and health informatics plays a central role in facilitating this process. EHRs and care coordination platforms enable seamless communication among multidisciplinary teams, including endocrinologists, emergency physicians, and primary care providers. These systems ensure that all team members are informed about the patient’s condition, treatment plan, and progress, leading to more cohesive and integrated care. In summary, health informatics significantly enhances the management of hyperglycemic crises by improving data management, supporting clinical decision-making, enabling real-time monitoring, leveraging data analytics, engaging patients, and facilitating care coordination. By integrating advanced technologies and data-driven approaches into clinical practice, health informatics contributes to better patient outcomes and more efficient management of these critical conditions.

Conclusion:

The management of hyperglycemic crises, such as Diabetic Ketoacidosis (DKA) and Hyperosmolar Hyperglycemic State (HHS), is crucial for preventing severe complications and improving patient outcomes. These crises are characterized by significant metabolic disturbances, including electrolyte imbalances and acidosis, which require meticulous and tailored treatment strategies. The primary objectives in managing these conditions include stabilizing the patient, correcting electrolyte imbalances, and mitigating complications. Electrolyte management is a cornerstone of treatment. Potassium replacement is essential due to its rapid depletion during treatment, and careful monitoring is necessary to prevent hypokalemia. Phosphate therapy is reserved for severe cases of hypophosphatemia, as excessive replacement can

lead to complications such as hypocalcemia. Bicarbonate therapy, while sometimes necessary for severe acidosis, is used selectively due to potential adverse effects including metabolic alkalosis and impaired myocardial function. Complications of hyperglycemic crises, such as seizures, organ failure, and cerebral edema, highlight the importance of vigilant monitoring and prompt intervention. For instance, cerebral edema, although rare in adults, is a significant concern in pediatric patients and requires preventive measures to avoid rapid changes in serum osmolality. The integration of health informatics plays a transformative role in managing hyperglycemic crises. By leveraging electronic health records (EHRs), decision support systems (DSS), and remote monitoring technologies, healthcare providers can access real-time data, adhere to best practices, and make informed decisions. Health informatics enhances the management of these conditions by improving data integration, supporting clinical decision-making, and enabling continuous monitoring. Artificial intelligence (AI) and machine learning further contribute to the management of diabetes by providing advanced tools for prediction and diagnosis. Techniques such as neural networks and support vector machines, when applied to comprehensive datasets, offer promising results in identifying patients at risk and refining diagnostic accuracy. In conclusion, the effective management of hyperglycemic crises requires a multifaceted approach that includes careful electrolyte management, prevention of complications, and the integration of health informatics and AI. These strategies collectively improve patient outcomes by ensuring accurate diagnosis, optimizing treatment protocols, and facilitating comprehensive care.

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