Saudi J. Med. Pub. Health **Vol. 2,** No. 2, pp 2377-2392 (2025)

Saudi Journal of Medicine and Public Health

https://saudijmph.com/index.php/pub
https://doi.org/10.64483/202522409

Integrated Multidisciplinary Management of Pediatric Diabetic Ketoacidosis: Nursing, Emergency Medical Services, Social Work, and Safety Systems Across the Care Continuum

Khaled Lafi Abdulkarim Al-Mutairi (1) , Fahad Bunaydir Shulaywih Almutairi (1) , Mjaed Metaib Atek Almutairi (1) , Fatimah Mohammed Salh Alamri (2) , Najmah Abdullah Aldandan (3) , Abdulaziz Mohammed Aqdi (4) , Abdullah Madsus Alanazi (5) , Bader Abdulhamid Mohammed Alharbi (5) , Mohammed Faris Alqahtani (5) , Fahad Abdul Aziz Alsaedi (6) , Zamzam Ali Sahli (7)

(1) Saudi Red Crescent Authority, Saudi Arabia,
(2) Erada Mental Health Complex,Ministry of Health, Saudi Arabia,
(3) Health Center in Al-Ahsa City,Ministry of Health, Saudi Arabia,
(4) Jazan Cluster,Ministry of Health, Saudi Arabia,
(5) Al-Ahsa Health Cluster,Ministry of Health, Saudi Arabia,
(6) Al-Ahsa Health Cluster – Maternity and Children's Hospital,Ministry of Health, Saudi Arabia,
(7) Irada Hospital For Mental Health,Ministry of Health, Saudi Arabia

Abstract

Background: Diabetic ketoacidosis (DKA) is a life-threatening metabolic emergency characterized by hyperglycemia, ketosis, and metabolic acidosis. Pediatric patients are particularly vulnerable due to limited physiological reserves and higher risk of cerebral edema.

Aim: To provide an integrated, multidisciplinary approach for managing pediatric DKA across emergency, nursing, social work, and safety systems, emphasizing evidence-based protocols and interprofessional collaboration.

Methods: This review synthesizes current guidelines and literature on pediatric DKA, detailing pathophysiology, epidemiology, diagnostic criteria, and treatment strategies. It highlights the roles of emergency medical services, nursing care, and psychosocial interventions in optimizing outcomes.

Results: DKA incidence remains significant, with up to 30% of children presenting in DKA at initial diabetes diagnosis. Mortality rates are low in high-resource settings (0.15–0.31%) but cerebral edema accounts for most fatalities. Effective management requires early recognition, controlled fluid resuscitation, continuous insulin infusion, proactive electrolyte replacement, and vigilant neurological monitoring. Multidisciplinary coordination reduces complications and recurrence risk, particularly in adolescents where psychosocial factors often drive repeated episodes.

Conclusion: Pediatric DKA demands rapid, protocol-driven care integrated with education and prevention strategies. Interprofessional teamwork and structured communication are essential to minimize morbidity and mortality.

Keywords: Diabetic ketoacidosis, pediatric diabetes, multidisciplinary care, cerebral edema, insulin therapy, electrolyte management, prevention strategies.

Introduction

Diabetic ketoacidosis (DKA) represents a life-threatening acute metabolic decompensation that arises from absolute or relative insulin deficiency and is most classically associated with type 1 diabetes mellitus. Nonetheless, DKA may also occur in type 2 diabetes when circulating insulin is insufficient to meet physiological demands, particularly during periods of intercurrent illness, stress, or delayed access to therapy. The syndrome is defined by a characteristic triad of hyperglycemia, ketosis, and metabolic acidosis, reflecting a profound shift in substrate utilization away from glucose and toward accelerated lipolysis and hepatic ketogenesis. The term "ketoacidosis" underscores the accumulation of water-soluble ketone bodies (KBs)—primarily beta-hydroxybutyrate and acetoacetate—which, when produced in excess and inadequately cleared, overwhelm buffering capacity and drive a systemic acidotic state with potentially catastrophic hemodynamic and neurological consequences [1][2]. In pediatric populations, DKA is particularly consequential because children have smaller physiological reserves, may present late in the course of illness, and are at risk for unique complications such as cerebral edema. Standardized diagnostic criteria therefore play a pivotal role in ensuring timely recognition and consistent triage. The International Society for Pediatric and Adolescent Diabetes defines DKA by the simultaneous presence of hyperglycemia, metabolic acidosis, and ketosis. Specifically, hyperglycemia is operationalized as a blood glucose

*Corresponding author e-mail: Sali.803@hotmail.com (Khaled Lafi Abdulkarim Al-Mutairi).
Receive Date: 01 December 2025, Revise Date: 28 December 2025, Accept Date: 30 December 2025

concentration exceeding 200 mg/dL (11 mmol/L), while metabolic acidosis is established by a venous pH below 7.3 or a serum bicarbonate level below 15 mEq/L (15 mmol/L). Ketosis is confirmed by elevated circulating ketones—commonly a beta-hydroxybutyrate concentration greater than 3 mmol/L—or by urine ketones categorized as “moderate” or “large” on standard testing [3]. These thresholds provide a pragmatic framework that supports early diagnosis, severity stratification, and prompt initiation of evidence-based resuscitation and insulin therapy.

The pathobiology of DKA is anchored in the body’s inability to appropriately utilize glucose at the cellular level. In the absence of effective insulin action, glucose uptake into insulin-sensitive tissues is impaired, hepatic gluconeogenesis and glycogenolysis are amplified, and counterregulatory hormones promote a catabolic milieu. As a result, adipose tissue lipolysis accelerates, releasing free fatty acids that are transported to the liver and converted into ketone bodies. Although ketone bodies are produced physiologically as alternative energy substrates, particularly during fasting, their generation becomes excessive in DKA. Importantly, KBs are not merely metabolic byproducts; they can serve as a critical fuel for the brain, myocardium, and skeletal muscle when glucose availability is limited or cellular glucose transport is compromised [4][5]. However, in DKA the rate of ketone production exceeds peripheral utilization and renal excretion, leading to ketonemia, osmotic diuresis, progressive dehydration, electrolyte derangements, and acidemia. These intersecting disturbances define DKA as a medical emergency that demands rapid identification, careful monitoring, and coordinated multidisciplinary care [3][4][5].

Etiology

Ketone bodies are continuously generated at low concentrations as part of normal intermediary metabolism; however, they rise to clinically significant levels when carbohydrate availability is reduced or when carbohydrate utilization is impaired. Physiological states such as fasting, starvation, and prolonged vigorous exercise can increase ketone production as the body transitions toward lipid-based energy metabolism. Pathological ketogenesis becomes most pronounced when insulin is deficient or ineffective, because insulin ordinarily suppresses lipolysis and limits hepatic ketone synthesis. In type 1 diabetes mellitus, absolute insulin deficiency provides the prototypical setting for unchecked ketone generation. In type 2 diabetes mellitus, insulin secretion may be preserved, yet remain insufficient relative to metabolic requirements, particularly during acute stress or intercurrent illness; under these conditions, insulin action may fall below the threshold needed to facilitate adequate cellular glucose uptake and to restrain lipolysis, thereby permitting the development of ketoacidosis [6][7]. The biochemical substrate for ketone production is predominantly derived from triglycerides, which constitute the principal form of fat storage in the human body. When accessible glucose stores decline or become functionally unavailable due to impaired insulin action, hormonal signals favor mobilization of adipose reserves. Hepatic processing of triglycerides yields free fatty acids and glycerol. The free fatty acids undergo β-oxidation, generating acetyl-CoA, which is subsequently diverted into ketogenesis when the capacity of the tricarboxylic acid cycle is limited by reduced carbohydrate flux. In parallel, glycerol can be converted into glucose through gluconeogenic pathways. Under normal circumstances, insulin-mediated transport enables tissues to utilize this glucose for energy. In insulin-deficient or insulin-resistant states, however, the glucose produced cannot be efficiently shunted into cells, leading to progressive hyperglycemia. Once renal thresholds are exceeded, glucose spills into the urine, promoting osmotic diuresis and exacerbating volume depletion—processes that further intensify counterregulatory hormone release and perpetuate ketone production. From a physiologic standpoint, ketone bodies can serve as a vital alternative fuel, particularly for the brain, which lacks meaningful energy storage capacity and relies primarily on circulating substrates. When blood glucose is low or when glucose cannot be effectively utilized because of insufficient insulin activity, ketones become a major energy source for cerebral tissue. This adaptive mechanism becomes maladaptive when ketone production overwhelms peripheral utilization and renal clearance, allowing ketones to accumulate and drive systemic acidosis. In contrast to the brain, skeletal muscle contains substantial glycogen reserves and can mobilize glucose locally via glycogenolysis. A large proportion of total body glycogen is stored in muscle tissue, providing a buffer against short-term fluctuations in energy supply. Nevertheless, in states of severe insulin deficiency, these compensatory pathways are insufficient to prevent escalating hyperglycemia and progressive ketogenesis, setting the stage for diabetic ketoacidosis [6][7].

Epidemiology

Diabetic ketoacidosis (DKA) remains a major public health and clinical burden in pediatric diabetes because it is both a frequent initial manifestation of disease and a leading cause of acute decompensation after diagnosis. In children with type 1 diabetes mellitus, DKA is commonly encountered at presentation and continues to represent a predominant driver of hospitalization, morbidity, and preventable mortality. Reported case fatality rates in pediatric DKA are low in absolute terms, yet clinically significant given the high incidence of events and the severity of associated complications; estimates commonly fall within approximately 0.15% to 0.31% of cases [8]. Although DKA can also occur in children and adolescents with type 2 diabetes mellitus, it is generally observed at lower overall rates than in type 1 diabetes, reflecting differences in underlying insulin deficiency, presentation patterns, and precipitating factors [9]. Epidemiologically, the incidence of DKA at the initial diagnosis of type 1 diabetes varies by region, healthcare access, and population risk factors. While some cohorts report relatively low proportions at diagnosis, DKA at first presentation has been documented in approximately 30% of children in the United States and Canada, emphasizing that delayed recognition of evolving hyperglycemia and insulin deficiency remains common even in high-resource settings [10]. The likelihood of DKA at diagnosis is not evenly distributed across pediatric subpopulations. Younger children are disproportionately vulnerable, particularly those under five years of age and most notably those under two years, in whom symptoms may be nonspecific and progression may be rapid. Increased risk is also associated with ethnic minority status and markers of socioeconomic disadvantage, including low household resources and reduced access to timely primary care. Importantly, children living in countries where the population prevalence of type 1 diabetes is low appear to experience higher rates of DKA at diagnosis, plausibly reflecting reduced clinical familiarity with early diabetes symptoms among caregivers and clinicians and, consequently, a higher probability of missed or delayed diagnosis [11][12]. Delayed recognition is a consistent epidemiological theme: as the interval between symptom onset and diagnosis lengthens, the probability of severe dehydration, ketosis, and acidemia increases.

The contribution of socioeconomic context has been substantiated in clinical reviews, including an analysis of newly diagnosed pediatric patients managed at a single U.S. center, which demonstrated that socioeconomic disadvantage was associated with a greater likelihood of DKA at presentation [13]. At the population level, the frequency of DKA at diagnosis has been shown to be inversely related to the background prevalence of type 1 diabetes, supporting the interpretation that where type 1 diabetes is less common, diagnostic suspicion may be lower and missed diagnoses more frequent [14]. Collectively, these findings underscore that DKA at diagnosis is not solely a biomedical phenomenon but also a health-systems indicator, reflecting gaps in awareness, access, and timely evaluation. Among children with established type 1 diabetes, DKA remains an important recurrent complication, with annual event rates commonly estimated at approximately 6% to 8% [15][16]. However, risk is concentrated rather than uniformly distributed. Factors associated with recurrent DKA include poor metabolic control, the peripubertal and pubertal period—particularly among adolescent girls—intercurrent illnesses such as gastroenteritis with vomiting and dehydration, and psychosocial vulnerabilities. These may include psychiatric comorbidity (notably eating disorders), family conflict or instability, and limited access to medical care, including underinsurance. Treatment-related drivers, especially omission of insulin, are highly salient and may occur intentionally or inadvertently; insulin pump failure or interruption of insulin delivery can precipitate rapid metabolic deterioration. The epidemiology of recurrent events demonstrates marked clustering: in a large prospective U.S. study, nearly 60% of DKA episodes among children with established diabetes occurred in only 5% of patients, indicating that a small, high-risk subgroup accounts for a disproportionate share of acute events [15]. Comparable concentration of risk has also been reported in the United Kingdom, suggesting that this pattern is not country-specific but rather reflects common intersections of behavioral, psychosocial, and structural determinants of health [8].

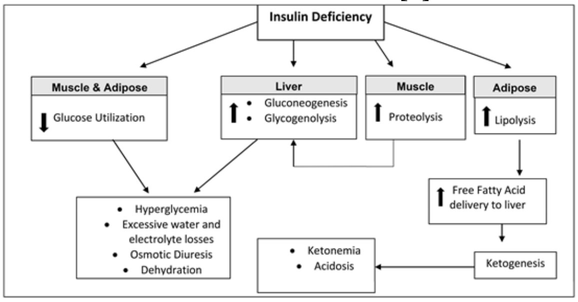

Fig. 1: Etiology of diabetic ketoacidosis.

In pediatric type 2 diabetes, ketosis and DKA occur less frequently but are clinically important when they do occur, often emerging in specific demographic contexts. Reports indicate that DKA in youth with type 2 diabetes is observed predominantly among adolescents with obesity, with a notable representation among African American populations in published cohorts [17]. In a retrospective review of adolescents presenting with DKA, a meaningful minority—approximately 13%—were ultimately classified as having type 2 diabetes, illustrating that DKA at presentation does not exclusively indicate type 1 diabetes and that diagnostic evaluation must remain broad, especially in contemporary pediatric populations where type 2 diabetes is increasingly prevalent [9]. Overall, the epidemiology of pediatric DKA highlights both biological vulnerability and modifiable system-level factors, emphasizing the importance of early recognition, equitable access to care, and targeted prevention strategies for high-risk groups [9][17].

Pathophysiology

Diabetic ketoacidosis (DKA) is a complex metabolic emergency in which absolute or relative insulin deficiency, coupled with excess counter-regulatory hormones, drives a coordinated cascade of hyperglycemia, ketogenesis, acidemia, dehydration, and electrolyte derangement. These processes are not independent; rather, they amplify one another through feedback loops that worsen circulatory compromise and impair renal clearance, thereby accelerating metabolic decompensation. At the core of DKA lies impaired cellular glucose utilization. Inadequate insulin action reduces glucose uptake in insulin-sensitive tissues and simultaneously promotes hepatic gluconeogenesis and glycogenolysis, leading to rising plasma glucose concentrations. Hyperglycemia increases serum osmolality and establishes the biochemical conditions for glucosuria once renal thresholds are exceeded. Glucosuria, in turn, acts as the proximal driver of osmotic diuresis, producing large obligate losses of water and electrolytes. In pediatric patients, these free-water deficits can evolve rapidly, culminating in significant intravascular volume depletion, reduced renal perfusion, and declining glomerular filtration. As renal function deteriorates, the kidney's capacity to excrete glucose and ketone anions diminishes, thereby further intensifying hyperglycemia and acidosis [17].

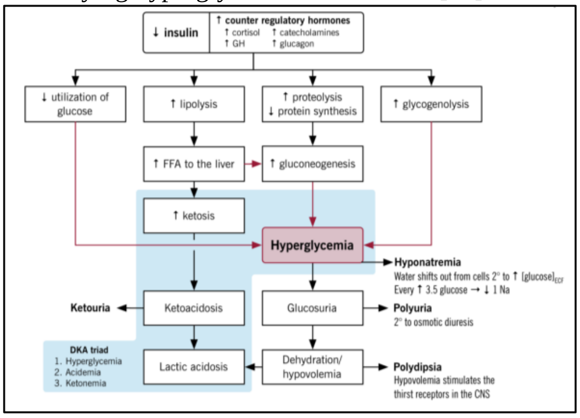

Fig. 2: Pathogenesis of diabetic ketoacidosis.

The osmotic diuresis of DKA is clinically consequential because it produces a combined deficit in water, sodium, potassium, phosphate, and other solutes. Dehydration contributes to tachycardia, hypotension, and poor tissue perfusion, while hyperosmolarity can provoke altered mental status and predispose to cerebral complications. Ketone body accumulation is the second defining metabolic axis. Excess production of ketoacids—primarily beta-hydroxybutyrate and acetoacetate—exceeds buffering capacity and generates a high-anion-gap metabolic acidosis. Respiratory compensation typically ensues, with hyperventilation increasing carbon dioxide elimination to partially mitigate acidemia. This compensatory pattern may be clinically evident as deep, labored breathing, reflecting the physiologic imperative to reduce $PaCO_2$ and thereby raise blood pH. Electrolyte abnormalities in DKA must be interpreted through the lens of total body depletion versus measured serum concentration. Potassium illustrates this distinction particularly well. Children with DKA generally have substantial total body potassium deficits, commonly estimated at approximately 3 to 6 mEq/kg, due to urinary losses driven by osmotic diuresis, aldosterone-mediated kaliuresis in response to hypovolemia, and the excretion of ketoacid anions that obligate cation loss. Paradoxically, serum potassium at presentation is frequently normal or mildly elevated. This occurs because insulin deficiency and metabolic acidosis promote transcellular potassium shifts from the intracellular to extracellular space, and dehydration-associated reductions in renal potassium clearance may further augment measured serum levels. As insulin therapy and acidosis correction are initiated, potassium shifts back into cells, unmasking the preexisting deficit and risking precipitous hypokalemia if not anticipated and replaced appropriately [17][18].

Sodium disturbances also require careful physiological interpretation. Measured serum sodium is often reduced in DKA, not necessarily because total body sodium is increased, but because hyperglycemia induces a dilutional effect as water shifts from the intracellular to the extracellular compartment. A commonly used correction factor estimates that the serum sodium concentration decreases by approximately 1.6 mEq/L for every 100 mg/dL increase in blood glucose above 100 mg/dL, producing a form of "pseudohyponatremia" that reflects osmotic water redistribution rather than true hypotonic hyponatremia [18]. Clinically, appreciating this corrected sodium is essential for guiding fluid therapy, interpreting osmolality trends, and minimizing risks associated with overly rapid shifts in serum tonicity during treatment. Phosphate physiology follows a similar pattern of hidden depletion with initially deceptive serum values. Osmotic diuresis promotes urinary phosphate losses, making total body phosphate deficiency common in pediatric DKA. However, initial serum phosphate concentrations are often normal or mildly elevated because insulin deficiency and acidosis drive phosphate out of cells into the extracellular compartment. As therapy proceeds and insulin-mediated cellular uptake resumes, this transcellular shift reverses, and serum phosphate frequently declines, sometimes to clinically significant levels [19]. Although routine phosphate replacement is not universally required, recognition of this trajectory is important, especially when severe hypophosphatemia threatens diaphragmatic function, myocardial performance, or hematologic integrity [18][19].

Renal indices provide additional insight into the severity of volume depletion and perfusion compromise. Elevated blood urea nitrogen (BUN) commonly correlates with hypovolemia and prerenal azotemia. Acute rises in serum creatinine may reflect acute kidney injury (AKI) due to reduced renal perfusion and, in some cases, additional tubular stress from osmotic load and inflammatory mediators. Renal impairment is not merely a laboratory finding; it amplifies DKA by limiting clearance of glucose, ketones, and acids, thereby sustaining hyperosmolarity and acidosis until effective volume resuscitation restores filtration and urinary excretion. The biochemical engine of ketoacidosis is ketone body production in the liver. Under normal physiological conditions, glucose is the principal circulating carbon substrate used to generate adenosine triphosphate (ATP) via glycolysis, the Krebs cycle, and oxidative phosphorylation. Ketone bodies function as alternative, water-soluble fuels derived from fatty acids and are used by multiple tissues—particularly during fasting or low carbohydrate availability. In DKA, ketogenesis becomes excessive because the hormonal milieu strongly favors lipid mobilization and hepatic fatty acid oxidation. Low insulin levels combined with high counter-regulatory hormone activity, especially glucagon, create a metabolic environment in which ketone production is both stimulated and insufficiently suppressed [20]. Physiological stress further amplifies this imbalance through catecholamine surges, which intensify insulin resistance and promote additional lipolysis [20].

A critical early step in this pathway is activation of hormone-sensitive lipase in adipose tissue, driven by an unfavorable insulin-to-glucagon ratio and reinforced by stress hormones. This activation accelerates the breakdown of triglycerides into long-chain fatty acids and glycerol. The fatty acids circulate largely bound to albumin and are delivered to the liver, where hepatocytes take them up for mitochondrial beta-oxidation. Within hepatic mitochondria, fatty acids are converted to fatty acyl–CoA derivatives and undergo beta-oxidation, producing acetyl–CoA as a central intermediate. Low insulin and elevated glucagon signaling facilitate the transport of fatty acyl–CoA into mitochondria via the carnitine-dependent transport system, mediated by sequential carnitine palmitoyltransferase reactions, thereby accelerating substrate flux into beta-oxidation and increasing acetyl–CoA availability [21][22]. Acetyl–CoA occupies a crossroads in metabolism, with several potential fates. Under balanced conditions, acetyl–CoA enters the Krebs cycle, where it is oxidized to carbon dioxide and water, generating reducing equivalents that drive ATP formation. Alternatively, acetyl–CoA can contribute to fatty acid synthesis in the cytoplasm when energy is abundant. In DKA, however, the surge in acetyl–CoA production, combined with altered hepatic redox state and reduced effective carbohydrate flux, saturates the oxidative capacity of the Krebs cycle. When the Krebs cycle cannot accommodate the acetyl–CoA load, excess acetyl–CoA is diverted into the ketogenic pathway. The initial ketone body formed is acetoacetic acid, which can then be reduced to beta-hydroxybutyric acid—an organic acid that often predominates in severe DKA—or undergo nonenzymatic decarboxylation to acetone [23]. Unlike acetoacetate and beta-hydroxybutyrate, acetone is not an acid and cannot be reconverted to acetyl–CoA; instead, it is eliminated via the urine and through exhalation, contributing to the characteristic “fruity” breath odor sometimes noted in DKA [21][22][23].

Although ketone bodies are physiologically adaptive as alternative fuels, their uncontrolled accumulation in DKA becomes pathologic. Beta-hydroxybutyrate and acetoacetate contribute directly to metabolic acidosis, while their renal excretion obligates cation loss, worsening electrolyte depletion. The resulting acidemia depresses myocardial contractility, impairs peripheral vascular responsiveness, and can exacerbate cerebral symptoms. Simultaneously, hyperosmolar dehydration compromises perfusion and renal function, limiting clearance and reinforcing the metabolic spiral. Thus, DKA can be understood as a tightly coupled syndrome in which insulin deficiency initiates hyperglycemia and ketogenesis, dehydration and renal dysfunction magnify both disturbances, and electrolyte shifts complicate the clinical course—together defining a medical emergency that requires carefully titrated fluid, insulin, and electrolyte therapy to reverse the underlying physiology [23].

Histopathology

Diabetes mellitus is fundamentally a chronic metabolic disorder, and diabetic ketoacidosis (DKA) typically represents an acute, episodic manifestation of inadequate glycemic control rather than a discrete histopathologic disease entity. Consequently, histopathologic interpretation in patients who experience recurrent DKA is often confounded by the cumulative tissue effects of longstanding hyperglycemia rather than by lesions uniquely attributable to ketoacidosis itself. In practice, repeated episodes of DKA are most frequently observed in individuals with persistently poor metabolic control, and chronically elevated glycated hemoglobin (HbA1c) serves as a robust surrogate marker of sustained hyperglycemic exposure. Over time, elevated HbA1c correlates with the development and progression of diabetes-related microvascular and macrovascular pathology. Microvascular injury is characterized by diffuse endothelial dysfunction, capillary basement membrane thickening, and pericyte loss, contributing to retinopathy, nephropathy, and neuropathy. Macrovascular disease reflects accelerated atherosclerosis with intimal thickening and plaque formation, increasing the long-term risk of ischemic events. While these lesions are not specific to DKA, they contextualize the broader pathological substrate in which recurrent DKA occurs and help explain why patients with frequent decompensations often exhibit compounding organ vulnerability [23].

The most clinically consequential acute “pathology-linked” complication associated with DKA, particularly in pediatric populations, is cerebral edema, which is thought to arise from complex osmotic and perfusion-related mechanisms during treatment rather than from a primary structural lesion present at baseline. Although cerebral edema occurs in a minority of cases—often estimated at up to approximately 1%—its implications are profound because it can rapidly progress to intracranial hypertension, herniation, and death. The pathophysiologic basis is commonly conceptualized as rapid shifts in serum osmolality and cerebral water movement during correction of hyperglycemia and dehydration, leading to brain swelling. From a clinical-pathological perspective, vigilance for early indicators of raised intracranial pressure is essential. Concerning features include new or worsening headache, irritability, papilledema, bradycardia, rising systemic blood pressure, and declining consciousness as reflected by a decreasing Glasgow Coma Scale score. These findings should be treated as emergent signals of cerebral compromise, prompting immediate reassessment of therapy and institution of measures to mitigate intracranial pressure. The mortality associated with DKA-related cerebral edema is high, approaching approximately one quarter of affected patients, and survivors frequently experience significant neurological morbidity, reflecting the vulnerability of developing neural tissue to pressure-related ischemia and injury [23].

Toxicokinetics

In the context of diabetic ketoacidosis (DKA), "toxicokinetics" is best understood as the production, interconversion, distribution, and elimination kinetics of ketone bodies whose accumulation contributes to metabolic acidosis and systemic illness. Three ketone-related molecules predominate in human physiology: beta-hydroxybutyrate (BHB), acetoacetate, and acetone. Although all three are commonly grouped under the umbrella term "ketones," they differ meaningfully in their biochemical behavior, diagnostic detectability, and clinical implications. BHB and acetoacetate are organic acids that directly contribute to the high–anion gap metabolic acidosis of DKA, whereas acetone is not an acid and does not itself drive acidemia; instead, it is a downstream metabolite that reflects ongoing or recent ketogenesis and contributes to characteristic odor through pulmonary excretion. BHB is the dominant ketone body in clinically significant DKA and is generally regarded as the most accurate marker of ketoacidosis severity. In many patients with DKA, BHB accounts for approximately three quarters of circulating ketone burden, a distribution shaped by hepatic redox state and the metabolic milieu favoring reduction of acetoacetate to BHB. Because of this predominance and its close alignment with acid generation, quantitative measurement of BHB in whole blood or serum provides a more direct assessment of disease severity and treatment response than urine ketone testing. Point-of-care whole blood ketone strips and laboratory-based serum assays can quantify BHB and are therefore well suited to monitoring resolution of ketoacidosis. By contrast, many commonly used urine dipsticks rely on nitroprusside-based reactions that primarily detect acetoacetate and, to a lesser extent, acetone. They do not reliably quantify BHB, which is the very ketone that dominates in severe DKA [23][24].

The interconversion kinetics among ketone bodies creates an important diagnostic timing effect. BHB often rises early and can be detected in the blood well before acetoacetate and acetone appear in urine in significant quantities, because BHB is subsequently converted into acetoacetate as the redox environment normalizes. Clinically, this means that blood BHB concentrations may signal evolving DKA up to roughly 24 hours before urine ketone testing becomes strongly positive. It also explains a common source of confusion during treatment: after effective therapy suppresses ongoing ketone production and BHB begins to fall, urine ketone readings may remain elevated—or even increase—because BHB is being converted back to acetoacetate, the very analyte detected by most urine strips. Consequently, urine ketone testing can misleadingly suggest persistent or worsening ketosis despite genuine biochemical improvement. Acetone adds another kinetic layer, as it is relatively lipophilic compared with the other ketone bodies, can be sequestered in adipose tissue, and may be released slowly back into the circulation. This gradual redistribution contributes to prolonged detectability of acetone in blood and urine even after the primary acidotic process has begun to resolve. Clinically used interpretive thresholds further illustrate why BHB measurement is preferred. Serum ketone (BHB) concentrations below 0.6 mmol/L are generally considered normal. Values between 0.6 and 1.5 mmol/L are often interpreted as low to moderate ketosis, while levels from 1.6 to 3.0 mmol/L represent significant ketosis with increased risk of developing DKA. Concentrations exceeding 3.0 mmol/L are strongly suggestive of DKA and warrant immediate emergency assessment and treatment [24]. Urine ketone strips are typically reported semiquantitatively. Absence of urine ketones is considered normal, whereas a single "plus" commonly corresponds to low-to-moderate ketone levels, "two plus" indicates high ketone levels, and "three plus" suggests severe ketonuria. However, these categories provide limited precision and correlate imperfectly with the clinical severity of acidosis, especially in early DKA or during treatment. Analytical limitations are also relevant to interpretation. Urine ketone tests can yield false-positive results with certain medications, including agents such as captopril and valproate, which may interfere with strip chemistry. False-negative results may occur when strips are expired, improperly stored, or when there is delay between urine collection and testing, allowing volatilization or degradation of detectable ketones. Because of these limitations, and because urine strips do not capture the predominant ketone in severe DKA, blood BHB measurement is widely regarded as the preferred tool for both diagnosis and treatment monitoring. When blood ketone testing is unavailable, urine ketones can still support diagnosis in the appropriate clinical context, but they are generally of limited value for tracking response to therapy and should be interpreted cautiously alongside clinical status and acid–base parameters [25].

History and Physical

A meticulous history and targeted physical examination are central to the early recognition of diabetic ketoacidosis (DKA), particularly in children and adolescents with type 1 diabetes mellitus, in whom clinical deterioration can occur rapidly. Any acutely unwell patient with type 1 diabetes should be evaluated for DKA, as ketoacidosis may develop in parallel with other illnesses or be precipitated by intercurrent stressors such as infection, trauma, or other systemic inflammatory processes. The presenting history often reflects a progression from early hyperglycemia-related symptoms to later catabolic and dehydrating manifestations. Families may describe increasing polydipsia and polyuria as cardinal features, driven by glucosuria and osmotic diuresis. Polyphagia can be present early as cellular energy deficit triggers hunger, while anorexia may emerge later as dehydration and acidosis intensify. Weight loss, fatigue, and a history of recurrent infections may be reported, reflecting sustained hyperglycemia and impaired immune function. In pediatric patients, symptom narratives frequently extend into behavioral and cognitive domains; parents and teachers may notice declining school performance, impaired concentration, irritability, or nonspecific malaise, and families may describe confusion or altered mental status when acidosis and hyperosmolarity become more pronounced. On examination, children with newly diagnosed type 1 diabetes who present in DKA often appear thin, dehydrated, and unwell. Clinical signs of dehydration are common and may include dry mucous membranes, reduced skin turgor, tachycardia, delayed capillary refill, and, in more advanced cases, hypotension. Thirst is frequently evident, and the history of frequent urination is typically concordant with physical findings of volume depletion, consistent with osmotic diuresis from glucosuria. Abdominal complaints are also prominent and can complicate diagnostic clarity. Diffuse abdominal tenderness, abdominal pain, nausea, and vomiting commonly accompany DKA and may misdirect clinicians toward primary gastrointestinal diagnoses; indeed, children experiencing their first episode of DKA are sometimes initially labeled as having viral gastroenteritis, particularly when vomiting and dehydration dominate the presentation. Careful integration of systemic symptoms, metabolic breathing patterns, and diabetes-specific history is therefore crucial to avoid delays in diagnosis. Respiratory examination can provide critical diagnostic cues. Metabolic acidosis typically elicits a compensatory respiratory response characterized by rapid, deep breathing—classically described as Kussmaul respirations—which reflects the physiologic drive to reduce carbon dioxide and partially mitigate acidemia. Additionally, a distinctive fruity odor on the breath may be appreciated, arising from pulmonary elimination of acetone, a volatile ketone byproduct. Neurological status in DKA spans a broad spectrum and often correlates with the severity of acidosis and dehydration. Patients may remain alert early in the course, but progressive acidemia, hyperosmolarity, and reduced cerebral perfusion can lead to lethargy, drowsiness, and, in severe cases, coma [26]. Because neurological decline may also signal complications such as cerebral edema during treatment, baseline mental status assessment and frequent reassessment are essential components of the physical evaluation [25][26].

Evaluation

The evaluation of diabetic ketoacidosis (DKA) is designed to confirm the diagnosis biochemically, define severity, identify precipitating factors, and establish a baseline for safe monitoring during treatment. Although the clinical picture often strongly suggests DKA—particularly in children with dehydration, vomiting, and Kussmaul respirations—the diagnosis is ultimately established through laboratory evidence of hyperglycemia accompanied by metabolic acidosis. Ketone testing is diagnostically supportive and frequently informative for risk stratification and follow-up, but it is not strictly required when hyperglycemia and acidemia are unequivocally present. Because DKA management is highly dependent on trends in acid–base status and electrolytes, early acquisition of essential laboratory studies is critical and should be coupled with frequent reassessment. Point-of-care testing and standard laboratory panels jointly support timely diagnosis and provide actionable physiologic targets [27]. A central concept in DKA assessment is the anion gap, calculated as $(Na+K) - (Cl+HCO3)$. In DKA, organic ketoacids—predominantly beta-hydroxybutyrate (BHB)—accumulate as “unmeasured” anions, widening the calculated gap and serving as a practical marker of high–anion gap metabolic acidosis. The anion gap is typically between 6 and 12 mEq/L under normal conditions, while values above 15 mEq/L are commonly seen in DKA [28][29][30]. Serial anion gap measurement is also clinically useful, as closure of the gap generally parallels resolution of ketoacidosis, even when blood glucose normalizes earlier during treatment [27][28][29].

Blood glucose is usually elevated above 200 mg/dL (11 mmol/L) and may occasionally exceed 1000 mg/dL, though pediatric DKA can occur with comparatively modest hyperglycemia relative to adults. This is an important practical point: clinicians should not dismiss DKA solely because glucose is not dramatically elevated, particularly in children. Direct measurement of serum or whole-blood BHB is often the most physiologically aligned marker of ketoacidosis severity, and BHB concentrations are typically elevated, with values above 31 mg/dL reported in many affected patients [31]. In addition to confirming ketosis, BHB trends can provide a more reliable reflection of metabolic improvement than urine ketones, which predominantly detect acetoacetate and acetone rather than BHB. Assessment of volume status and renal function is essential, making blood urea nitrogen (BUN) and creatinine routine components of the evaluation. Elevations may reflect dehydration and prerenal azotemia, though acute kidney injury can also occur and has implications for electrolyte management and clearance of acids. Comprehensive serum electrolytes should be obtained early because sodium, potassium, chloride, phosphate, and bicarbonate abnormalities are common and dynamic. Venous blood gas analysis is typically sufficient for acid–base assessment and provides the venous pH and partial pressure of carbon dioxide (pCO2), allowing clinicians to quantify the severity of acidosis and the adequacy of respiratory compensation. A venous pH below 7.2 is generally associated with more severe disease, a higher risk profile, and a greater likelihood of requiring intensive care monitoring, particularly in pediatric settings where cerebral edema risk is a key concern [29][30][31].

Urinary ketone testing remains widely used in many healthcare facilities because it is inexpensive and readily available; however, clinicians must interpret it in light of its methodological limitations. Nitroprusside-based urine dipsticks detect acetoacetate and acetone but do not measure BHB, which predominates in severe DKA. As a result, urine ketones may lag behind the true clinical course and can remain elevated despite improving BHB and pH, making them less valuable for monitoring treatment response. Blood lactate measurement may be useful when the differential diagnosis includes lactic acidosis or when sepsis is suspected as a precipitant; lactate is also a prognostic marker in systemic infection, which may coexist with or trigger DKA. Hemoglobin A1c (HbA1c) provides context regarding antecedent glycemic control, helping to distinguish chronic poor control from a more abrupt deterioration and informing post-acute management planning. In newly diagnosed patients or those in whom diabetes type is uncertain, selected immunologic and endocrine tests can clarify classification without directly altering acute DKA treatment. Diabetes-associated autoantibodies—such as glutamic acid decarboxylase antibodies, insulin autoantibodies, islet cell antibodies, and zinc transporter 8 antibodies—are not required to manage the acute metabolic emergency, but their presence supports a diagnosis of type 1 diabetes in approximately 80% to 85% of new cases [32]. C-peptide measurement can further assist differentiation by reflecting endogenous beta-cell function; values below 0.2 nmol/L are associated with insulin-deficient diabetes consistent with type 1 diabetes mellitus. This information can be important for longer-term management and counseling, particularly in adolescents whose phenotype may overlap type 1 and type 2 diabetes features [32].

Severity classification is a key output of the evaluation because it informs level-of-care decisions and anticipates complication risk. Pediatric DKA is commonly categorized as mild, moderate, or severe based on venous pH and serum bicarbonate. Mild DKA is characterized by venous pH 7.2 to <7.3 and bicarbonate 10 to <15 mEq/L; moderate DKA by pH 7.1 to <7.2 and bicarbonate 5 to 9 mEq/L; and severe DKA by pH <7.1 with bicarbonate <5 mEq/L. Some guidelines allow higher bicarbonate thresholds for vulnerable populations—such as very young children or patients in resource-limited settings—to support early escalation and monitoring, for example defining severe DKA at bicarbonate <7 mEq/L or mild DKA at bicarbonate <18 mEq/L. In practice, severity assessment should be individualized, incorporating mental status, hemodynamic stability, and comorbid conditions alongside laboratory thresholds to guide safe disposition and monitoring intensity [32].

Treatment / Management

Management of diabetic ketoacidosis (DKA) is an urgent, protocol-driven process that prioritizes physiologic stabilization, reversal of ketoacidosis, correction of dehydration and electrolyte deficits, and identification of precipitating factors to prevent recurrence. Treatment begins immediately with a structured assessment of airway, breathing, and circulation (ABCs) and proceeds to fluid resuscitation as the first therapeutic intervention. Insulin therapy—most commonly delivered as a continuous intravenous infusion—should be initiated after initial stabilization and in a manner that anticipates dynamic potassium shifts and avoids iatrogenic complications, particularly in pediatric patients who are vulnerable to cerebral edema [1][33][34][35]. The overarching goals are to restore intravascular volume, improve tissue perfusion, suppress hepatic ketogenesis, correct acid–base disturbances, and normalize serum osmolality gradually while maintaining adequate cerebral perfusion. Initial resuscitation is centered on cardiopulmonary support and establishment of reliable access. Supplemental oxygen is provided liberally, and clinicians should maintain a low threshold for advanced airway management when there is depressed consciousness, compromised protective reflexes, severe respiratory fatigue, or impending respiratory failure. Intubation may be required in select cases; however, if performed, ventilation strategy must be carefully controlled to avoid abrupt shifts in carbon dioxide and pH that could adversely affect cerebral blood flow. In patients who are comatose or at high aspiration risk, placement of a nasogastric tube may be appropriate for gastric decompression, and a urinary catheter may be used to ensure accurate monitoring of urine output and to help assess renal perfusion response. Early placement of dependable intravenous access—ideally two large-bore cannulas—is strongly preferred, with one line reserved for insulin administration and the other for serial blood sampling, fluid administration, and additional medications. Because dosing fluids, insulin, and electrolytes is weight-based in children, obtaining an accurate patient weight is a practical cornerstone of safe care and should be performed as early as feasible [33][34][35].

Simultaneously with stabilization, clinicians must perform a focused clinical assessment to identify potential precipitants such as infection, missed insulin doses, pump failure, trauma, or other systemic stressors. Fever, focal symptoms, hemodynamic instability, or laboratory indicators of infection should prompt targeted antimicrobial evaluation and therapy when warranted, while recognizing that stress leukocytosis and inflammatory markers may be nonspecific in DKA. Addressing the precipitating cause is not ancillary; it is integral to ensuring durable resolution and preventing early relapse after metabolic correction. Intravenous fluid therapy is the first-line treatment for dehydration and contributes materially to glucose reduction by improving renal perfusion and enhancing glucosuria clearance. Initial fluid resuscitation commonly begins with a bolus of isotonic crystalloid, such as normal saline or lactated Ringer’s solution, at approximately 10 mL/kg. If clinical shock is present—manifested by hypotension, poor perfusion, or altered mentation attributable to circulatory collapse—a second 10 mL/kg bolus may be administered while reassessing perfusion response. Following initial boluses, ongoing fluid replacement is tailored to estimated deficit, maintenance needs, and hemodynamic response, with careful attention to avoiding overly rapid correction of hyperosmolarity. A critical nuance in DKA is the interpretation and monitoring of sodium. Hyperglycemia produces dilutional reductions in measured serum sodium, and as glucose falls, sodium may rise as extracellular water shifts normalize. Continuous sodium monitoring is therefore essential, and if sodium fails to improve or declines during therapy, clinicians may need to adjust the sodium concentration of infused fluids to prevent worsening effective hyponatremia and to support safer osmolar trajectories [36]. This is particularly important in children because large, rapid shifts in tonicity have been associated with cerebral edema risk [36].

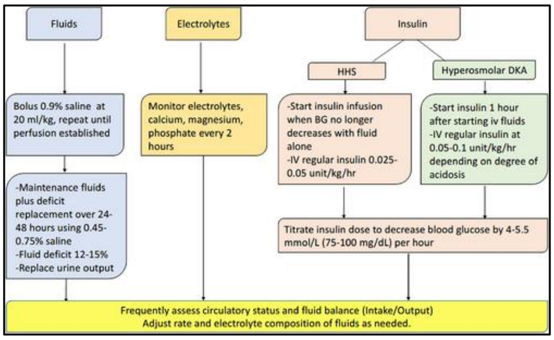

Fig. 3: Management of diabetic ketoacidosis.

Insulin therapy is initiated to halt lipolysis and ketone production, promote cellular glucose utilization, and correct acidosis. Regular insulin is typically administered as a continuous infusion at approximately 0.1 unit/kg/hour [27]. Subcutaneous insulin regimens may be considered in mild DKA or in settings where infusion pumps are not available, but continuous intravenous infusion remains standard for moderate-to-severe disease because it provides predictable pharmacokinetics and allows tight titration. In pediatric DKA, there is no established role for an initial insulin bolus; bolus dosing is generally avoided because it may precipitate rapid osmolar shifts and has been associated with increased risk of cerebral edema. Another essential safety principle is potassium-aware timing: because insulin drives potassium into cells and can acutely lower serum potassium, it is prudent to confirm serum potassium early and, in cases of hypokalemia, to delay insulin initiation until potassium replacement has begun. Even a “normal” potassium level in an acidotic child may mask a profound total-body deficit; accordingly, potassium management must be proactive rather than reactive. As insulin lowers serum glucose, dextrose must be introduced into intravenous fluids to prevent hypoglycemia while allowing continued insulin delivery until ketoacidosis resolves. Dextrose is commonly added when glucose decreases to approximately 250 mg/dL [27]. If glucose continues to fall—particularly below 150 mg/dL—higher dextrose concentrations, such as 10% to 12.5%, may be used to sustain sufficient glucose availability while maintaining the insulin infusion. This strategy is crucial because the therapeutic endpoint in DKA is not normalization of glucose alone, but correction of acidosis and closure of the anion gap through cessation of ketone production and enhanced ketone metabolism. Ideally, clinicians reduce the insulin infusion rate only after ketoacidosis is corrected or nearly corrected. However, individualized adjustments may be necessary in malnourished patients or those with heightened insulin sensitivity to prevent recurrent hypoglycemia while maintaining adequate suppression of ketogenesis [27].

Criteria for discontinuing the insulin infusion reflect both clinical readiness and biochemical resolution. The infusion is typically stopped when the patient can tolerate oral intake or oral medications, blood glucose is below 200 mg/dL, ketone burden has substantially resolved as evidenced by closure of the anion gap or a marked reduction in BHB (for example, BHB less than or equal to 10.4 mg/dL), and acid–base status has normalized or near-normalized, such as a venous pH greater than 7.3 or serum bicarbonate above 15 mEq/L. Transitioning off intravenous insulin must be managed deliberately to avoid rebound ketosis. Long-acting basal insulin should be administered before discontinuing the infusion to ensure continuous insulin coverage during the transition to subcutaneous therapy and to prevent recurrence of ketogenesis. Electrolyte replacement, particularly potassium, is a continuous process that must be guided by frequent laboratory reassessment and clinical monitoring. Because total body potassium is depleted in most children with DKA, replacement is often necessary once renal function and urine output are confirmed. If initial potassium is elevated, replacement is typically withheld until potassium levels begin to normalize, urinary output is established, and renal function is adequate. Conversely, normal or low serum potassium generally indicates the need for replacement after excluding significant renal impairment, given the likelihood of substantial total body depletion. In cases of frank hypokalemia, potassium repletion should take priority and insulin initiation should be delayed until potassium is being corrected, because insulin-driven intracellular shifts can precipitate life-threatening arrhythmias. Electrocardiographic monitoring can be used when potassium abnormalities are severe, when rapid shifts are anticipated, or when clinical status warrants additional surveillance. Resolution of ketoacidosis is typically defined by normalization of the anion gap, reduction of serum BHB to a low level such as ≤10.4 mg/dL, and improvement of venous pH to ≥7.3. These endpoints reflect the combined effects of insulin suppressing hepatic ketone generation, peripheral tissues metabolizing ketones more effectively, and improved renal clearance as rehydration restores perfusion [27][37]. Lactic acidosis, when present, also tends to correct with restoration of circulating volume and improved tissue perfusion, although persistent lactate elevation should prompt reassessment for sepsis or other ongoing causes [27][37].

Bicarbonate therapy is generally avoided in pediatric DKA because of concerns about paradoxical central nervous system acidosis, potassium shifts, and potential association with cerebral edema. Exceptions may exist in extreme circumstances, such as peri-arrest or cardiac arrest states, life-threatening hyperkalemia, or profound acidemia with pH below 6.9 accompanied by severe clinical compromise. Even in these scenarios, bicarbonate use should be cautious, protocol-driven, and coupled with close monitoring. High-quality nursing care and frequent bedside assessment are essential throughout DKA treatment, as clinical deterioration can occur despite improving laboratory values. Regular evaluations of mental status, perfusion, respiratory effort, and fluid balance should be paired with frequent biochemical monitoring, often at intervals such as every two hours for key markers during the acute phase, to ensure safe correction of glucose, electrolytes, and acid–base status. Particular vigilance is required for neurological changes that could signal cerebral edema, including headache, irritability, bradycardia, hypertension, declining level of consciousness, or abnormal pupillary findings. Early recognition of such features is critical because timely intervention may be lifesaving. Once ketoacidosis has resolved, the anion gap has closed, and the patient demonstrates sustained clinical improvement, oral intake can be reintroduced and a structured transition to subcutaneous insulin initiated. Education and prevention planning should begin before discharge. Determining the cause of the acute DKA episode—whether infection, missed insulin, psychosocial barriers, access limitations, or equipment failure—is essential to reducing recurrence risk. Clinicians should work collaboratively with the child and caregivers to reinforce sick-day rules, ensure availability and correct use of insulin and monitoring supplies, address barriers to adherence, and coordinate outpatient follow-up with diabetes educators and the broader care team. In this way, acute metabolic rescue is linked to durable prevention, aligning immediate stabilization with long-term risk reduction [37].

Differential Diagnosis

The differential diagnosis of diabetic ketoacidosis (DKA) is broad because its defining clinical features—vomiting, abdominal pain, dehydration, tachypnea, altered mental status, and metabolic acidosis—overlap with numerous medical and toxicologic conditions. A systematic approach is therefore required, integrating symptom chronology, diabetes history, bedside examination, and targeted laboratory evaluation to distinguish DKA from alternative causes of acid–base disturbance and shock. Gastroenteritis is a frequent diagnostic competitor, particularly in children presenting with vomiting and dehydration; however, gastroenteritis alone does not typically produce a high–anion gap metabolic acidosis with ketonemia and marked hyperglycemia. That said, DKA may coexist with infectious gastroenteritis, and persistent vomiting should not exclude DKA when polyuria, polydipsia, weight loss, or Kussmaul respirations are present. Hyperosmolar hyperglycemic nonketotic syndrome (HHS) must be considered in patients with severe hyperglycemia and dehydration, especially in type 2 diabetes. HHS is characterized by extreme hyperosmolarity with minimal or absent ketosis and less prominent acidosis, whereas DKA features substantial ketone accumulation and acidemia. Starvation ketosis can also mimic aspects of DKA by producing ketones and mild acidosis, particularly in patients with prolonged fasting or poor intake, but it is typically associated with normal or low glucose concentrations and a less severe acid–base disturbance. Alcoholic ketoacidosis similarly presents with high–anion gap acidosis and ketonemia, often in the setting of heavy alcohol use and reduced oral intake; glucose is frequently low to normal, and the clinical context is usually distinctive [37][38].

Several life-threatening conditions can both resemble and precipitate DKA, requiring active exclusion. Sepsis may present with dehydration, tachypnea, hypotension, and lactic acidosis; lactate measurement and careful infectious evaluation are important, especially because sepsis can trigger DKA in patients with diabetes. Acute pancreatitis is another critical alternative diagnosis, given its association with abdominal pain, vomiting, and systemic inflammation; it can also be a precipitant of DKA, making serum lipase assessment and imaging considerations relevant when clinical suspicion is high. Myocardial infarction, while less common in pediatric populations, remains a key consideration in adults with diabetes and may present with atypical symptoms and metabolic stress. Uremia from renal failure can cause metabolic acidosis, altered mental status, and electrolyte abnormalities; elevated creatinine and a clinical history of kidney disease help differentiate it, though renal dysfunction may also complicate severe DKA. Toxicologic exposures constitute an especially important subset because they can produce high–anion gap metabolic acidosis and altered consciousness. Ingestions such as ethylene glycol and methanol, as well as salicylates, can mimic DKA and require assessment for osmolar gap, toxic alcohol levels where available, and characteristic co-findings. Diabetic medication overdose, particularly with insulin or insulin secretagogues, may cause hypoglycemia rather than hyperglycemia, but mixed presentations can occur in complex cases, reinforcing the need for careful medication history and serial glucose monitoring. Finally, primary respiratory disorders—including respiratory acidosis and respiratory distress syndrome—may present with tachypnea and altered blood gas values, yet their acid–base pattern differs, with elevated $PaCO_2$ and a primary respiratory process rather than the low $PaCO_2$ compensatory response typical of DKA [37][38].

Prognosis

The prognosis of pediatric diabetic ketoacidosis (DKA) has improved substantially over recent decades, largely due to advances in early recognition, standardized treatment protocols, and the availability of modern pediatric critical care. In high-resource settings, contemporary case fatality rates are low, with reported mortality typically ranging from approximately 0.15% to 0.31% in the United States and other resource-developed countries such as Canada and the United Kingdom [38]. Nevertheless, DKA remains a high-acuity emergency because death, when it occurs, is often sudden and frequently linked to neurological injury rather than to metabolic derangements alone. Indeed, a substantial proportion of fatalities are attributable to cerebral injury, including cerebral edema and related intracranial complications that can evolve before, during, or after initiation of therapy [39]. This reality underscores a key prognostic principle: survival is not determined solely by correcting glucose and acidosis, but also by preventing and rapidly treating cerebral complications and other organ failures during the resuscitation course. Prognosis varies markedly across health systems and patient populations. Although mortality is relatively low in well-resourced environments with rapid access to pediatric intensive care and experienced multidisciplinary teams, outcomes may be significantly worse in resource-limited settings where delayed presentation, limited monitoring capacity, and restricted access to intensive therapies are more common. In such contexts, higher mortality reflects both greater illness severity at arrival and constraints in implementing close neurologic surveillance, frequent laboratory monitoring, and timely escalation when complications arise. Beyond survival, prognosis also includes morbidity. Many children recover fully after appropriately managed DKA, yet severe episodes can be associated with short- and long-term sequelae, including neurocognitive effects, renal dysfunction, and recurrence risk in vulnerable adolescents. Thus, prognostic assessment must incorporate the acuity and severity of the presenting episode, the presence of comorbid illness (particularly infection or shock), markers of dehydration and renal impairment, and the quality and timeliness of clinical monitoring and intervention. Importantly, recurrent DKA is a prognostic red flag, often reflecting persistent barriers to diabetes management and signaling increased risk for future life-threatening events. Effective prognosis communication should therefore extend beyond immediate survival to emphasize prevention strategies and systems-based supports that reduce recurrence and protect neurological outcomes [38][39].

Complications

The most feared complication of pediatric DKA is cerebral injury, commonly discussed in relation to cerebral edema, because it carries both high mortality and a significant burden of neurologic morbidity among survivors. Cerebral edema is estimated to occur in approximately 0.3% to 0.9% of pediatric DKA episodes [38]. When it develops, outcomes can be grave; reported mortality commonly ranges from about 21% to 24% [38][40][41][40][38]. Several clinical and biochemical features are associated with increased risk, including severe acidosis, pronounced dehydration, elevated blood pressure, and markedly increased blood urea nitrogen, all of which may reflect the combined effects of hypoperfusion, hyperosmolar stress, and systemic illness severity [39]. The precise etiology remains incompletely defined. Historically, rapid intravenous fluid administration was considered a central causative factor, but this interpretation has become more controversial; notably, a large PECARN study published in 2018 did not demonstrate differences in neurological outcomes across fluid regimens, challenging a simplistic causal attribution to fluid rate alone [42]. Clinically, cerebral injury may present at any point in the illness trajectory—before treatment, during therapy, or after initial biochemical improvement—though onset is often described within the first 12 hours of treatment initiation [39]. Warning signs include altered mental status, new or worsening headache, recurrent vomiting, urinary incontinence, and physiological indicators of raised intracranial pressure such as the Cushing triad (bradycardia, irregular respirations, and hypertension). Importantly, early neuroimaging can be falsely reassuring: cerebral edema may not be apparent on initial CT, and treatment may need to be initiated on clinical suspicion even when imaging is normal [43]. When suspicion is high, emergent therapy includes osmotherapy with mannitol (0.5–1 g/kg IV over 15 minutes, with a repeat dose if no response) or hypertonic 3% saline (2.5 mL/kg over 30 minutes), alongside urgent neurosurgical consultation and escalation of critical care support [40][41]. Beyond cerebral injury, pediatric DKA can be complicated by a wide array of systemic effects. These include cognitive impairment, venous thrombosis [44], pancreatic enzyme elevations, acute kidney injury [45], electrolyte disturbances such as hypokalemia, treatment-related hypoglycemia, rhabdomyolysis, pulmonary edema, multiple organ dysfunction syndrome, and cardiac arrhythmias. Many of these complications reflect the combined impact of dehydration, acidosis, catecholamine surge, and shifting electrolytes during therapy, emphasizing why frequent reassessment and protocolized monitoring are essential to safe management [38][39][40][41][42][43][44][45].

Patient Education

Prevention of DKA depends on comprehensive education that equips children and caregivers with the knowledge and practical skills needed to manage diabetes reliably during both routine life and intercurrent illness. Education should cover the disease process, including short- and long-term complications, and should emphasize that DKA is often preventable through consistent insulin administration, regular glucose monitoring, and timely response to rising glucose and ketone levels. Parents and children should be trained on when and how to check blood glucose, how to interpret results, and how to respond to abnormal values with appropriate corrective actions. Education must also address medication use in detail, including insulin administration techniques, dosing schedules, side effects, and the critical importance of adherence. Where oral hypoglycemic agents are relevant—primarily in type 2 diabetes—families should similarly understand dosing, interactions, and what to do during illness. “Sick-day” guidance is particularly important: caregivers should be taught not to stop insulin during illness, to increase monitoring frequency, to maintain hydration, and to seek early medical evaluation when vomiting, persistent hyperglycemia, ketonemia, or altered mental status occurs. Dietitians, nurses, and multidisciplinary home-health support can be pivotal in translating education into sustainable routines, tailoring meal planning, and addressing barriers such as health literacy, access to supplies, or psychosocial stressors. Education is most effective when reinforced repeatedly, assessed through teach-back methods, and linked to follow-up pathways that ensure ongoing support rather than relying on a single discharge conversation [44][45].

Other Issues

Recurrent DKA is a particularly serious clinical problem in adolescents, in whom episodes may be frequent, severe, and potentially fatal. A key clinical pearl is that recurrence often signals modifiable behavioral, psychosocial, or structural barriers rather than purely biomedical failure. Early help is advised as soon as DKA is suspected or diagnosed, and prevention efforts should begin during the acute admission, not after discharge. Common precipitating factors include poor adherence to insulin therapy or inadequate understanding of regimen requirements, intercurrent infections, alcohol and substance use disorders, psychological stress and major lifestyle changes, and comorbid psychiatric disorders. Adolescents may face unique challenges, including autonomy transitions, risk-taking behavior, stigma, peer influence, and disordered eating patterns, all of which can undermine consistent insulin use. Clinicians should therefore adopt a nonjudgmental, systems-based approach that identifies barriers, connects families to mental health and social support resources, ensures reliable access to insulin and monitoring supplies, and establishes clear, achievable follow-up plans. Another practical pearl is that clinical improvement in glucose levels does not guarantee resolution of ketoacidosis or safety from cerebral complications; continued monitoring of mental status, electrolytes, and acid–base markers remains essential until biochemical endpoints are met. Finally, because many severe complications are time-sensitive, teams should maintain explicit escalation thresholds for neurological change, hemodynamic instability, or electrolyte deterioration to ensure prompt intervention [45].

Enhancing Healthcare Team Outcomes

Pediatric DKA is best managed through an interprofessional model that integrates rapid emergency stabilization with specialized endocrine care and continuous critical care monitoring. Optimal teams typically include an emergency department clinician, pediatric endocrinologist, pediatrician, intensivist, critical care nursing staff, and pharmacists, with many children requiring ICU-level care due to the need for frequent neurological assessment, strict fluid and insulin titration, and serial laboratory monitoring. While clinicians deliver initial hydration and insulin therapy to correct acidosis, the team must simultaneously investigate precipitating causes such as infection, missed insulin dosing, pump malfunction, or psychosocial barriers. Nurses play a central role in continuous bedside monitoring, accurate intake/output measurement, timely recognition of neurological change, and execution of protocol-based insulin and fluid adjustments. Pharmacists contribute by verifying weight-based dosing, monitoring for medication interactions, supporting safe electrolyte replacement, and counseling caregivers regarding insulin administration and supply use. Diabetes educators and primary caregivers collaborate to reinforce adherence strategies, teach sick-day management, and ensure that families understand how to monitor glucose and ketones at home. High-quality outcomes depend on disciplined communication and documentation. Every interprofessional member is responsible for recording observations, interventions, and patient responses, and for promptly informing colleagues when clinical status changes so that corrective actions can be instituted without delay. Because pediatric DKA can evolve rapidly, any detected deterioration—particularly neurological decline—should trigger immediate documentation and direct notification of the treating team to ensure timely escalation and reduce preventable morbidity and mortality [46][28][47]. Interprofessional care, grounded in shared protocols and rapid communication loops, remains the most effective methodology for managing pediatric DKA and for protecting patients through the most vulnerable phases of treatment [46][47][48] .

Conclusion:

Pediatric diabetic ketoacidosis remains a critical emergency with potentially fatal complications, most notably cerebral edema. Despite advances in standardized protocols and critical care, outcomes hinge on timely recognition, meticulous fluid and insulin management, and continuous monitoring of neurological and biochemical parameters. The complexity of DKA extends beyond acute metabolic correction; it reflects systemic gaps in education, access, and psychosocial support. Recurrence, particularly among adolescents, underscores the need for holistic strategies that address behavioral and structural barriers to adherence. Effective prevention begins during hospitalization, linking acute stabilization with long-term education, caregiver engagement, and coordinated outpatient follow-up. Sick-day rules, reliable insulin access, and psychosocial interventions are pivotal in reducing recurrence risk. Interprofessional collaboration—spanning emergency clinicians, endocrinologists, nurses, pharmacists, and social workers—ensures comprehensive care and rapid escalation when complications arise. Ultimately, pediatric DKA management is not merely a technical exercise but a systems-based endeavor that integrates acute care with durable prevention. By coupling evidence-based protocols with patient-centered education and multidisciplinary teamwork, healthcare providers can significantly reduce morbidity, mortality, and the burden of recurrent episodes, safeguarding both immediate survival and long-term quality of life.

References:

1. Abulebda K, Whitfill T, Montgomery EE, Kirby ML, Ahmed RA, Cooper DD, Nitu ME, Auerbach MA, Lutfi R, Abu-Sultaneh S. Improving Pediatric Diabetic Ketoacidosis Management in Community Emergency Departments Using a Simulation-Based Collaborative Improvement Program. Pediatric emergency care. 2021 Nov 1:37(11):543-549. doi: 10.1097/PEC.0000000000001751.
2. Agarwal HS. Subclinical cerebral edema in diabetic ketoacidosis in children. Clinical case reports. 2019 Feb:7(2):264-267. doi: 10.1002/ccr3.1960.
3. Mayer-Davis EJ, Kahkoska AR, Jefferies C, Dabelea D, Balde N, Gong CX, Aschner P, Craig ME. ISPAD Clinical Practice Consensus Guidelines 2018: Definition, epidemiology, and classification of diabetes in children and adolescents. Pediatric diabetes. 2018 Oct:19 Suppl 27(Suppl 27):7-19. doi: 10.1111/pedi.12773.
4. Flood K, Nour M, Holt T, Cattell V, Krochak C, Inman M. Implementation and Evaluation of a Diabetic Ketoacidosis Order Set in Pediatric Type 1 Diabetes at a Tertiary Care Hospital: A Quality-Improvement Initiative. Canadian journal of diabetes. 2019 Jul:43(5):297-303. doi: 10.1016/j.jcjd.2018.12.005.
5. Danne T, Garg S, Peters AL, Buse JB, Mathieu C, Pettus JH, Alexander CM, Battelino T, Ampudia-Blasco FJ, Bode BW, Cariou B, Close KL, Dandona P, Dutta S, Ferrannini E, Fourlanos S, Grunberger G, Heller SR, Henry RR, Kurian MJ, Kushner JA, Oron T, Parkin CG, Pieber TR, Rodbard HW, Schatz D, Skyler JS, Tamborlane WV, Yokote K, Phillip M. International Consensus on Risk Management of Diabetic Ketoacidosis in Patients With Type 1 Diabetes Treated With Sodium-Glucose Cotransporter (SGLT) Inhibitors. Diabetes care. 2019 Jun:42(6):1147-1154. doi: 10.2337/dc18-2316.
6. Al Zahrani AM, Al Shaikh A. Glycemic Control in Children and Youth With Type 1 Diabetes Mellitus in Saudi Arabia. Clinical medicine insights. Endocrinology and diabetes. 2019:12():1179551418825159. doi: 10.1177/1179551418825159.
7. Jawaid A, Sohaila A, Mohammad N, Rabbani U. Frequency, clinical characteristics, biochemical findings and outcomes of DKA at the onset of type-1 DM in young children and adolescents living in a developing country - an experience from a pediatric emergency department. Journal of pediatric endocrinology & metabolism : JPEM. 2019 Feb 25:32(2):115-119. doi: 10.1515/jpem-2018-0324.
8. Edge JA, Hawkins MM, Winter DL, Dunger DB. The risk and outcome of cerebral oedema developing during diabetic ketoacidosis. Archives of disease in childhood. 2001 Jul:85(1):16-22
9. Sapru A, Gitelman SE, Bhatia S, Dubin RF, Newman TB, Flori H. Prevalence and characteristics of type 2 diabetes mellitus in 9-18 year-old children with diabetic ketoacidosis.

Journal of pediatric endocrinology & metabolism : JPEM. 2005 Sep:18(9):865-72

10. Wolfsdorf J, Glaser N, Sperling MA, American Diabetes Association. Diabetic ketoacidosis in infants, children, and adolescents: A consensus statement from the American Diabetes Association. Diabetes care. 2006 May:29(5):1150
11. Kao KT, Islam N, Fox DA, Amed S. Incidence Trends of Diabetic Ketoacidosis in Children and Adolescents with Type 1 Diabetes in British Columbia, Canada. The Journal of pediatrics. 2020 Jun:221():165-173.e2. doi: 10.1016/j.jpeds.2020.02.069.
12. Rewers A, Klingensmith G, Davis C, Petitti DB, Pihoker C, Rodriguez B, Schwartz ID, Imperatore G, Williams D, Dolan LM, Dabelea D. Presence of diabetic ketoacidosis at diagnosis of diabetes mellitus in youth: the Search for Diabetes in Youth Study. Pediatrics. 2008 May:121(5):e1258-66. doi: 10.1542/peds.2007-1105.
13. Mallare JT, Cordice CC, Ryan BA, Carey DE, Kreitzer PM, Frank GR. Identifying risk factors for the development of diabetic ketoacidosis in new onset type 1 diabetes mellitus. Clinical pediatrics. 2003 Sep:42(7):591-7
14. Lévy-Marchal C, Patterson CC, Green A, EURODIAB ACE Study Group. Europe and Diabetes. Geographical variation of presentation at diagnosis of type I diabetes in children: the EURODIAB study. European and Dibetes. Diabetologia. 2001 Oct:44 Suppl 3():B75-80
15. Rewers A, Chase HP, Mackenzie T, Walravens P, Roback M, Rewers M, Hamman RF, Klingensmith G. Predictors of acute complications in children with type 1 diabetes. JAMA. 2002 May 15:287(19):2511-8
16. Cengiz E, Xing D, Wong JC, Wolfsdorf JI, Haymond MW, Rewers A, Shanmugham S, Tamborlane WV, Willi SM, Seiple DL, Miller KM, DuBose SN, Beck RW, T1D Exchange Clinic Network. Severe hypoglycemia and diabetic ketoacidosis among youth with type 1 diabetes in the T1D Exchange clinic registry. Pediatric diabetes. 2013 Sep:14(6):447-54. doi: 10.1111/pedi.12030.
17. Neufeld ND, Raffel LJ, Landon C, Chen YD, Vadheim CM. Early presentation of type 2 diabetes in Mexican-American youth. Diabetes care. 1998 Jan:21(1):80-6
18. Katz MA. Hyperglycemia-induced hyponatremia--calculation of expected serum sodium depression. The New England journal of medicine. 1973 Oct 18:289(16):843-4
19. Kebler R, McDonald FD, Cadnapaphornchai P. Dynamic changes in serum phosphorus levels in diabetic ketoacidosis. The American journal of medicine. 1985 Nov:79(5):571-6
20. Barnes AJ, Bloom SR, Goerge K, Alberti GM, Smythe P, Alford FP, Chisholm DJ. Ketoacidosis in pancreatectomized man. The New England journal of medicine. 1977 Jun 2:296(22):1250-3
21. Miles JM, Haymond MW, Nissen SL, Gerich JE. Effects of free fatty acid availability, glucagon excess, and insulin deficiency on ketone body production in postabsorptive man. The Journal of clinical investigation. 1983 Jun:71(6):1554-61
22. Edgerton DS, Ramnanan CJ, Grueter CA, Johnson KM, Lautz M, Neal DW, Williams PE, Cherrington AD. Effects of insulin on the metabolic control of hepatic gluconeogenesis in vivo. Diabetes. 2009 Dec:58(12):2766-75. doi: 10.2337/db09-0328.
23. Owen OE, Trapp VE, Skutches CL, Mozzoli MA, Hoeldtke RD, Boden G, Reichard GA Jr. Acetone metabolism during diabetic ketoacidosis. Diabetes. 1982 Mar:31(3):242-8
24. Kangin M, Talay MN, Tanriverdi Yilmaz S, Unal E, Demiral M, Asena M, Ozbek MN. A Retrospective Analysis of Children and Adolescents With Diabetic Ketoacidosis in the Intensive Care Unıt: Is It Significant that the Blood Ketone Level Becomes Negative in Diabetic Ketoacidosis? Cureus. 2020 Oct 8:12(10):e10844. doi: 10.7759/cureus.10844.
25. Tantiwong P, Puavilai G, Ongphiphadhanakul B, Bunnag P, Ngarmukos C. Capillary blood beta-hydroxybutyrate measurement by reagent strip in diagnosing diabetic ketoacidosis. Clinical laboratory science : journal of the American Society for Medical Technology. 2005 Summer:18(3):139-44
26. Edge JA, Roy Y, Bergomi A, Murphy NP, Ford-Adams ME, Ong KK, Dunger DB. Conscious level in children with diabetic ketoacidosis is related to severity of acidosis and not to blood glucose concentration. Pediatric diabetes. 2006 Feb:7(1):11-5
27. Wolfsdorf JI, Glaser N, Agus M, Fritsch M, Hanas R, Rewers A, Sperling MA, Codner E. ISPAD Clinical Practice Consensus Guidelines 2018: Diabetic ketoacidosis and the hyperglycemic hyperosmolar state. Pediatric diabetes. 2018 Oct:19 Suppl 27():155-177. doi: 10.1111/pedi.12701.
28. Glaser N, Kuppermann N. Fluid treatment for children with diabetic ketoacidosis: How do the results of the pediatric emergency care applied research network Fluid Therapies Under Investigation in Diabetic Ketoacidosis (FLUID) Trial change our perspective? Pediatric diabetes. 2019 Feb:20(1):10-14. doi: 10.1111/pedi.12795.
29. Abbas Q, Arbab S, Haque AU, Humayun KN. Spectrum of complications of severe DKA in children in pediatric Intensive Care Unit. Pakistan journal of medical sciences. 2018 Jan-Feb:34(1):106-109. doi: 10.12669/pjms.341.13875.

30. Baalaaji M, Jayashree M, Nallasamy K, Singhi S, Bansal A. Predictors and Outcome of Acute Kidney Injury in Children with Diabetic Ketoacidosis. Indian pediatrics. 2018 Apr 15:55(4):311-314
31. Wolfsdorf JI. The International Society of Pediatric and Adolescent Diabetes guidelines for management of diabetic ketoacidosis: Do the guidelines need to be modified? Pediatric diabetes. 2014 Jun:15(4):277-86. doi: 10.1111/pedi.12154.
32. Dabelea D, Pihoker C, Talton JW, D'Agostino RB Jr, Fujimoto W, Klingensmith GJ, Lawrence JM, Linder B, Marcovina SM, Mayer-Davis EJ, Imperatore G, Dolan LM, SEARCH for Diabetes in Youth Study. Etiological approach to characterization of diabetes type: the SEARCH for Diabetes in Youth Study. Diabetes care. 2011 Jul:34(7):1628-33. doi: 10.2337/dc10-2324.
33. Weinberger K, Seick Barbarini D, Simma B. Adherence to Guidelines in the Treatment of Diabetic Ketoacidosis in Children: An Austrian Survey. Pediatric emergency care. 2021 May 1:37(5):245-249. doi: 10.1097/PEC.0000000000001551.
34. Gunn ER, Albert BB, Hofman PL, Cutfield WS, Gunn AJ, Jefferies CA, Starbase Diabetes Working Group, Paediatric Diabetes Service, Starship Children's Hospital, Auckland, New Zealand. Pathways to reduce diabetic ketoacidosis with new onset type 1 diabetes: Evidence from a regional pediatric diabetes center: Auckland, New Zealand, 2010 to 2014. Pediatric diabetes. 2017 Nov:18(7):553-558. doi: 10.1111/pedi.12456.
35. Abulebda K, Abu-Sultaneh S, White EE, Kirby ML, Phillips BC, Frye CT, Murphy LD, Lutfi R. Disparities in Adherence to Pediatric Diabetic Ketoacidosis Management Guidelines Across a Spectrum of Emergency Departments in the State of Indiana: An Observational In Situ Simulation-Based Study. Pediatric emergency care. 2024 Nov 1:40(11):e265-e269. doi: 10.1097/PEC.0000000000001494.
36. Glaser NS, Stoner MJ, Garro A, Baird S, Myers SR, Rewers A, Brown KM, Trainor JL, Quayle KS, McManemy JK, DePiero AD, Nigrovic LE, Tzimenatos L, Schunk JE, Olsen CS, Casper TC, Ghetti S, Kuppermann N, Pediatric Emergency Care Applied Research Network (PECARN) DKA FLUID Study Group. Serum Sodium Concentration and Mental Status in Children With Diabetic Ketoacidosis. Pediatrics. 2021 Sep:148(3):. pii: e2021050243. doi: 10.1542/peds.2021-050243.
37. Noyes KJ, Crofton P, Bath LE, Holmes A, Stark L, Oxley CD, Kelnar CJ. Hydroxybutyrate near-patient testing to evaluate a new end-point for intravenous insulin therapy in the treatment of diabetic ketoacidosis in children. Pediatric diabetes. 2007 Jun:8(3):150-6
38. Lawrence SE, Cummings EA, Gaboury I, Daneman D. Population-based study of incidence and risk factors for cerebral edema in pediatric diabetic ketoacidosis. The Journal of pediatrics. 2005 May:146(5):688-92
39. Glaser N, Barnett P, McCaslin I, Nelson D, Trainor J, Louie J, Kaufman F, Quayle K, Roback M, Malley R, Kuppermann N, Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics. Risk factors for cerebral edema in children with diabetic ketoacidosis. The Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics. The New England journal of medicine. 2001 Jan 25:344(4):264-9
40. Marcin JP, Glaser N, Barnett P, McCaslin I, Nelson D, Trainor J, Louie J, Kaufman F, Quayle K, Roback M, Malley R, Kuppermann N, American Academy of Pediatrics. The Pediatric Emergency Medicine Collaborative Research Commitee. Factors associated with adverse outcomes in children with diabetic ketoacidosis-related cerebral edema. The Journal of pediatrics. 2002 Dec:141(6):793-7
41. Scibilia J, Finegold D, Dorman J, Becker D, Drash A. Why do children with diabetes die? Acta endocrinologica. Supplementum. 1986:279():326-33
42. Kuppermann N, Ghetti S, Schunk JE, Stoner MJ, Rewers A, McManemy JK, Myers SR, Nigrovic LE, Garro A, Brown KM, Quayle KS, Trainor JL, Tzimenatos L, Bennett JE, DePiero AD, Kwok MY, Perry CS 3rd, Olsen CS, Casper TC, Dean JM, Glaser NS, PECARN DKA FLUID Study Group. Clinical Trial of Fluid Infusion Rates for Pediatric Diabetic Ketoacidosis. The New England journal of medicine. 2018 Jun 14:378(24):2275-2287. doi: 10.1056/NEJMoa1716816.
43. Krane EJ, Rockoff MA, Wallman JK, Wolfsdorf JI. Subclinical brain swelling in children during treatment of diabetic ketoacidosis. The New England journal of medicine. 1985 May 2:312(18):1147-51
44. Worly JM, Fortenberry JD, Hansen I, Chambliss CR, Stockwell J. Deep venous thrombosis in children with diabetic ketoacidosis and femoral central venous catheters. Pediatrics. 2004 Jan:113(1 Pt 1):e57-60
45. Hursh BE, Ronsley R, Islam N, Mammen C, Panagiotopoulos C. Acute Kidney Injury in Children With Type 1 Diabetes Hospitalized for Diabetic Ketoacidosis. JAMA pediatrics. 2017 May 1:171(5):e170020. doi: 10.1001/jamapediatrics.2017.0020.
46. Foster NC, Beck RW, Miller KM, Clements MA, Rickels MR, DiMeglio LA, Maahs DM, Tamborlane WV, Bergenstal R, Smith E, Olson BA, Garg SK. State of Type 1 Diabetes

Management and Outcomes from the T1D Exchange in 2016-2018. Diabetes technology & therapeutics. 2019 Feb:21(2):66-72. doi: 10.1089/dia.2018.0384. E

47. Sildorf SM, Breinegaard N, Lindkvist EB, Tolstrup JS, Boisen KA, Teilmann GK, Skovgaard AM, Svensson J. Poor Metabolic Control in Children and Adolescents With Type 1 Diabetes and Psychiatric Comorbidity. Diabetes care. 2018 Nov:41(11):2289-2296. doi: 10.2337/dc18-0609.