Hyperosmolar Hyperglycemic State (HHS) Symptoms and Treatment

Hyperosmolar hyperglycemic state(HHS) is a serious acute metabolic complication of diabetes mellitus that is characterized by hyperglycemia (>600 mg/dl), hyperosmolarity (>330 mOsm/L) and, dehydration without ketosis or acidosis.

Hyperosmolar hyperglycemic state is the most serious complication in patients with type 2 diabetes mellitus and whenever it occurs, it is a medical emergency

It usually occurs in middle aged or elderly individuals with type 2 diabetes mellitus and it may be the presenting feature in around 25% of individuals.

HHS is the type 2 diabetes equivalent of diabetic ketoacidosis (DKA) in type 1 diabetes individuals. Its metabolic differences occur because in individuals with type 2 diabetes mellitus there is a small quantity of insulin remaining enough to suppress lipolysis and the associated acidosis.

This complication is more common is Afro-Caribbean.

HHS occurs less frequently when compared to diabetic ketoacidosis but once it occurs it has a higher mortality rate of about 15%.

What are the Precipitating causes of hyperosmolar hyperglycaemic state?

Hyperosmolar hyperglycemic state is not a disease per-se, but a consequence to another condition or an underlying pathology associated with an increase in the levels of the counter-regulatory hormones.

The most common precipitating causes for hyperosmolar hyperglycemic state are;

- Infection (The most common factor with the most commonly encountered infection being pneumonia and urinary tract infections),
- Myocardial infarction (Heart attack), stroke or trauma. These patients usually have an acute dramatic increase of stress hormone ‘cortisol’ and glucagon and an associated adrenaline levels.
- Drugs such as the use of diuretics
- Steroid medications
- Inadequate or reduced fluid intake
- Omission of oral hypoglycaemic drugs
- Insulin deficiency.
- Renal failure.
- States of increased glucagon, cortisol, and catecholamine levels (counteregulatory hormones) may cause uncontrolled hyperglycemia.

Hyperosmolar hyperglycaemic state may be complicated by thromboembolism or rhabdomyolysis

(muscle breakdown).

Characteristics of hyperglycemic hyperosmolar state

Hyperosmolar hyperglycemic state is characterized by;

- Severe hyperosmolality,
- Hyperglycemia, and
- Dehydration.
- No ketoacidosis.

These features are in comparison with diabetic ketoacidosis that is characterized by hyperglycemia, dehydration, and acidosis because of an accumulation of ketone bodies in the blood.

Epidemiology

The exact incidence of hyperosmolar hyperglycemic state is unknown but it is estimated that HHS accounts up to 1% of all hospital admissions in diabetic patients.

Hyperglycemic hyperosmolar state is more common in the elderly patients and the one with type 2 diabetes mellitus as compared to diabetic ketoacidosis that is more common in the young patients and ones with type 1 diabetes mellitus.

Its mortality rate is about 15-20% as compared to 2% mortality in patients with diabetic ketoacidosis.

Its outcome is usually dependent on the cause, degree of dehydration, underlying comorbidities and, the patient's age.

Pathophysiology of Hyperosmolar Hyperglycemic State

The main triggers for hyperglycemic hyperosmolar state is a relative insulin deficiency and inadequate fluid intake. The state of insulin deficiency impairs glucose utilization in skeletal muscle and increases the production of glucose in the liver through glycogenolysis and gluconeogenesis process.

Failure of glucose entry to cells for utilization causes an increase in the levels of the counter-regulatory hormones(catecholamines) as a result of increased gluconeogenesis, hastened conversion of glycogen to glucose, and inadequate utilization of glucose by peripheral tissues due to insulin resistance.

High blood glucose level (hyperglycemia) causes osmotic diuresis that leads to intravascular volume depletion. Together with dehydration, the hydration status of the individual is exacerbated.

Since the insulin deficiency I hyperglycemic hyperosmolar state is relative and not absolute deficiency, there is no development of ketosis because the available insulin is sufficient to prevent production of ketone bodies. There is also a possibility that the liver is less capable of ketone body

synthesis or the available insulin/glucagon ratio does not favor ketogenesis.

HHS is associated with lower levels of counterregulatory hormones and free fatty acids have than in DKA in some studies.
Patients who present with severe hyperglycemia have higher chances of developing osmotic diuresis, severe dehydration and polyuria. This leads to development of severe dehydration and the patient would eventually enter a hyperosmolar state. Due to this reason, patients in hyperosmolar hyperglycemic state usually have a much higher serum glucose level when compared to those with diabetic ketoacidosis.

Most of this glucose the sera of these patient is as a result of increased hepatic production of glucose.

Normally, a severe hyperglycemia draws water from the cells as a result of a created osmolar gradient leading to diuresis; therefore, these patients in hyperosmolar hyperglycemic state have severe dehydration, a contraction in the extracellular and the intracellular volume.

Diagnosis of Hyperosmolar Hyperglycemic State

The criteria for the diagnosis of hyperosmolar hyperglycemic state (HHS)syndrome can be summarized as:

- A marked plasma glucose concentration more than 600 mg/Dl,
- Hyperosmolarity (effective serum osmolality above 320 mOsm/L),
- An arterial pH above 7.3 (No acidosis),
- A serum bicarbonate concentration above 18 mEq/L,
- Absent urine or serum ketone bodies.
- Serum beta-hydroxybutyrate that is below 3 mmol/L,
- Patients may have a variable mental status but, most patients are in stupor coma.
- Prerenal azotemia.
- An anion gap is variable but a small anion-gap metabolic acidosis may be present secondary to increased production of lactic acid.
- Moderate ketonuria, if present, is secondary to starvation

The measured serum sodium may be normal or slightly low despite the marked hyperglycemia. The corrected serum sodium is usually increased.

Clinical Features a Patient with of Hyperosmolar Hyperglycemic State

Patients who develop hyperosmolar hyperglycemic state syndrome have an altered mental status such as stupor and coma.

Features of dehydration such as tachycardia, hypotension, sunken eyes, decreased skin turgor are present secondary to the severe dehydration.

If the underlying cause of HHS is a myocardial infarction, the patient may present with arrhythmia or other cardiac rhythms different from sinus tachycardia.

These patients may also present with:

- Fever
- Rales on chest auscultation
- Dullness to chest percussion
- Bronchial breathing sounds
- Change in the urine color

These patients will present with features of predisposing factors or the underlying disease condition such as features of pneumonia and urinary tract infections.

Diabetic patients who present with polyuria, may have an associated severe dehydration.

A stroke patient who has hyperosmolar hyperglycemic state may develop some lateralizing signs in response to pain.

Nausea, vomiting, and abdominal pain and the Kussmaul type of respirations are notably absent but present in diabetic ketoacidosis.

Like mentioned above, HHS is often precipitated by a serious, concurrent illness such as myocardial infarction or stroke. Sepsis, pneumonia, or any other serious infections are frequent precipitants and should be ruled out.

Diagnostics and Diagnostic Workup

Suspected patients who present with a coma should have their plasma glucose levels checked to exclude hypoglycemia and hyperglycemia.

Arterial blood gases analysis is indicated to rule out acidosis. Usually patients with hyperosmolar hyperglycemic state have a PH of above 7.3 and serum bicarbonate levels are above 18 mEq/L.

Determine effective serum osmolality, by calculating using the formula: 2 (Na) + 18/glucose.

Serum electrolyte levels. Evaluation of serum electrolytes should be done to determine the concentration of sodium because these are the two main constituents in the serum that affect the osmolar gradient.

Kidney function tests should be done to find out the nature and severity of present electrolyte derangements.

Complete blood count to identify the likelihood of inflammation shown by an elevated white blood cells.

A blood cultures and acute phase reactants assays are performed to check for the source of infection.

Treatment of Hyperosmolar Hyperglycemic State

The management hyperosmolar hyperglycemic states is similar to the treatment of diabetic

ketoacidosis with rehydration therapy and electrolyte replacement together with intravenous insulin.

The management is divided into three sections

1. Treatment of underlying precipitating factor
2. Insulin therapy and
3. Rehydration

These patients will need to be admitted and managed as inpatients.

Rehydration

Rehydration to correct the volume depletion is key. This is because in HHS, fluid losses and dehydration are usually more pronounced than in DKA