

Hyperosmolar Hyperglycemic State (HHS) — Symptoms and Treatment

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The hyperosmolar hyperglycemic state is characterized by severe hyperosmolality, hyperglycemia, and dehydration. Patients in a hyperosmolar hyperglycemic state do not have ketoacidosis. Diabetic ketoacidosis, on the other hand, is characterized by hyperglycemia, dehydration, and acidosis due to ketone bodies accumulation in the blood; thus, the condition was also known as hyperosmolar non-ketotic state (HONKS) or non ketotic hyperosmolar states (NKHS)



Definition

It is an acute complication of diabetes mellitus that sets in as a metabolic derangement characterized by hyperglycemia (>600 mg/dl), hyperosmolality (>330 mOsm/L) and dehydration but no ketoacidosis.

Epidemiology of Hyperosmolar Hyperglycemic State

The incidence of hyperosmolar hyperglycemic state is unknown. It has been estimated that up to 1% of hospital admissions in [diabetic patients](#) are due to hyperosmolar hyperglycemic state. The condition is more common in the elderly and in patients with [type 2 diabetes](#). Diabetic ketoacidosis is more common in the young and in patients with [type 1 diabetes](#).

Mortality in patients with hyperosmolar hyperglycemic state has been estimated to be as high as 20%. Mortality in patients with diabetic ketoacidosis is 2%. The prognosis of hyperosmolar hyperglycemic state is dependent on the degree of [dehydration](#), the presence of comorbidities, the patient's age, and the cause of the hyperosmolar hyperglycemic state. Hyperosmolar hyperglycemic state was previously known as diabetic coma.

Pathophysiology of Hyperosmolar Hyperglycemic State

Insulin deficiency and inadequate fluid intake, coupled with resulting hyperglycemia, are the main trigger agents for HHS. A lack of glucose entry to cells for use leads to an increase in the levels of the counter-regulatory hormones that is associated with increased gluconeogenesis, accelerated conversion of glycogen to glucose, and inadequate use of glucose by peripheral tissues due to insulin resistance.

The deficiency of insulin is not severe enough to trigger ketoacidosis as seen with DKA.

Patients with severe hyperglycemia might develop osmotic diuresis, polyuria, and severe [water deficit](#). This can lead to severe dehydration and the patient would eventually enter a hyperosmolar state; therefore, patients in hyperosmolar hyperglycemic state usually have a much higher serum glucose level compared to those with diabetic ketoacidosis.

Most of the glucose found in the sera of patients with hyperosmolar hyperglycemic state comes from **increased hepatic production**. Elevated serum glucose levels create an osmolar gradient that withdraws water from the cells. Moreover, the elevated serum glucose levels lead to [diuresis](#); therefore, patients in hyperosmolar hyperglycemic state have severe dehydration, contraction in the extracellular volume, and contraction in the intracellular volume.

Triggers of Hyperosmolar Hyperglycemic State

Like diabetic ketoacidosis, hyperosmolar hyperglycemic state syndrome is not a disease per-se, but more of a **consequence to another pathology that is associated with an increase in the levels of the counter-regulatory hormones**.

- Infection is the most common cause of hyperosmolar hyperglycemic state. The most commonly encountered infection in patients within a hyperosmolar hyperglycemic state is [pneumonia](#), followed by [urinary tract infections](#).
- Patients with stroke, acute myocardial infarction, or trauma usually have an acute and dramatic increase in the levels of glucagon and cortisol in addition to an elevation in norepinephrine and epinephrine levels; therefore, these conditions are also common causes of hyperosmolar hyperglycemic state in type 2 diabetics.
- Children with type 1 or type 2 diabetes who develop an acute circulatory, nervous, or genitourinary disease might develop hyperosmolar hyperglycemic state.
- Insulin deficiency.
- Inadequate fluid intake.
- Renal failure.
- Use of diuretics.

- Increased levels of glucagon and counterregulatory hormones, such as catecholamines, cortisol and growth hormone, lead to uncontrolled hyperglycemia.

Diagnostic Criteria of Hyperosmolar Hyperglycemic State

The current American diabetes association criteria for the diagnosis of hyperosmolar hyperglycemic state syndrome can be summarized in the following points:

- A plasma glucose concentration more than 600 mg/dL
- An arterial pH above 7.3
- A serum bicarbonate concentration above 18 mEq/L
- Urine or serum ketones are absent.
- Serum beta-hydroxybutyrate below 3 mmol/L
- Effective serum osmolality above 320 mOsm/L
- Mental status is variable, but, most commonly, patients are in stupor coma.
- The anion gap is variable.

Clinical Presentation of Hyperosmolar Hyperglycemic State

Patients who develop hyperosmolar hyperglycemic state syndrome usually become stupor and comatose. Because of the severe dehydration, you expect to see tachycardia, hypotension, decreased skin turgor, and sunken eyes; however, if the cause of the hyperosmolar hyperglycemic state is myocardial infarction, you might see other cardiac rhythms different from sinus tachycardia.

Patients might have:

- Fever
- Rales on chest auscultation
- Dullness to percussion
- Bronchial breathing sounds
- Change in the urine color
- The presence of predisposing factor to urinary tract infections (catheter might be observed)
- Polyuria, which can worsen the severity of the dehydration

A physical examination of a stroke patient who is in hyperosmolar hyperglycemic state might develop some lateralizing signs in response to pain. For instance, if the stroke was within the right hemisphere, response to pain by motor withdrawal might be limited or absent in the left upper and lower extremities.

Diagnostic Workup for Hyperosmolar Hyperglycemic State

Patients who are in a coma should receive a **plasma glucose test to exclude hypoglycemia and hyperglycemia**; both are common conditions associated with an altered mental status.

Arterial blood gases examination is indicated to exclude acidosis. The pH in patients with hyperosmolar hyperglycemic state is above 7.3. Serum bicarbonate levels are above 18 mEq/L.

Effective serum osmolality, which is calculated by the formula: $2(\text{Na}) + 18/\text{glucose}$, should be determined as it is part of the diagnostic criteria in hyperosmolar hyperglycemic state. Accordingly, serum electrolytes should be evaluated to determine the concentration of sodium. These are the two main constituents in the serum that affect the osmolar gradient. Total serum osmolality is equal to $2(\text{Na}) + 18/\text{glucose} + \text{BUN}/2$.

Renal function tests to determine the nature and severity of electrolyte derangements.

Blood cultures and acute phase reactants assays to check for the source of infection.

Complete blood counts may suggest the likelihood of an inflammatory process by an elevated white blood cell count.

Treatment of Hyperosmolar Hyperglycemic State

The current American diabetes association recommendations for the treatment of hyperglycemic state can be summarized in the following points:

Insulin therapy	<ul style="list-style-type: none"> • Initial bolus dose of 0.1 unit per kg intravenously. • 1 unit per kg per hour until glucose concentration is below 250 mg/dL. • 0.5 unit per kg per hour until euglycemia.
Fluid therapy	<ul style="list-style-type: none"> • Normal saline at the rate of 500 to 1000 ml/h for the first 2 to 4 hours. • Followed by 0.45% saline at the rate of 250 to 500 mL/h.

The treatment of hyperosmolar hyperglycemic state syndrome in pediatrics has been updated in 2011. The current recommendations for the **treatment of the syndrome in children** can be summarized in the following points:

Insulin therapy	<ul style="list-style-type: none"> • No bolus. • Start fluid therapy first. • Start insulin infusion only if glucose levels were not declining with fluid therapy alone. • Patient has hyperosmolar hyperglycemic state, no ketoacidosis & glucose levels were not declining with fluid therapy: insulin at the dose of 0.025 to 0.05 units per kg per hour. • Patient has hyperosmolar diabetic ketoacidosis: insulin at the dose of 0.05 to 0.1 units per kg/hour.
Fluid therapy	<ul style="list-style-type: none"> • 20 mL/kg in bolus, and can be repeated until there is adequate tissue perfusion. • Dantrolene might be administered to induce muscle relaxation.

References

Pasquel FJ, Umpierrez GE. Hyperosmolar Hyperglycemic State: A Historic Review of the Clinical Presentation, Diagnosis, and Treatment. *Diabetes Care*. 2014;37(11):3124-3131. doi:10.2337/dc14-0984.

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