# Chapter 48
# Approach to Hyperglycemia in the ICU


## 48.1 Introduction

Hyperglycemic crises, particularly diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic syndrome (HHS), are life-threatening emergencies common in ICU settings. Their occurrence can be associated with both type 1 and type 2 diabetes and, without timely intervention, can lead to severe complications and high healthcare costs. The structured approach outlined here offers a comprehensive guide for identifying, assessing, and managing these crises to optimize outcomes and reduce risks [1–5]. [Ref: Algorithm 48.1].

## 48.2 Epidemiological and Economic Impact

- Increased Incidence: In recent years, the incidence of both DKA and HHS has surged, often due to delayed diagnosis and the rising prevalence of diabetes globally. This trend has placed a substantial burden on healthcare systems, with DKA and HHS admissions escalating the demand for ICU resources.
- Economic Burden: Management of recurrent hyperglycemic crises is costly. DKA and HHS are responsible for high hospitalization costs, especially with recurrent episodes, which frequently lead to repeat ICU admissions. For effective long-term management, reducing recurrence is paramount to controlling these costs [6].



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### *48.2.1 Risk Factors and Preventative Measures*

- Risk Factors: Key risk factors include infections, intercurrent illnesses, psychological stress, and omission or insufficient use of insulin therapy. Of these, infection is the most common trigger worldwide. Urinary tract infection and pneumonia are the most common infectious causes leading to DKA and HHS. Stroke, alcohol and substance use, pancreatitis, pulmonary embolism, myocardial infarction, and trauma are the other acute factors that can precipitate DKA. Among the type 1 diabetes patients, omission of insulin therapy, often in the setting of psychological and socioeconomic factors, is a major cause of DKA. Younger age, prior history of hyperglycemic and hypoglycemic crises, presence of kidney disease, neuropathy, depression, smoking, alcohol and substance abuse, and high HbA1c are the other factors leading to increased chances of DKA in type 1 diabetes population. For people with type 2 diabetes, presence of comorbidities is another risk factor in addition to the factors mentioned.
- The risk factors for recurrence are insulin omission, psychiatric conditions (such as depression or substance abuse), and poor social support, all of which can increase the likelihood of repeat episodes. Recognizing and addressing these factors can prevent future crises.
- Preventative Education: Educating patients and families on early signs and symptoms, such as excessive thirst, frequent urination, and fatigue, is critical. Awareness of triggers and preventive strategies can empower patients and reduce the severity and frequency of hyperglycemic events [7].

## 48.3 Pathophysiology and Diagnostic Nuances

- Differentiation of DKA and HHS:
- Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic syndrome (HHS) represent two distinct clinical syndromes along the spectrum of hyperglycemic crises, each with unique pathophysiology and management implications.
- DKA occurs predominantly in patients with type 1 diabetes but can also affect those with type 2 diabetes under extreme stress or during critical illness. It is characterized by an absolute insulin deficiency, which leads to an unregulated breakdown of fatty acids, resulting in ketonemia (elevated ketones) and anion gap metabolic acidosis. In DKA, hyperglycemia is typically present but is less pronounced than in HHS.
- HHS often occurs in patients with type 2 diabetes, particularly elderly individuals with concomitant infections or other stressors. Here, relative insulin deficiency allows for severe hyperglycemia, which causes an osmotic diuresis and leads to extreme dehydration and hyperosmolality (often exceeding 320 mOsm/

kg). However, because there is usually a minimal increase in lipolysis, ketosis and acidosis are absent or mild.

- Differentiating DKA from HHS is essential as they involve different risks and treatment approaches. DKA requires prompt correction of acidosis and careful electrolyte management, while HHS management emphasizes gradual correction of hyperosmolality and rehydration to avoid complications like cerebral edema. This distinction guides treatment priorities, especially regarding fluid management and insulin therapy initiation.
- Euglycemic DKA:
- Euglycemic DKA (eDKA) is a variant of DKA where patients present with the classical metabolic acidosis and ketonemia of DKA but with normal to only moderately elevated blood glucose levels (often <250 mg/dL). This condition is increasingly recognized, especially in patients treated with SGLT2 inhibitors, which promote urinary glucose excretion and can obscure the hyperglycemia typically associated with DKA. Identifying euglycemic DKA can be challenging due to its atypical presentation, as clinicians often rely on elevated glucose levels as a diagnostic marker for hyperglycemic crises. Therefore, in patients taking SGLT2 inhibitors or those with symptoms consistent with DKA (nausea, vomiting, abdominal pain, altered mental status), it is crucial to assess blood ketone levels and blood gas values to detect acidosis.
- Managing eDKA involves similar principles to DKA, focusing on correcting acidosis, managing ketonemia, and stabilizing electrolytes, with the added emphasis on monitoring for hypoglycemia since blood glucose levels may not be significantly elevated. Regular ketone monitoring and close observation for acidosis resolution are necessary throughout treatment [8].
- Diagnostic criteria DKA:
  - Glucose ≥200 mg/dL (11.1 mmol/L) OR prior history of diabetes.
  - β-Hydroxybutyrate concentration ≥ 3.0 mmol/L (3.8 mg/dL) OR urine ketone strip 2+ or greater,
  - pH < 7.3 and/or bicarbonate levels <18 mmol/L.

  Presence of all 3 is necessary to make a diagnosis of DKA.

Serum ketone (β-hydroxybutyrate) levels are more specific than urine ketone (acetoacetate). Urine ketone testing can underestimate the severity of ketonemia early in the course of DKA because of a lag in the formation of acetoacetate, and conversely, overestimate its severity later in the course of DKA when β-hydroxybutyrate is being cleared and converted into acetoacetate. DKA patients usually present with a high anion gap metabolic acidosis.

DKA can be graded into mild, moderate, and severe based on metabolic acidosis, ketonemia, and mental status.

| | Mild DKA | Moderate DKA | Severe DKA |
|---|---|---|---|
| Blood glucose levels/history of DM | Glucose ≥200 mg/dL | Glucose ≥200 mg/dL | Glucose≥200 mg/dL |
| Ketonemia | β-Hydroxybutyrate 3.8–7.6 mg/dL | β-Hydroxybutyrate 3.8–7.6 mg/dL | β-Hydroxybutyrate>7.6 mg/dL |
| Acidosis | pH >7.25 to<7.30 and Bicarbonate 15–18 mmol/L | pH 7.00–7.25 and Bicarbonate 10–15 mmol/L | pH <7.00 and Bicarbonate <10 mmol/L |
| Mental status | Alert | Alert/drowsy | Stupor/coma |

- Diagnostic criteria HHS: hyperglycemia and hyperosmolality in the absence of severe ketonemia and metabolic acidosis.
  - Plasma glucose ≥600 mg/dL (33.3 mmol/L).
  - Calculated effective serum osmolality >300 mOsm/kg (calculated as [2xNa + (mmol/L) + glucose (mmol/L)]), OR total serum osmolality >320 mOsm/kg [(2xNa + (mmol/L) + glucose (mmol/L) + urea (mmol/L)].
  - β-Hydroxybutyrate concentration <; 3.8 mg/dL or urine ketone showing <;2+ on strip.
  - pH ≥7.3 and bicarbonate concentration ≥ 15 mmol/L (absence of acidosis).

Clinical presentation:
DKA:

- Develops over hours to days.
- Usually alert.
- Polyuria, polydipsia, weight loss, and dehydration.
- Nausea, vomiting, and abdominal pain.
- Kussmaul respiration.

HHS:

- Develops over days to a week.
- Change in cognitive state common.
- Polyuria, polydipsia, weight loss, and dehydration.
- Often co-presenting with other acute illness.

## 48.4 Fluid Management and Electrolyte Considerations

- Guidelines on Fluid Replacement:
- Fluid resuscitation is the cornerstone of initial management for both DKA and HHS, addressing the severe dehydration common in both conditions.

- Initiation: Start with isotonic saline (0.9% NaCl) to quickly expand intravascular volume and prevent hypovolemic shock. In patients with normal cardiac and renal function, give 500–1000 mL/h during the first 2–4 h. The infusion rate is adjusted based on factors like blood pressure, heart rate, and clinical signs of perfusion. In the first few hours, rapid repletion may be necessary to restore hemodynamic stability. In patients with cardiac and renal compromise, small boluses of 250 mL intravenous isotonic crystalloids must be given, and regular hemodynamic assessment must be done.
- Ongoing Management: Estimated fluid deficit should be corrected in 24–48 hours. 5% Dextrose may be used when blood glucose levels are <250 mg/dL, but the ketonemia is not corrected, mandating continuous need of insulin infusion. After initial stabilization, further fluid management is tailored to serum sodium and osmolality levels. For example, in cases of hypernatremia, fluid replacement may shift to hypotonic solutions to avoid worsening hyperosmolarity and minimize the risk of cerebral edema.

In HHS patients, rate of decline in osmolality should be 3–8 mOsm//kg/hr., and sodium correction should be 10 mmol/day.

- Potassium Replacement Protocol:

- Potassium management is a crucial element in treating DKA and HHS due to the shifts in potassium levels induced by insulin therapy and rehydration.
- Initial Assessment: Before initiating insulin therapy, assess serum potassium levels. If potassium levels are low (<3.3 mmol/L), insulin should be delayed until potassium is corrected to avoid life-threatening hypokalemia.
- Replacement Strategy: If serum potassium is within normal range (3.3–5.5 mmol/L), potassium should be supplemented as insulin and fluids are administered, with typical dosing at 20–40 mmol/L in IV fluids. In patients with initial hyperkalemia (>5.5 mmol/L), potassium should be monitored closely, and replacement deferred until levels decrease due to redistribution from insulin and fluid therapy. Regular monitoring every 2–4 hours is essential to adjust potassium replacement based on ongoing levels and avoid hypo- or hyperkalemia [9, 10].

Routine sodium bicarbonate is not recommended. Fluids and insulin usually reverse the deleterious effect of DKA. Bicarbonate may only be given if the pH is <7.0 to reduce several vascular effects like refractory hypotension.

## 48.5 Monitoring Guidelines and Complication Management

If DKA or HHS is suspected, initial samples should be taken for glucose, serum electrolytes, venous blood gases, complete blood count, and blood or urine ketone levels.

Resolution of DKA is defined as achieving plasma ketone <0.6 mmol/L and venous pH ≥7.3 or bicarbonate ≥18 mmol/L [2]. Ideally, the blood glucose concentration should also be<200 mg/dL (11.1 mmol/L). The anion gap should not be used as a criterion, as it may be misleading because of the presence of hyperchloremic metabolic acidosis caused by large volumes of 0.9% sodium chloride solution. Because β-hydroxybutyrate is converted into acetoacetate as the acidosis improves, urinary ketone measurement should be avoided as a criterion of DKA resolution.

HHS is resolved when the measured or calculated serum osmolality falls to<300 mOsm/kg, hyperglycemia has been corrected, urine output is >0.5 mL/kg/h, cognitive status has improved, and the blood glucose is<250 mg/dL.

- Bedside Monitoring with Ketone Meters:
- Bedside measurement of blood ketones, specifically 3-β-hydroxybutyrate, provides a direct marker of ketonemia and metabolic derangement, offering a more precise assessment of DKA resolution compared to blood glucose alone.
- Clinical Practice: Ketone levels should be measured frequently, typically every 1–2 hours during the initial phases of treatment. As ketosis resolves and glucose levels approach target ranges, monitoring frequency may be reduced based on clinical stability.
- Managing Cerebral Edema:
- Cerebral edema is a life-threatening complication, particularly in pediatric DKA patients. It is thought to result from rapid osmolar shifts during rehydration, where excessive fluid shifts into the brain, causing swelling.
- Early Warning Signs: Symptoms such as headache, decreased heart rate, altered neurological status (restlessness, drowsiness), and rising blood pressure are early indicators of cerebral edema. Immediate intervention with hypertonic saline or mannitol is critical in suspected cases to reduce intracranial pressure.
- Preparedness: In pediatric and high-risk cases, hyperosmolar therapy supplies should be readily available, and staff trained to respond promptly to early signs of cerebral edema.

**Aims of Treatment**

- Rate of fall of ketones of at least 0.5 mmol/L/h OR bicarbonate rise 3 mmol/L/h and blood glucose fall 3 mmol/L/h.
- Maintain serum potassium in normal range.
- Avoid hypoglycemia.

## 48.6 Insulin Therapy Adjustments

Confirmation of hyperglycemia: To confirm that hyperglycemia is persistent and not secondary to another condition or factor that could be causing elevated blood glucose levels, such as medications (e.g., corticosteroids), infections, or underlying medical conditions. Once these other potential causes are ruled out, the focus shifts

to treating the hyperglycemia directly with insulin. Short-acting insulin given intravenously is the preferred choice to lower blood glucose levels.

**Rationale for Starting IV Insulin Infusion**

- Persistent Hyperglycemia Management: When blood glucose levels remain above 200 mg/dL without any identifiable alternative cause, it suggests that the patient may have inadequate insulin activity relative to glucose levels. At this stage, initiating IV insulin infusion is necessary to control glucose levels, as oral agents or subcutaneous insulin may not provide adequate or timely glucose reduction.
- Insulin Infusion Advantages: Intravenous insulin allows for rapid and precise control of blood glucose levels, which is critical in ICU patients where swift adjustments are often required. IV insulin bypasses the absorption variability associated with subcutaneous injections, ensuring immediate availability and better response in acute settings.
- Low-Dose Insulin Protocols:
- Initiating insulin therapy at low doses (0.05–0.1 U/kg/hr) is recommended after adequate fluid resuscitation, especially in HHS, to prevent rapid osmolar shifts. A bolus of 0.1 U/kg is given as a bolus, and then a continuous infusion is started. The target blood glucose levels must be around 200 mg/dL. 5% Dextrose may be started if blood glucose levels fall below the desired levels. Nurse/institute-driven protocol may also be used to titrate the infusion of Insulin. Insulin infusion can be brought down to as low as 0.05 U/kg/hr. However, it must be kept in mind that insulin infusion is to be continued till the correction of acetonemia.
- Benefits of Low-Dose Protocols: Low-dose insulin achieves a gradual reduction in blood glucose without causing a precipitous drop, which can be dangerous in cases of extreme hyperosmolality in HHS. This approach minimizes the risk of hypoglycemia and reduces the potential for electrolyte imbalances.
- Administration Timing: Starting insulin after 1–2 hours of fluid resuscitation allows for initial hemodynamic stabilization and helps assess the patient's potassium status to prevent complications like hypokalemia.
- Continuation of Basal Insulin:
- For patients with a baseline requirement for long-acting (basal) insulin, it is often beneficial to continue their usual dose during crisis management, even while they are receiving insulin infusions. Continuation of basal insulin prevents rebound hyperglycemia once the insulin infusion is tapered and may stabilize glycemic control, facilitating the transition back to subcutaneous insulin therapy. Long-acting basal insulin should be initiated subcutaneously at 0.15–0.3 units/kg.

## 48.7 Management Algorithm

### *48.7.1 Initial Glucose Assessment*

Begin by measuring blood glucose levels to determine if the patient is experiencing significant hyperglycemia, which in the ICU setting is defined as blood glucose above 200 mg/dL. If glucose is below this threshold, there is no immediate concern for a hyperglycemic crisis, and regular monitoring at standard intervals should continue to ensure stability, especially if the patient has risk factors for metabolic disturbances. However, when blood glucose exceeds 200 mg/dL, this may indicate a potential metabolic crisis such as diabetic ketoacidosis (DKA) or hyperosmolar hyperglycemic syndrome (HHS), both of which require prompt evaluation and intervention due to their potential severity in critically ill patients.

### *48.7.2 Symptom and Vital Sign Assessment*

For patients with glucose levels over 200 mg/dL, assess for signs of severe metabolic imbalance. Key symptoms to look for include dehydration (e.g., dry mucous membranes, poor skin turgor, hypotension, urine output <0.5 mL/kg body weight), altered mental status (such as confusion, lethargy, or coma), and Kussmaul respirations, which are characteristic of acidosis. These symptoms are often indicative of DKA or HHS, and their presence supports the need for immediate diagnostic confirmation and therapeutic intervention. DKA typically presents with rapid breathing and altered mental status due to acidosis, whereas HHS may involve extreme dehydration and profound mental status changes owing to hyperosmolarity. If such symptoms are absent, continue monitoring glucose while exploring other potential causes of hyperglycemia, such as medication effects or stress responses, to avoid unnecessary intervention.

### *48.7.3 Presence of Ketones and pH Levels*

The next step involves determining whether ketones are present in the blood and assessing blood pH levels to differentiate between DKA and HHS, as both conditions can present with high glucose but require different treatment approaches. Elevated ketones combined with a low pH (below 7.3) strongly suggest DKA, whereas HHS is typically indicated by high serum osmolality (often exceeding 320 mOsm/kg) without significant ketonemia and a pH greater than 7.3. Accurate differentiation between DKA and HHS is essential because each condition requires distinct management: DKA focuses on correcting acidosis and reducing ketones,

while HHS management prioritizes gradual reduction of hyperosmolality to prevent cerebral edema.

### *48.7.4 DKA Management*

In cases where ketones are positive and pH is below 7.3, DKA is likely, and immediate management is necessary to prevent progression of acidosis and related complications. Begin fluid resuscitation with isotonic saline to restore intravascular volume. After initial stabilization, fluids may be adjusted to 0.45% saline based on serum sodium levels, aiming for gradual volume replacement over 24–48 hours to minimize the risk of cerebral edema. Following fluid resuscitation, initiate an IV insulin infusion at 0.05–0.1 U/kg/h to gradually reduce glucose levels, inhibit ketogenesis, and correct acidosis. Insulin therapy is crucial for stopping ketone production, while slow, controlled fluid replacement reduces the risk of cerebral edema, particularly in younger patients and those prone to rapid osmolar shifts.

### *48.7.5 HHS Management*

If ketones are absent, pH is above 7.3, and serum osmolality exceeds 320 mOsm/kg, HHS is the likely diagnosis, requiring a treatment plan centered on fluid rehydration to safely reduce hyperosmolarity. Aggressive rehydration with isotonic saline is essential to restore hydration and gradually reduce serum osmolality, thereby preventing dehydration-related complications. Careful monitoring of fluid administration is vital to avoid rapid shifts that could elevate the risk of cerebral edema. Insulin therapy, if needed, is initiated at a low dose (0.025–0.05 U/kg/h) only if blood glucose does not decrease adequately with fluid management alone, thereby preventing unnecessary insulin-related complications. The primary focus in HHS is on achieving fluid balance and osmolar correction, with insulin introduced only when fluid therapy alone proves insufficient for glucose control.

### *48.7.6 Monitoring Potassium Levels*

Potassium monitoring is crucial throughout DKA and HHS management, as insulin and fluid therapy can drive potassium into cells, risking hypokalemia, which poses a serious risk for cardiac arrhythmias. If potassium levels are below 5.5 mmol/L, initiate potassium replacement to maintain levels within the safe range of

4–5 mmol/L, typically adding potassium to IV fluids in accordance with the insulin infusion rate and real-time potassium levels. For patients with initial potassium levels above 5.5 mmol/L, immediate replacement may not be necessary, but levels should be monitored closely to detect any rapid declines. Frequent monitoring and appropriate potassium adjustments are essential to prevent cardiac complications, ensuring that electrolyte levels remain stable throughout treatment.

This structured approach to hyperglycemia management in the ICU ensures that each critical step—glucose assessment, symptom evaluation, diagnostic differentiation, and appropriate interventions—is addressed to optimize patient outcomes and reduce the risks associated with DKA and HHS.

## 48.8 Special Considerations and Populations

- Elderly Patients and Comorbidities: Elderly patients, frequently presenting with HHS, are at higher risk due to comorbid infections or cardiovascular conditions. These patients require gradual osmolar correction and careful monitoring for precipitating conditions that may impact recovery and increase mortality risk.

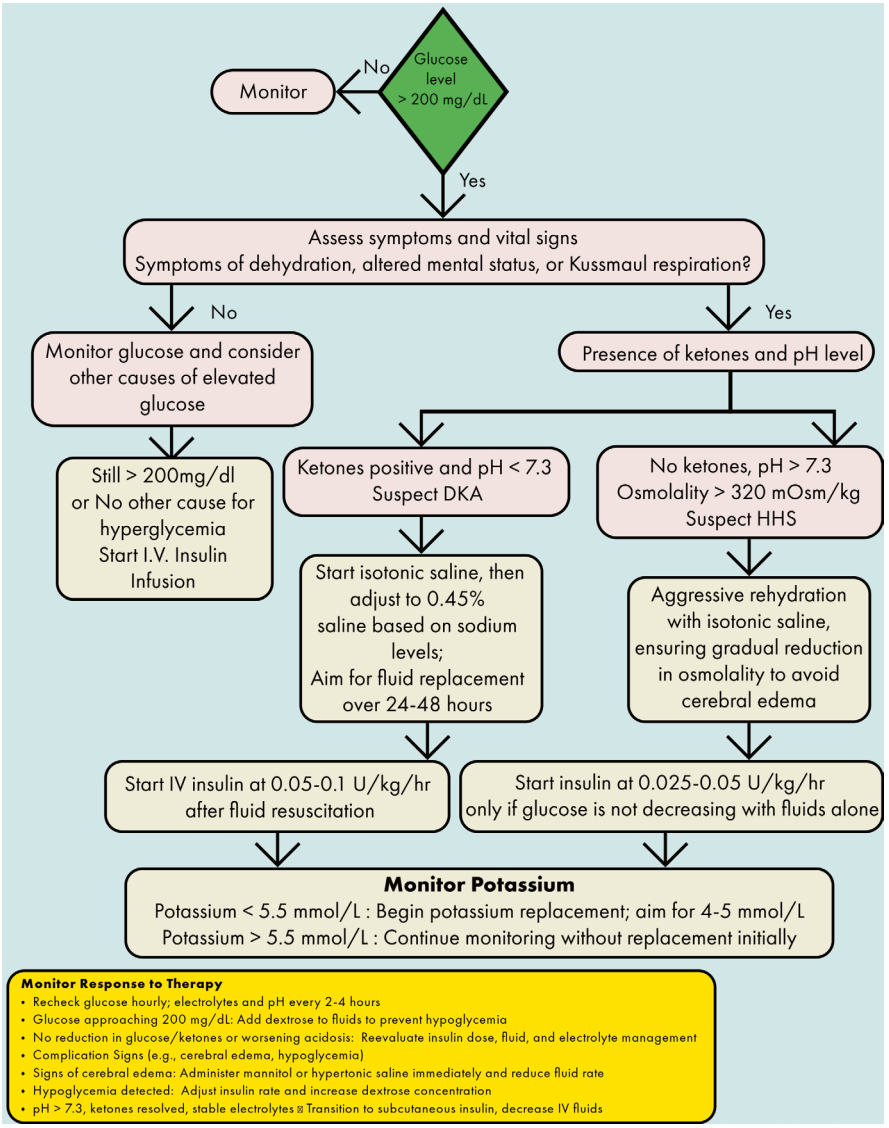
## 48.9 Long-Term and Psychosocial Follow-Up

- Psychosocial Interventions for High-Risk Patients: Integrating mental health assessments, social support, and substance use screenings into postcrisis follow-up can prevent recurrent episodes, especially for patients with significant psychosocial barriers. Regular follow-up with diabetes education and social services support can improve adherence and reduce long-term morbidity associated with hyperglycemic crises.

## 48.10 Conclusion

This structured approach to DKA and HHS management addresses both acute treatment and long-term prevention, emphasizing the importance of individualized care, psychosocial support, and early recognition of complications. Adhering to these guidelines optimizes patient outcomes, decreases healthcare costs, and reduces the frequency of recurrent ICU admissions for hyperglycemic crises.

**Algorithm 48.1: Approach to hyperglycemia in the ICU**



## Bibliography

1. American Diabetes Association Professional Practice Committee. 13. Older adults: standards of Care in Diabetes-2024. Diabetes Care. 2024;47(Suppl 1):S244–S57.
2. American Diabetes Association Professional Practice Committee. 16. Diabetes Care in the Hospital: standards of Care in Diabetes-2024. Diabetes Care. 2024;47(Suppl 1):S295–306.
3. American Diabetes Association Professional Practice Committee. 2. Diagnosis and classification of diabetes: standards of Care in Diabetes-2024. Diabetes Care. 2024;47(Suppl 1):S20–42.
4. American Diabetes Association Professional Practice Committee. 3. Prevention or delay of diabetes and associated comorbidities: standards of Care in Diabetes-2024. Diabetes Care. 2024;47(Suppl 1):S43–51.
5. American Diabetes Association Professional Practice Committee. 9. Pharmacologic approaches to Glycemic treatment: standards of Care in Diabetes-2024. Diabetes Care. 2024;47(Suppl 1):S158–S78.
6. Calimag APP, Chlebek S, Lerma EV, Chaiban JT. Diabetic ketoacidosis. Dis Mon. 2023;69(3):101418.
7. Duhon B, Attridge RL, Franco-Martinez AC, Maxwell PR, Hughes DW. Intravenous sodium bicarbonate therapy in severely acidotic diabetic ketoacidosis. Ann Pharmacother. 2013;47(7–8):970–5.
8. Fayfman M, Pasquel FJ, Umpierrez GE. Management of hyperglycemic crises: diabetic ketoacidosis and hyperglycemic hyperosmolar state. Med Clin North Am. 2017;101(3):587–606.
9. Wolfsdorf JI, Allgrove J, Craig ME, Edge J, Glaser N, Jain V, et al. ISPAD clinical practice consensus guidelines 2014. Diabetic ketoacidosis and hyperglycemic hyperosmolar state. Pediatr Diabetes. 2014;15(Suppl 20):154–79.
10. Wolfsdorf JI, Glaser N, Agus M, Fritsch M, Hanas R, Rewers A, et al. ISPAD clinical practice consensus guidelines 2018: diabetic ketoacidosis and the hyperglycemic hyperosmolar state. Pediatr Diabetes. 2018;19(Suppl 27):155–77.