Current trends in Medical and Clinical Case Reports[R] ISSN 2679-7088 Volume 10

Case Report Open Access

Therapy Approach in Mixed Hyperglycemic Hyperosmolar State and Diabetic Ketoacidosis in an Obese Boy

Smiljka Kovacevic[1], Vera Zdravkovic[1,2], Jelena Blagojevic[1], Milos Jesic[2,3], Stefan S Djordjevic[2,4] and Maja Jesic[1,2*]

[1]Endocrinology Department, University Children's Hospital, Belgrade, Serbia

[2]Faculty of Medicine, Belgrade, Serbia

[3]Neonatology Department, University Children's Hospital, Belgrade, Serbia

[4]Rheumatology Department, University Children's Hospital, Belgrade, Serbia

***Corresponding author:**

Maja Jesic,
Endocrinology Department, University Children's Hospital, Belgrade, Serbia and Faculty of Medicine, Belgrade, Serbia

Received: 23 Oct 2025
Accepted: 11 Nov 2025
Published: 22 Nov 2025
J Short Name: CTMCCR

Keywords:

Mixed Hyperglycemic Hyperosmolar State-Diabetic Ketoacidosis; Adolescent; Type 2 Diabetes

Citation:

Maja Jesic, Therapy Approach in Mixed Hyperglycemic Hyperosmolar State and Diabetic Ketoacidosis in an Obese Boy. Current Trends in Med and Clin Case Rep® 2025; V15(1): 1-5

1. Abstract

1.1. Background

Hyperglycemic hyperosmolar state (HHS) and diabetic ketoacidosis (DKA) are severe acute complications of type 1 (T1D) and type 2 diabetes (T2Ds) that can occur separately or together.

1.2. Case Presentation

We present a 14-year-old boy who was admitted to the Endocrinology department at the University Children's Hospital in Belgrade, Serbia, due to hyperglycemia and hypernatremia. He received intensive intravenous replacement therapy together with a small IV insulin infusion. After 37 hours of treatment, once normal serum osmolarity and pH levels were achieved and glucose levels stabilized, the intravenous therapy was discontinued. Extreme obesity, alon, g with a clinical sign of insulin resistance, acanthosis nigricans, suggested that the boy might have developed an acute complication of unrecognized T2D. The high percentage of HbA1c, elevated C-peptide levels, and low titers of antibodies against pancreatic islet antigens confirmed our suspicion of T2D. Metabolic disturbance resulted from long-standing, unrecognized T2D.

1.3. Conclusions

Since there are no established protocols for treating mixed HHS-DKA in the pediatric population, this case report aimed to provide a detailed hourly treatment of an acute emergency in an adolescent with newly diagnosed T2D.

2. Introduction

Hyperglycemic hyperosmolar state (HHS) and diabetic ketoacidosis (DKA) are severe acute complications of type 1 (T1D) and type 2 diabetes (T2D) that can occur separately or together. Mixed HHS-DKA is a rare diagnosis in children characterized by high osmolarity ≥320 mOsm/kg, high glucose ≥600 mg/dL, acidosis (pH ≤7.3), and ketonuria and/or elevated serum beta-hydroxybutyrate [1]. When comparing these two conditions, HHS has a ten times higher mortality rate than DKA [2-4].

The combination of HHS and DKA is more common in adults with diabetes, with a prevalence estimated to be 30-33% according to various studies [5,6].

Sometimes, the presentation of newly diagnosed T2D in children and adolescents can resemble T1D. Although DKA is much more common as an acute complication of T1D, HHS is typically seen in children with T2D. Because patients with HHS or mixed HHS-DKA often face more common life-threatening complications, it is essential to distinguish HHS from DKA, as their treatments and associated complications differ [1,4,7,8,9]. Management strategies for mixed HHS-DKA are not clearly defined in the protocol; therefore, this report presents a clinical course and highlights the difficulties in recognizing and treating such a condition.

3. Case Presentation

A 14-year-old boy was admitted to the Endocrinology department at the University Children's Hospital in Belgrade, Serbia, due to hyperglycemia and hypernatremia. Over the past few days, he has complained of headaches and malaise. He has had a history of polyuria and polydipsia for the last four weeks. He had no previous infection or other precipitating factors for hyperglycemia. His birth history and measurements were normal. After the fourth month, he experienced weight gain issues due to feeding difficulties. By the age of five, he started overeating and

gaining excessive weight, leading to ongoing obesity. Psychomotor development was diagnosed late. He received treatment for epilepsy until he turned eight. Due to intellectual challenges and learning disabilities, he attends a special school. His family history showed no chronic illnesses. Both parents were severely obese, but did not have T2D. Informed consent for publication was obtained from the parents. On admission to the hospital, his height was 167 cm (79th percentile), weight 137 kg (above 99th percentile), and body mass index (BMI) 49.12 kg/m² (above 99th percentile). He was hypotensive and dehydrated, exhibiting Kussmaul breathing and somnolence due to hyperosmolarity and acidosis (vital signs: respiratory rate 24/minute, heart rate 90/minute, blood pressure 100/60 mmHg, pulse oximetry 99 % on room air). Acanthosis and striae rubrae were prominent on the skin of the neck and axilla. The pubertal stage was 2. The neurological examination revealed a Glasgow Coma Scale score of 13, with a response to speech, eye opening, and a mildly confused verbal response. The motor response was normal. He complained of a headache, and no other neurological alterations were reported. The laboratory findings are presented in Tables 1 and 3. Laboratory findings revealed significant hyperglycemia (46 mmol/L or 828 mg/dL), a decreased blood pH (7.21), and bicarbonate levels (19.3 mmol/L), along with mild ketonuria and glycosuria. The sodium level was elevated (173 mmol/L), potassium levels were normal (4.3 mmol/L), and serum osmolarity increased (403 mOsm/kg). He was dehydrated, with elevated creatinine (151 mmol/L) and urea (11 mmol/L) (Table 1). The patient was diagnosed with combined HHS and DKA.

The course of treatment during the first 20 hours is shown in Tables 2 and 4. For the first two hours, he received intensive replacement therapy with isotonic saline (0.9% NaCl), administering 15 ml/kg IV during the first hour, followed by 10 ml/kg during the next hour, then switching to hypotonic saline (0.45 % NaCl) (Table 2). During the fourth hour, a small IV insulin infusion was initiated at a dose of 0.045 units/kg/hour alongside the IV fluids. Two hours after starting insulin, the dose was reduced to 0.025-0.030 units per hour due to a rapid decline in blood sugar levels. At the sixth hour, 5% glucose was added to the hydration solution, along with a reduction in insulin dose, to prevent a rapid drop in glucose levels. After decreasing insulin, glucose levels decreased by 3-5 mmol/L per hour, while sodium levels declined at no more than 1 mmol/hour (Table 1). The acidosis resolved after 10 hours. After 16 hours of treatment, with acidosis resolved and glycemia suboptimal, the patient began minimal oral intake. After 28 hours of treatment, sodium levels normalized. Diuresis remained normal. Tables 3 and 4 show laboratory parameters and insulin dosage during 10-20 hours of therapy. After 37 hours of treatment, once normal serum osmolarity and pH levels were achieved and glucose levels stabilized, the intravenous infusion was discontinued. He received total of 17 litres of intravenous infusion (3.3 ml/kg/h). The total daily intravenous insulin dose was 0.45 IU/kg/day during the first day. Consequently, subcutaneous basal-bolus insulin therapy was started. The average total daily dose of subcutaneous insulin was 120 IU per 24 hours, or 0.88 units per kilogram per day. After two days of subcutaneous insulin therapy, Metformin was added twice daily.

During treatment, vital signs and laboratory data were monitored closely every hour. The patient didn't complain about headaches and did not develop neurological or other complications. Also, the patient did not have treatment-related hypokalemia or hypoglycemia.

Laboratory analyses revealed a high percentage of hemoglobin A1c (HbA1c) 11.4 %, high levels of C-peptide (3.24 ng/mL), and a low titer of antibodies against pancreatic islet antigens (ICA 1.8 IU/mL, GAD 2 IU/mL, IA2 2.6 IU/mL). After 3 days of subcutaneous insulin and Metformin therapy, the boy achieved optimal premeal glucose, so basal-bolus insulin therapy was stopped. Metformin therapy was continued twice daily, and glucose levels were optimal. After 3 months of Metformin therapy, lifestyle changes, diet, and physical activity, the HbA1c level was reduced to 8.4%. Genetic testing, including a Chromosomal Microarray, was normal.

Table 1: Laboratory parameters during the first 10 hours of treatment.

	1h	2h	3h	4h	5h	6h	7h	8h	9h	10h
Ph	7.21	7.23	7.23	7.23	7.23	7.28	7.28	7.33	7.33	7.35
HCO3 (mmol/l)	19.3	20.2	20.1		18	20.2	22.1	22.7	22.5	22.5
Glucose (mmol/l)	46.0	32.0	30.3	26.6	19.9	15	16.8	15.4	12.8	12.2
Na (mmol/l)	173	172	173	172	172	172	169	167	165	164
K (mmol/l)	4.3	4.4	4.5	3.8	3.7	4.4	3.8	3.9	3.7	4
Osmolality (mOsm/kg)	403			379			360		348	
Urea (mmol/l)	11			8.2			5.5		5.0	
Creatinine (mmol/l)	151			110			95		89	

Table 2: Insulin and fluid therapy during the first 10 hours of treatment.

	1h	2h	3h	4h	5h	6h	7h	8h	9h	10h
IV fluid therapy (ml/h)	0.9% saline 1800	0.9% saline1500	0.45% saline 1000	0.45% saline 1000	0.45% saline 1000	GS 5% 500	GS 5% 500	GS 5% 300	GS 5% 300	GS 5%300
Insulin (IJ/kg/h)	/	/	/	0.045	0.045	0.025	0.025	0.03	0.03	0.03
Diuresis (ml/h)	350	50	120	110	60			450	410	530

Table 3: Laboratory parameters during 10-20 hours of treatment.

	11h	12h	13h	14h	15h	16h	17h	18h	19h	20h
Ph	7.33		7.35		7.36	7.42		7.47	7.36	7.36
HCO3 (mmol/l)	22.7		21.5		22.6	19.5		19.9	22.0	22.1
Glucose (mmol/l)	12.2	11.4	15.0	13.1	10.8	11.5	13.9	11.7	12.6	12.2
Na (mmol/l)	166		165		164	162		160	159	157
K (mmol/l)	3.7		4		3.9	3.7		4.1	4.1	3.6

Table 4: Insulin and fluid therapy during 10-20 hours of treatment.

	11h	12h	13h	14h	15h	16h	17h	18h	19h	20h
IV fluid therapy (ml/h)	0.9% saline300	0.9% saline 300	0.45% saline 300ml	0.45% saline 450	0.45% saline 450	GS 5% 400	GS 5% 450	GS 5% 450	GS 5% 450	GS 5% 450
Insulin (IJ/kg/h)	0.03	0.03	0.03	0.03	0.02	0.02	0.03	0.05	0.05	0.05
Diuresis (ml/h)	370	280		450		410		760	350	310

4. Discussion

A study involving 916 children and adolescents with diabetes mellitus found that those presenting with hyperglycemic emergencies included 0.8% with HHS and 13.8% with a mixed presentation. 3 Among all patients, only 2.6% had T2D. All other patients were diagnosed with T1D. This study, along with others, demonstrates that combined HHS and DKA are rare presentations of T2D.

In our patient, initial analyses could not distinguish between T1D and T2D. Sometimes, during hyperglycemic emergencies, the presentation of a newly diagnosed T2D in children and adolescents can resemble that of T1D. Gradually increasing polyuria and polydipsia as signs of diabetes went unnoticed, leading to severe dehydration and electrolyte losses at presentation. Dehydration and fluid deficit lead to more common complications in mixed presentations compared to DKA [3]. It is known that fluid losses in HHS are estimated to be twice those in DKA. (1) An additional issue with our patient was intellectual impairment, as studies show that it carries a higher risk of hyperosmolarity, likely due to reduced fluid intake [3,10]. Additionally, a study by Agrawal et al. demonstrated that patients with HHS or mixed presentations have a 3.7-fold greater risk of developing complications compared to those with DKA [3].

Extreme obesity, along with a clinical sign of insulin resistance, acanthosis nigricans, suggested that the boy might have developed an acute complication of unrecognized T2D. Obese children carry higher metabolic risk factors, and those with a family history of T2D seem to face the greatest risk of developing T2D [6].

The high percentage of HbA1c, elevated C-peptide levels, and low titers of antibodies against pancreatic islet antigens confirmed our suspicion of T2D. Metabolic disturbance resulted from long-standing, unrecognized T2D.

In this patient, treatment was complicated by severe hypernatremia and high serum osmolarity. The initial goal was to normalize sodium levels, correct hyperosmolality and dehydration, while the second goal was to resolve ketoacidosis. Glycosuria causes osmotic diuresis, which, along with hypernatremia, leads to a hyperosmolar state, intracellular dehydration, and hypovolemia. A particular challenge in treatment was fluid replacement due to extreme obesity. Obesity leads to great difficulty in recognizing a degree of dehydration. Since there are no established protocols for intravenous fluid replacement in mixed HHS-DKA cases, various authors recommend initial boluses ranging from 6-20 ml/kg/h [11,12]. Because of the mixed HHS-DKA, we employed a more aggressive approach for replacing intravascular

volume compared to DKA to prevent vascular collapse, which enhances mortality [1,9]. Reported a case of mismanaged HHS due to underestimating the severity of dehydration, resulting in the death of an adolescent patient [11]. At the beginning of treatment, a bolus of 20 ml/kg of isotonic saline is recommended to restore 12-15 % of total body weight over the next 24-48 hours [2,13,14]. Excessive fluid replacement carries the risk of cerebral edema; therefore, the patient was closely monitored for neurological complications, urinary output, vital signs, and clinical status. Initially, isotonic saline is preferred for fluid replacement and to maintain circulatory volume. Over the next few hours, depending on sodium levels, fluid therapy was adjusted to hypotonic saline to gradually lower sodium and glucose levels. Throughout therapy, laboratory analyses of glucose, sodium, potassium, and osmolarity were performed hourly.

Although there are no clearly defined protocols for treating mixed DKA-HHS, insulin doses are lower than those used in DKA. Some authors suggest that using low-insulin dose protocols is preferable to prevent a rapid drop in blood glucose levels, which can cause cerebral edema, as well as life-threatening complications of hypokalemia. 15 Frequently, these patients present with potassium levels in the normal range but may experience low potassium levels during 48 hours of insulin treatment, increasing the risk of mortality [15]. Our patient received intravenous potassium replacement once insulin was initiated.

In patients with T2D who present with mixed HHS-DKA, it is possible to discontinue insulin therapy after resolving acidosis and achieving a stable period of euglycemia. Oral diabetic agents therapy followed by resolving acidosis, since it's at risk of lactic acidosis and metabolic derangement during ketoacidosis. During DKA, patients with T2D exhibit a significant reduction in insulin secretion; however, treatment and recovery of ketoacidosis is usually followed by recovery of beta-cell function and insulin sensitivity [16-18]. Three months after resolving mixed HHS-DKA and taking Metformin, the patient achieved better glycaemic control. After four years, he remained free of acute diabetic emergencies. He achieved optimal metabolic control (HbA1c 4.9 %), but since he is still obese (BMI 46 kg/m2), he is receiving Liraglutide treatment.

In conclusion, since there are no established protocols for treating mixed HHS-DKA in the paediatric population, this case report aimed to provide a detailed hourly treatment of an acute emergency in an adolescent with newly diagnosed T2D. Also, it shows the importance and necessity of intensive fluid replacement for rescuing a patient with mixed HHS-DKA in a paediatric population. For healthcare professionals, it is essential to recognize that T2D in the paediatric population is being diagnosed at increasingly younger ages than previously observed. Since a delay in diagnosis of T2D is often, it is crucial to recognize those at risk for developing T2D to avoid acute complications as HHS and DKA.

References

1. Wolfsdorf JI, Glaser N, Agus M. ISPAD Clinical Practice Consensus Guidelines 2018: Diabetic ketoacidosis and the hyperglycemic hyperosmolar state. Pediatr Diabetes. 2018; 27: 155-177.
2. Kitabchi AE, Nyenwe EA. Hyperglycemic crises in diabetes mellitus: diabetic ketoacidosis and hyperglycemic hyperosmolar state. Endocrinol Metab Clin North Am. 2006; 35: 725-51.
3. Agrawal S, Baird GL, Quintos JB. Pediatric Diabetic Ketoacidosis with Hyperosmolarity: Clinical Characteristics and Outcomes. Endocr Pract. 2018; 24: 726-732.
4. Price A, Losek J, Jackson B. Hyperglycaemic hyperosmolar syndrome in children: Patient characteristics, diagnostic delays and associated complications. J Paediatr Child Health. 2016; 52: 80-4.
5. Wachtel TJ, Tetu-Mouradjian LM, Goldman DL, Ellis SE, O'Sullivan PS. Hyperosmolarity and acidosis in diabetes mellitus: a three-year experience in Rhode Island. J Gen Intern Med. 1991; 6: 495-502.
6. Pulgaron ER, Delamater AM. Obesity and type 2 diabetes in children: epidemiology and treatment. Curr Diab Rep. 2014; 14: 508.
7. Klingensmith GJ, Connor CG, Ruedy KJ. Presentation of youth with type 2 diabetes in the Pediatric Diabetes Consortium. Pediatr Diabetes. 2016; 17: 266-73.
8. Pasquel FJ, Umpierrez GE. Hyperosmolar hyperglycemic state: a historic review of the clinical presentation, diagnosis, and treatment. Diabetes Care. 2014; 37: 3124-31.
9. Zeitler P, Haqq A, Rosenbloom A, Glaser N; Drugs and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society. Hyperglycemic hyperosmolar syndrome in children: pathophysiological considerations and suggested guidelines for treatment. J Pediatr. 2011; 158: 9-14.
10. Rosenbloom AL, Silverstein JH, Amemiya S, Zeitler P, Klingensmith GJ. International Society for Pediatric and Adolescent Diabetes. ISPAD Clinical Practice Consensus Guidelines 2006-2007. Type 2 diabetes mellitus in the child and adolescent. Pediatr Diabetes. 2008; 9: 512-26.
11. Tsai SL, Hadjiyannakis S, Nakhla M. Hyperglycemic hyperosmolar syndrome at the onset of type 2 diabetes mellitus in an adolescent male. Paediatr Child Health. 2012; 17: 24-6.
12. Nwosu BU, Adhami S, Rogol AD. Stroke in a child with Adams-Oliver syndrome and mixed diabetic ketoacidosis and hyperglycemic hyperosmolar syndrome. J Pediatr Endocrinol Metab. 2012; 25: 357-61.
13. Kitabchi AE, Umpierrez GE, Fisher JN, Murphy MB, Stentz FB. Thirty years of personal experience in hyperglycemic crises: diabetic ketoacidosis and hyperglycemic hyperosmolar state. J Clin Endocrinol Metab. 2008; 93: 1541-52.
14. Kitabchi AE, Umpierrez GE, Murphy MB. Management of hyperglycemic crises in patients with diabetes. Diabetes Care. 2001; 24: 131-53.
15. Pasquel FJ, Tsegka K, Wang H. Clinical Outcomes in Patients with Isolated or Combined Diabetic Ketoacidosis and Hyperosmolar Hyperglycemic State: A Retrospective, Hospital-Based Cohort Study. Diabetes Care. 2020; 43: 349-357.

16. Umpierrez GE, Smiley D, Kitabchi AE. Narrative review: ketosis-prone type 2 diabetes mellitus. Ann Intern Med. 2006; 144: 350-7.

17. Maldonado M, Hampe CS, Gaur LK. Ketosis-prone diabetes: dissection of a heterogeneous syndrome using an immunogenetic and beta-cell functional classification, prospective analysis, and clinical outcomes. J Clin Endocrinol Metab. 2003; 88: 5090-8.

18. Mauvais-Jarvis F, Sobngwi E, Porcher R. Ketosis-prone type 2 diabetes in patients of sub-Saharan African origin: clinical pathophysiology and natural history of beta-cell dysfunction and insulin resistance. Diabetes. 2004; 53: 645-53.

19. Smiley D, Chandra P, Umpierrez GE. Update on diagnosis, pathogenesis and management of ketosis-prone Type 2 diabetes mellitus. Diabetes Manag (Lond). 2011; 1: 589-600.