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Hyperosmolar hyperglycemic syndrome: A comprehensive review of clinical presentation, diagnosis, and treatment strategies in hyperglycemic crises

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ABSTRACT

Introduction and Purpose

Hyperosmolar Hyperglycemic State (HHS), a severe type 2 diabetes complication, presents with profound hyperglycemia, hyperosmolality, and dehydration sans ketosis, posing distinct challenges in diagnosis and treatment compared to diabetic ketoacidosis (DKA). This article aims to enhance medical community awareness by examining HHS features, prevalence, and associated risk factors, contributing to improved clinical management. Emphasizing tailored treatment strategies for dehydration, coexisting illnesses, and metabolic decompensation, it ultimately seeks to enhance outcomes for type 2 diabetes individuals.

Material and methods

Conducting a systematic review of medical articles from 1972 to 2023 using PubMed, this study analyzed keywords such as hyperglycemic hyperosmolar state, HHS, diabetes mellitus, hyperglycemia, and dehydration. Inclusion of pertinent articles ensured a comprehensive exploration of Hyperosmolar Hyperglycemic State (HHS) literature during the specified timeframe.

Brief description of the state of knowledge.

Hyperosmolar Hyperglycemic Syndrome (HHS) predominantly affects elderly type 2 diabetes individuals, often triggered by infections like pneumonia or urinary tract infections. Clinical presentation includes fatigue, weakness, polydipsia, polyuria, nausea, and altered consciousness. Diagnosis relies on criteria such as elevated blood glucose levels and increased osmolality. HHS management involves a multidisciplinary approach, addressing fluid depletion, compromised cerebral perfusion, and achieving gradual normalization of osmolality and blood glucose levels to prevent complications.

Summary

Hyperosmolar Hyperglycemic Syndrome (HHS), a severe metabolic disorder linked to diabetes, extends beyond hyperglycemia, necessitating a comprehensive understanding. This review sheds light on HHS etiology, clinical manifestations, diagnostic criteria, and treatment modalities, emphasizing its critical nature in diabetes care.

Keywords: hyperglycemic hyperosmolar state, HHS, diabetes mellitus, hyperglycemia, dehydration,

INTRODUCTION

Hyperosmolar Hyperglycemic State (HHS) is a severe condition marked by profound hyperglycemia, hyperosmolality, and dehydration, occurring without ketosis. It differs from diabetic ketoacidosis (DKA), necessitating a distinct treatment approach. Although predominantly observed in those aged over 45 with type 2 diabetes, occurrences in children and young adults have been noted. HHS poses a significantly higher risk compared to diabetic ketoacidosis. Prognosis is influenced by factors such as dehydration severity, coexisting illnesses, and advanced age. Treatment focuses on correcting volume deficits, hyperosmolality, hyperglycemia, and electrolyte imbalances, alongside addressing the underlying cause of metabolic decompensation. [1,2]

Diabetes mellitus, characterized by elevated blood glucose levels, stems from an insufficient production of insulin, either absolutely or relatively. Insulin, an anabolic hormone secreted by the pancreatic beta cells in the islets of Langerhans, plays a pivotal role in regulating glucose levels. Its primary functions include facilitating glucose uptake by adipose tissue and skeletal muscle (glycogenesis) while inhibiting fat breakdown in adipose tissue (lipolysis). Hormones like glucagon and catecholamines counterbalance insulin's metabolic effects. [3,4]

Type 1 diabetes is an immune-mediated diabetes, constituting only 5–10% of diabetes cases, was previously referred to as insulin-dependent or juvenile-onset diabetes. It results from a cellular-mediated autoimmune attack on the pancreatic β-cells. Indicators of this immune destruction include islet cell autoantibodies, autoantibodies to insulin, GAD (GAD65), and tyrosine phosphatases IA-2 and IA-2β. Approximately 85–90% of individuals exhibit one or more of these autoantibodies when fasting hyperglycemia is first detected.

Type 2 diabetes, representing 90–95% of cases, encompasses a spectrum from insulin resistance with relative insulin deficiency to an insulin secretory defect with resistance. Formerly termed non–insulin-dependent or adult-onset diabetes, it primarily affects individuals with insulin resistance and often relative, rather than absolute, insulin deficiency. Initial insulin treatment is typically unnecessary. The causes are varied, excluding autoimmune β-cell destruction. Most patients are obese, with obesity-induced insulin resistance being prevalent. Even non-obese individuals may exhibit abdominal fat distribution. Diagnosis can be delayed due to gradual hyperglycemia development without severe symptoms. Despite seemingly normal or elevated insulin levels, there is defective insulin secretion, insufficient to counter insulin resistance. While weight reduction and pharmacological treatments may enhance insulin resistance, complete restoration is uncommon. Risk factors encompass age, obesity, sedentary lifestyle, prior gestational diabetes, hypertension, dyslipidemia, and genetic predisposition, with complex genetic factors at play. [5]

Hyperosmolar Hyperglycemic Syndrome (HHS) is a critical and potentially life-threatening complication associated with type 2 diabetes. HHS is infrequent, constituting only 13% of hyperglycemia-related emergency admissions in the United States. Despite its lower occurrence, HHS exhibits a higher mortality rate compared to Diabetic Ketoacidosis (DKA). HHS typically evolves gradually over several days, resulting in more pronounced dehydration and metabolic disturbances than observed in DKA. The critical distinction between transient elevations of blood glucose seen in many individuals with diabetes and HHS lies in the prolonged duration of hyperglycemia and the associated severe dehydration.[6]

MATERIAL AND METHODS

This study conducted a systematic review of medical articles retrieved from the PubMed database, covering the period from 1972 to 2023. The search strategy involved the analysis of keywords, including hyperglycemic hyperosmolar state, HHS, diabetes mellitus, hyperglycemia, and dehydration.The inclusion of pertinent articles ensured a thorough exploration of the literature, providing a comprehensive overview of the topics related to Hyperosmolar Hyperglycemic State (HHS) within the specified timeframe.

REVIEW AND DISCUSSION

Clinical presentation of patients with HHS

Hyperosmolar Hyperglycemic Syndrome (HHS) predominantly affects elderly individuals with type 2 diabetes. Infection, particularly pneumonia and urinary tract infection, is the most common precipitating factor for HHS. A significant number of HHS cases arise in individuals without a pre-existing history of diabetes. Typical initial symptoms encompass fatigue, weakness, polydipsia, polyuria, nausea, and altered consciousness. Medical conditions such as stroke, myocardial infarction, and trauma can induce the release of counterregulatory hormones, impairing access to water. This process may result in severe dehydration and the initiation of Hyperosmolar Hyperglycemic Syndrome (HHS). [1, 7, 8]

Abnormalities in physical examination

System	Signs and symptoms
General condition	fatigue and dizziness, confusion, polydipsia
Skin	prolonged capillary refill, poor skin turgor
Respiratory system	tachypnea
Cardiovascular system	tachycardia, orthostatic hypotension, weak pulse
Genitourinary	polyuria, prerenal kidney failure
Central Nervous System	neurological deficit, somnolence, stupor, coma

Criteria for Diagnosing HHS

HHS primarily occurs in adults and elderly patients, with an evolution lasting from several days to weeks, often marked by altered mental status. In HHS, insulin levels are sufficient to prevent ketogenesis but fail to counteract hyperglycemia. The disease onset is primarily attributed to extremely high hyperglycemic levels and consequent osmotic diuresis.

Despite significant electrolyte losses and total body volume depletion, individuals with HHS may not exhibit apparent dehydration due to hypertonicity preserving intravascular volume (shifting water from intracellular to extracellular spaces). Diagnosis of HHS should not rely solely on biochemical parameters. However, blood glucose levels are notably elevated (usually ≥30 mmol/l), along with increased osmolality (usually ≥320 mOsm/kg). Osmolality serves as an indicator of severity and aids in treatment monitoring. While serum osmolality is often reported in biochemical profiles in a calculated or measured form, it can be calculated using the formula [(2×Na+) + glucose + urea]. While this formula provides a close

approximation of measured osmolality, a more precise formula exists. Although urea is not a significant compound, its inclusion in calculations is crucial in hyperosmolar states, serving as an indicator of severe dehydration. [9, 10,11, 12,13]

Diagnostic Criteria for Hyperosmolar Hyperglycemic Syndrome

Laboratory parameters	Values typical for HHS
glucose	>33,3 mmol/l (>600 mg/dl)
pH	>7,30
HCO3-	>15 mmol/l
Na+	>150 mmol/l
Serum concentrations of urea, creatinine, and uric acid	usually increased
ketones in urine	None, < +
Plasma osmolarity	>320 mOsm/kg H2O

Treatment strategies

The management of Hyperosmolar Hyperglycemic Syndrome (HHS) necessitates a multidisciplinary approach, involving consultations with an endocrinologist and an intensive care specialist. Altered mental status in Hyperosmolar Hyperglycemic Syndrome (HHS) may arise from notable fluid depletion and compromised cerebral perfusion. In such cases, securing the airway is recommended, particularly if the Glasgow Coma Score is less than 8. [4] The goals of treatment of hyperosmolar hyperglycemic syndrome (HHS) include causal treatment and achieving gradual normalization of osmolality, safe replenishment of fluid and electrolyte losses, gradual normalization of blood glucose levels, prevention of thrombosis and prevention of complications such as cerebral edema and osmotic demyelination syndrome, and foot ulcers.

The goal of treating Hyperosmolar Hyperglycemic Syndrome (HHS) is to replace around 50% of estimated fluid loss in the first 12 hours and the remaining amount in the subsequent 12 hours. The speed of correction is influenced by the initial severity, renal function, and coexisting conditions. The initial glucose target is 10-15 mmol/L, transitioning to an individualized target (6–10 mmol/L) when normal eating and drinking resume. Ideally, individuals recover quickly enough to orally replace the water deficit. [14, 15]

Initial therapy focuses on expanding intravascular and extravascular volume to restore peripheral perfusion. Recommended fluids include crystalloids, particularly 0.9% sodium chloride solution with added potassium as needed. Caution is advised against rapid changes in osmolality, with continuous monitoring and adjustment of fluid replacement rates. The rate of fall of serum sodium should not exceed 10 mmol/L in 24 hours, and the safe rate of plasma glucose decline should not exceed 5 mmol/h. If osmolality is not decreasing despite adequate fluid replacement, consideration may be given to using 0.45% sodium chloride solution. Complete normalization of electrolytes and osmolality may take up to 72 hours. [16]

In Hyperosmolar Hyperglycemic Syndrome (HHS), osmolality is a critical parameter, with sodium and glucose being the main contributors. Rapid changes can lead to dangerous fluid shifts, risking neurological complications like cerebral edema and osmotic demyelination. Total body water distribution is influenced by osmotically effective substances, and various osmoles play a crucial role in water movement across cell membranes. Serum sodium, a close osmolality approximation, may appear normal or low in hyperglycemia due to the osmotic shift caused by added glucose. [17]

Different formulae calculate osmolality, with [(2×Na+) + glucose + urea] offering a close approximation. Urea's exclusion allows tonicity calculation, crucial for assessing the risk of cerebral edema in hyponatremia. Effective osmolality considers the impact of glucose and urea on osmolality. Monitoring osmolality is vital for assessing severity and treatment response. Fluid replacement alone lowers glucose concentrations, and the initiation of fixed-rate intravenous insulin infusion (FRIII) should be delayed unless significant ketonemia is present. The risk of early insulin administration includes larger osmotic shifts and potential circulatory

collapse. Generally, it is recommended to initiate intravenous insulin at a dose of 0.5 U/kg/h once osmolality ceases to decline. The infusion rate can be increased by 1.0 unit/h. Initiate glucose infusion (5% or 10%) once blood glucose falls below 14 mmol/L, running concurrently with Fixed-Rate Intravenous Insulin Infusion (FRIII) and other fluid replacement. Appropriate fluid and FRIII management should achieve a fall in serum osmolality within the target range of 3.0–8.0 mOsm/kg/h to minimize the risk of neurological complications. [18,19, 6]

Hypokalemia in Hyperosmolar Hyperglycemic Syndrome (HHS) results from osmotic diuresis, hypertonicity, and fluid shifts, causing intracellular potassium loss. Hypoperfusion and vomiting exacerbate potassium depletion. In DKA, insulin deficiency and ketone accumulation contribute to intracellular-to-extracellular potassium shifts. Insulin treatment aids in restoring intracellular potassium, addressing hypokalemia in HHS. [6] Potassium replacement in Hyperosmolar Hyperglycemic Syndrome (HHS) should begin once hyperkalemia is excluded or resolved with rehydration and insulin therapy. If potassium levels are between 3.3–5.5 mmol/l, administer 20 mmol/hour initially, aiming to maintain levels above 4.0 mmol/l by adjusting the infusion rate. If levels are below 3.3 mmol/l, insulin therapy initiation should be delayed until potassium is corrected by infusing at 40 mmol/hour. If potassium exceeds 5.5 mmol/l, withhold potassium until concentrations are within the target range. [9,23]

In Hyperosmolar Hyperglycemic Syndrome (HHS), there is a heightened occurrence of thrombotic complications such as myocardial infarction, stroke, or peripheral arterial thrombosis compared to other diabetic crises. The effectiveness of prophylaxis using low-dose LMWH or anti-platelet therapy remains uncertain, and the use of full therapeutic doses is undetermined. Individuals with diabetes, particularly those with HHS, face an increased risk of arterial and venous thromboembolic events. Prophylactic low molecular weight heparin (LMWH) is recommended throughout the hospital stay unless contraindicated, while therapeutic anticoagulation is considered only for those with suspected thrombosis or acute coronary syndrome. [20,21,22]

Prognosis and prevention

Hyperosmolar Hyperglycemic Syndrome (HHS) typically has a low overall mortality, usually attributed to the underlying illness triggering the hyperglycemic crisis. Prognosis is poorer in elderly patients with severe coma and hypotension. Recovery time is influenced by age, comorbidities, and the underlying precipitants.. Key aspects of management include early mobilization, proper nutrition, and discontinuation of IV insulin upon oral intake resumption. Prolonged IV fluids might be needed for those with inadequate oral intake. Transition to subcutaneous insulin is common, and consideration of appropriate medications is given to those previously undiagnosed or well-controlled on oral agents after stability. Continuous involvement of diabetes specialists is essential to prevent recurrence and address long-term complications. [1]

Education and effective communication are essential for preventing admissions related to HHS in individuals with diabetes. This involves teaching individuals about sick day management, emphasizing when to contact a healthcare provider, understanding blood glucose goals, using supplemental insulin during illness, never discontinuing insulin, initiating a suitable diet when regular intake is not possible, and increasing blood glucose monitoring frequency during acute illness. [9]

SUMMARY

Hyperosmolar Hyperglycemic Syndrome (HHS) primarily affects elderly individuals with type 2 diabetes, often triggered by infections like pneumonia or urinary tract infections. Initial symptoms include fatigue, weakness, polydipsia, polyuria, nausea, and altered consciousness. Clinical examination reveals signs such as prolonged capillary refill, poor skin turgor, tachypnea, tachycardia, orthostatic hypotension, weak pulse, polyuria, neurological deficits, and altered mental status.

Diagnosis of HHS involves elevated blood glucose levels (>33.3 mmol/l), increased osmolality (>320 mOsm/kg), and other laboratory parameters. Treatment strategies require a multidisciplinary approach, focusing on gradual normalization of osmolality, fluid and electrolyte replenishment, blood glucose control, and prevention of complications. Initial therapy involves expanding volume with fluids,

cautioning against rapid changes in osmolality. Potassium replacement is crucial, initiated based on levels. Thrombotic complications may occur, warranting prophylaxis with low molecular weight heparin.

The prognosis of HHS is influenced by age, comorbidities, and underlying precipitants, with recovery typically taking up to 72 hours. Management includes early mobilization, proper nutrition, and transitioning to subcutaneous insulin. Education on sick day management is vital for preventing HHS-related admissions in individuals with diabetes.

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Lidia Bartoszek – writing-rough preparation, writing—review and editing, methodology

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References

1. Pasquel FJ, Umpierrez GE. Hyperosmolar hyperglycemic state: a historic review of the clinical presentation, diagnosis, and treatment. Diabetes Care. 2014 Nov;37(11):3124-31. doi: 10.2337/dc14-0984.

2. Zubkiewicz-Kucharska A, Chrzanowska J, Noczyńska A. Hyperosmolar hyperglycaemic state (HHS) as the first manifestation of type 2 diabetes in a child. Pediatr Endocrinol Diabetes Metab. 2019;25(2):85-89. doi: 10.5114/pedm.2019.85819

3. Röder PV, Wu B, Liu Y, Han W. Pancreatic regulation of glucose homeostasis. Exp Mol Med. 2016 Mar 11;48(3):e219 doi: 10.1038/emm.2016.6

4. Adeyinka A, Kondamudi NP. Hyperosmolar Hyperglycemic Syndrome. StatPearls Publishing; 2023 Jan. 2023 Aug 12.

5. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 2010 Jan; 33(Suppl 1): S62–S69. doi: 10.2337/dc10-S062

6. Mustafa OG, Haq M, Dashora U, Castro E, Dhatariya KK, the Joint British Diabetes Societies (JBDS) for Inpatient Care Group. Management of Hyperosmolar Hyperglycaemic State (HHS) in Adults: An updated guideline from the Joint British Diabetes Societies (JBDS) for Inpatient Care Group. Diabetic Medicine 2023 Mar; 40(3): e15005. doi: 10.1111/dme.15005

7. Wachtel TJ.The diabetic hyperosmolar state. Clin Geriatr Med. 1990 Nov;6(4):797-806.

8. Berger W. [Diabetic emergencies]. Praxis (Bern 1994). 1997 Feb 18;86(8):308-13.

9. English P, Williams G. Hyperglycaemic crises and lactic acidosis in diabetes mellitus. Postgrad Med J 2004;80:253–261. doi: 10.1136/pgmj.2002.004291

10. Bartoli E, Bergamasco L, Castello L, Sainaghi PP. Methods for the quantitative assessment of electrolyte disturbances in hyperglycaemia. Nutr Metab Cardiovasc Dis. 2009;19(1):67-74. doi: 10.1016/j.numecd.2008.10.005

11. Zeitler P, Haqq A, Rosenbloom A, Glaser N. Hyperglycemic hyperosmolar syndrome in children: pathophysiological considerations and suggested guidelines for treatment. J Pediatr. 2011;158(1):9-14. doi: 10.1016/j.jpeds.2010.09.048

12. Fadini GP, De Kreutzenberg SV, Rigato M, Brocco S, Marchesan M, Tiengo A, Avogaro A. Characteristics and outcomes of the hyperglycemic hyperosmolar non-ketotic syndrome in a cohort of 51 consecutive cases at a single center. Diabetes Res Clin Pract. 2011;94:172–179. doi: 10.1016/j.diabres.2011.06.018.

13. Dhatariya K K, Vellanki P. Treatment of Diabetic Ketoacidosis (DKA)/Hyperglycemic Hyperosmolar State (HHS): Novel Advances in the Management of Hyperglycemic Crises (UK Versus USA). Curr Diab Rep. 2017; 17(5): 33., doi: 10.1007/s11892-017-0857-4

14. Gershkovich B, English SW, Doyle MA, Menon K, McIntyre L. Choice of crystalloid fluid in the treatment of hyperglycemic emergencies: a systematic review protocol. Syst Rev. 2019;8(1):228. doi: 10.1186/s13643-019-1130-5

15. Hockaday TD, Alberti KG. Diabetic coma. Clin Endocrinol Metab. 1972 Nov;1(3):751-88.

16. Katz MA. Hyperglycemia-induced hyponatremia - calculation of expected serum sodium depression. N Engl J Med. 1973;16(289):843-844.

17. Bhave G, Neilson EG. Volume depletion versus dehydration: how understanding the difference can guide therapy. Am J Kidney Dis. 2011;58(2):302-309.

18. Scott A, on behalf of the Joint British Diabetes Societies (JBDS) for Inpatient Care Management of hyperosmolar hyperglycaemic state in adults with diabetes. Diabetic Med. 2015;32:714–724. doi: 10.1111/dme.12757.

19. Zahran NA1, Jadidi S. Pediatric Hyperglycemic Hyperosmolar Syndrome: A Comprehensive Approach to Diagnosis, Management, and Complications Utilizing Novel Summarizing Acronyms. Children (Basel). 2023 Oct 31;10(11):1773. doi: 10.3390/children10111773.

20. Carr ME. Diabetes mellitus: a hypercoagulable state. J Diabetes Complicat. 2001;15(1):44-54.

21. Petrauskiene V, Falk M, Waernbaum I, Norberg M, Eriksson JW. The risk of venous thromboembolism is markedly elevated in patients with diabetes. Diabetologia. 2005;48(5):1017-1021. doi: 10.1007/s00125-005-1715-5

22. Wordsworth G, Robinson AH, Ward A, Atkin M. HHS—full or prophylactic anticoagulation? British Journal of Diabetes. 2014;14(2):64-66.

23. Kitabchi AE, Umpierrez GE, Murphy MB, et al. Management of hyperglycemic crises in patients with diabetes. Diabetes Care 2001. Jan;24(1):131-53. doi: 10.2337/diacare.24.1.131.