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Hyperosmolar Hyperglycemic State (HHS) and Diabetic Kidney Disease (DKD) as Acute and Chronic Complications of Type 2 Diabetes Mellitus in End-Stage Chronic Kidney Disease (CKD): a Case Report

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KEYWORDS

HHS, DKD, Diabetes Mellitus types 1 and 2

ABSTRACT

Hyperosmolar hyperglycemic state (HHS) is a life-threatening metabolic emergency that occurs in patients with type 1 or type 2 *diabetes mellitus* (DM). It is characterized by severe hyperglycemia, hyperosmolarity, dehydration, and mild or absent ketosis. Another chronic complication frequently associated with long-standing DM is *diabetic kidney disease* (DKD), which increases the risk of morbidity and mortality. However, the coexistence of acute HHS and chronic DKD in a single patient presents complex clinical challenges and requires prompt management. This case report presents a 61-year-old male patient with a 20-year history of type 2 DM who was referred due to decreased consciousness persisting for five days. Clinical findings included severe hyperglycemia (680 mg/dL), hyperosmolarity (360 mOsm/kg), an increased anion gap (>12), and urinary tract infection (UTI) as the precipitating factor of HHS. Laboratory results also revealed moderate normochromic-normocytic anemia, massive proteinuria, and decreased renal function, indicating DKD. This report highlights the critical interplay between acute metabolic crises and chronic diabetic complications. Early recognition and management of HHS, alongside evaluation of underlying chronic conditions such as DKD, are essential to reduce morbidity and mortality. The findings emphasize the importance of comprehensive diabetic care, timely infection control, and regular renal monitoring in patients with long-term diabetes.

INTRODUCTION

Hyperosmolar hyperglycemic state (HHS) is a life-threatening condition that often occurs in patients with type 1 and 2 diabetes mellitus characterized by a hyperglycemic crisis without a mild increase or no ketones in blood and urine (Stoner, 2017; Umpierrez et al., 2024). Although HHS can occur in type 1 and 2 DM, it is generally more common in the elderly with type 2 diabetes, where insulin production still occurs but is not adequate to overcome hyperglycemia. Signs of HHS include hyperglycemia that causes a hyperosmolar state, severe dehydration, changes in mental status, without severe ketosis and acidosis. HHS triggers include infections such as UTIs and pneumonia, acute illnesses, and others. HHS occurs due to an increase in counter-regulatory hormones in response to low insulin levels in the blood; these hormones include glucagon, growth hormone, cortisol, and catecholamines, which all stimulate glucose production through the processes of gluconeogenesis and glycogenolysis.

However, the increase in glucose production is not offset by utilization in tissues. In HHS, there is still a minimal amount of residual insulin that is not adequate to overcome hyperglycemia (Umpierrez et al., 2024; Karslioglu French et al., 2019; Aldhaeefi et al., 2022). However, the presence of this insulin residue prevents the burning of fatty acids that would otherwise produce ketones, so in HHS there is no ketosis or only mild ketosis (Umpierrez et al., 2024). The HHS mortality rate ranges from 10-50%, depending on the severity of dehydration, age, level of consciousness, and other comorbidities (Stoner, 2017; Umpierrez & Korytkowski, 2016). The management of hyperglycemic crises generally involves correcting dehydration, hyperglycemia, electrolyte disorders, and identification and treatment of the precipitating factors. Monitoring of vital signs, fluid input and output, insulin dose, and laboratory parameters such as electrolytes, blood glucose, bicarbonate, and anion gap should be performed to assess therapeutic response (Fayfman et al., 2017).

Another chronic complication of diabetes mellitus is diabetic kidney disease (DKD). Patients with DKD will generally progress to end-stage renal disease (ESRD) and develop other complications such as cardiovascular disease and infection. Poor glycemic control and blood pressure dysregulation lead to changes in kidney hemodynamics, chronic inflammation, and fibrosis. Kidney structural changes that occur in DKD include loss of capillary fenestration, apoptosis and depletion of podocyte cell processes, loss of slit diaphragm, expansion of the mesangial matrix, and glomerular hypertrophy (Alicic et al., 2017; Thomas et al., 2015). These structural changes can begin to be observed 5 to 7 years after the diagnosis of type 1 DM. Similar changes are also observed in type 2 DM but are more heterogeneous (Alicic et al., 2017). A classic sign as well as an independent risk factor for the development of ESRD is proteinuria or macroalbuminuria. However, some patients experience nonproteinuric diabetic kidney disease, which is characterized by decreased kidney function without proteinuria (Yamanouchi et al., 2020). The median time for people with DM to start developing proteinuria is 15 years from the time of initial diagnosis (Alicic et al., 2017). Management strategies for DKD include strict glycemic and blood pressure control; the use of nephroprotective agents such as ACE inhibitors, ARBs, SGLT-2 inhibitors, and GLP-1 agonists can be considered (Młynarska et al., 2024).

Rahman et al. (2024) conducted a comprehensive cohort study which found that patients presenting with hyperglycemic crises (HC), particularly hyperosmolar hyperglycemic state (HHS), at the initial diagnosis of type 2 diabetes had a 2-fold increased risk of developing chronic kidney disease (CKD) compared to those without HC, with an adjusted hazard ratio (aHR) for HHS of 2.47. While this study elucidates the long-term renal risk associated with HHS, it did not focus on acute in-hospital management or simultaneous chronic complications like DKD. Conversely, Tuttle & Heerspink (2022) highlighted the emerging phenotype of non-albuminuric *diabetic kidney disease*—characterized by eGFR decline without notable proteinuria—which affects approximately 20–40% of diabetic patients and follows a distinct pathophysiology involving tubulointerstitial damage. However, they largely addressed chronic progression and did not explore how acute metabolic crises like HHS may exacerbate or interact with non-albuminuric DKD.

This case study aims to illustrate the intertwined presentation of HHS and DKD in a long-standing diabetic patient, highlighting the diagnostic and therapeutic challenges they pose. Clinically, it underscores the necessity of prompt, multifaceted management—correcting hyperosmolarity, dehydration, and electrolyte imbalances—alongside renal assessment. The findings contribute valuable, practice-oriented knowledge for physicians managing complex diabetic emergencies, reinforcing the benefit of integrating acute and chronic care strategies to reduce morbidity and mortality in similar patient populations.

RESEARCH METHOD

A 61-year-old male patient was referred with decreased consciousness since 5 days of SMRS. The decrease in consciousness is said to be gradual, starting with restlessness, but the patient can still be talked to, then aggravates until 2 days of SMRS, the patient does not respond to the call. The patient also complained of experiencing tightness since 5 days of SMRS, tightness was said to have disappeared, did not improve with a change in position. Another complaint in the form of weakness of the whole body was also felt by patients since 1 month which was aggravating since the last 2 weeks. Swelling in both lower limbs began to be experienced since the last 1 week. A history of fever, cough, and urinary disorders is denied. Previously, the patient had been treated at the nearest hospital, but due to a decrease in consciousness, the patient was then referred to Tabanan Hospital. The patient has a history of type 2 diabetes mellitus since the age of 20, had used insulin for 3 years from 2020 to 2023 but was stopped due to recurrent hypoglycemia. The patient was then given OADs in the form of Metformin 500mg and Glimepiride 2 mg daily. The history of hypertension has only been known for the last 10 years with treatment but the patient's family has forgotten the name of the drug.

On physical examination, it was found that GCS E2V2M3 contact was inadequate awareness, a vital sign within normal limits. The conjunctiva of anemic patients, in the neck of JVP 5+2 mmH2O, no additional breathing sounds such as rhonki and wheezing were found. In the abdomen, there was no ascites or organomegaly such as hepatomegaly and spleenomegaly, ballottement negative. In both lower extremities, pitting edema, CRT<2 seconds, was obtained. In patients with a dower catheter. Patients were subjected to laboratory examinations such as DL, UL, Electrolyte, AGD, blood chemistry, iron profile, thorax x-ray, and urine culture.

Table 1. Serial complete blood test

Parameter	22/12/24	26/12/2024	28/12/24	Reference Value
HGB	7.4	6.9	9.6	13.2-17.3
HCT	23.5	20.8	28.7	40-52
RBC	2.9	2.75	3.54	4.4-5.9
WBC	10.7	10.94	11.3	3.8-10.6
PLT	272	301	295	150-440
MCV	81.0	75.6	81	80-100
MCH	25.5	25.1	27	26-34
MCHC	31.5	33.3	33	32-36
%NEW	95.1	88.4	92	50-70
%LYMPH	3.3	5.0	5	25-40

%MONO	4.6	5.9	3	2-8
%EOS	0.0	0.6	0.0	2-4
%BASO	0.0	0.1	0.0	0-1

Source: author

Table 2. Blood chemistry examination, and screening for Hepatitis B and C infections.

Parameter	22/12/24	28/12/2024	Reference Value
GDS	680	293	74-106
SGOT	255	-	0-50
SGPT	199	-	0-50
Urea	171	90.7	10-50
Creatinin	6.56	6.24	0.7-1.1
Feritin	-	1069	Male 27-375 Female 12-135
HBsAg	-	Non-reactive	Non-reactive
Anti-HCV	-	Non-reactive	Non-reactive
Gout	-	10.80	2.0-7.0
Sodium	124	133	135-147
Potassium	7.9	7.3	3.5-5.0
Chlorida	99	115	95-105

Source: author

Table 3. AGD Examination

Parameter	23/12/24	Reference Value
pH	7.29	7.350-7.450
PaCO2	34.5	35-48
PaO2	93	
HCO3	15.7	22-26
BE	-11	-3- (3)
Saturase O2	99	

Source: author

Table 4. Complete Urine Test

Parameter	22/12/24	26/12/24	Reference Value
Makroskopis			
Color	Yellow	Yellow	The End of the Day
Turbidity	Turbid	Turbid	Clear
Chemistry			
Leukosit	+3	+1	Negative
Nitrite	Negative	Negative	Negative
Glukosa	+3	+3	Negative
Protein	+3	+3	Negative
Keton	Negative	Negative	Negative
Urobilinogen	Usual	Usual	Usual
Bilirubin	Negative	Negative	Negative
Blood	+2	+1	Negative
Sedimen Urine			
Leukosit	26-28	1-3	Negative
Red blood cell	15-17	2-4	Negative
Silinder	Negative	Negative	Negative
Epithelium	3-5	1-3	Negative
Crystal	Negative	Negative	Negative

Bacteria	Negative	+2	Negative

Source: author

The results of a complete blood test are known that patients have moderate anemia that tends to lead to chronic disease anemia. The WBC parameter showed an increase in the total number exceeding normal values with a shift to the left predominantly neutrophils indicating a tendency to bacterial infection. In a complete urine examination, the patient is diagnosed with UTI, but a urine culture is needed to confirm the diagnosis. The results of the AGD showed the presence of mild acidosis in the patient. From the laboratory data above in the patient, the serum osmolarity calculation was carried out which was 346 and an anion gap >12.

RESULT AND DISCUSSION

Hyperosmolar hyperglycemic state (HHS) is one of the disorders in Diabetes Mellitus, both type 1 and 2 DM but is more common in type 2 DM. HHS is more common in the elderly, although it can also occur in children with a 10x higher mortality rate than DKA. The mortality rate from HHS is exacerbated by the comorbidities, the severity of the dehydration and the severity of the triggering factors, and the age of the sufferer. It is triggered by several conditions such as infections especially UTIs and pneumonia, acute medical conditions such as myocardial infarction, CVA, pulmonary embolism, trauma, etc. (Alicic et al., 2017; Gosmanov et al., 2021). Pneumonia is known to occur in 57% of cases mainly caused by gram-negative bacteria, followed by UTIs and sepsis as much as 21% (Gosmanov et al., 2021). A typical sign found in HHS is severe hyperglycemia ≥ 600 mg/dL, hyperosmolar condition with serum osmolarity reaching ≥ 320 mOsm/kg, severe dehydration, and minimal or no ketosis. In HHS there is generally metabolic alkalosis where pH is >7.3, and bicarbonate >18 mmol/L. Some cases may indicate mild acidosis. This can be found in patients who experience mild ketosis due to inadequate insulin activity. Other conditions such as severe dehydration cause the body to fall into a state of hypoperfusion to peripheral tissues so that the body conducts anaerobic metabolism and produces lactic acid as a byproduct of anaerobic metabolism (Long et al., 2021). Increased anion gap with metabolic acidosis can be found in lactate accumulation and uremia conditions in patients with comorbid renal failure (Adeyinka & Kondamudi, 2023).

Clinically, patients may show symptoms and signs such as malaise, lethargy, or changes in mental status such as delirium or even coma due to decreased blood flow to the brain. Tachycardia, a weak pulse can be found due to compensation for a drop in blood pressure. Tachypneue can be found in some sufferers if acidosis is present (Adeyinka & Kondamudi, 2023). In the case of the patient, it was complained of a gradual decline in consciousness from restlessness to somnolen. In patients, signs of dehydration were found such as cowong eyes and dry lip mucosa. Pitting edema was also found in both lower limbs of the patient. The patient is known to have comorbidities with a decline in kidney function that has only been known since the last 3 months.

Complete blood laboratory tests showed the presence of microcyteric hypochromic moderate anemia at the initial examination, but in the next examination the anemia was more towards normochromic-normocyter. From the WBC parameters, patients experienced

neutrophil predominantly leukocytosis which indicates a tendency for acute bacterial infection. To find out the locus of infection in the patient, a thoracic x-ray and a complete urine examination were performed. The results of the x-ray examination showed the presence of cardiomegaly but no signs of lung infection such as consolidation or infiltrate were found. In the urine, leukocytees were first found with urine sediments of 26-28 cells/LPB. To establish UTIs in this patient, a urine culture examination was carried out which resulted in 103 cell colonies. This is likely due to the fact that urine culture was carried out a few days after the start of treatment at the Referral Hospital where the patient had been treated at a different hospital and received therapy in the form of intravenous antibiotics before. The patient's serum ormolarity was calculated using laboratory data of blood glucose, electrolyte, and AGD. The GDS level of the first patient was 680 mg/dL which if the serum osmoloaricity calculation was carried out, the result was 360 mOsm/kg. The anion gap was also calculated by subtracting the number of cations (Na+ and K+) by the anions (Cl- and HCO3-) and the result was an anion gap = 17.2. These findings are in accordance with the HHS diagnosis theory above which is obtained massive hyperglycemia, hyperosmolarity, and increased anion gap. On the examination of AGD, patients tended to experience mild metabolic acidosis with a pH of 7.29 and serum bicarbonate of 15.7. This may be related to comorbidities of kidney failure suffered by patients from which a state of uremia with BUN 171 and Sc 6.56 was obtained from the examination of the kidney failure. Potassium levels in HHS can be found to be high or low, low insulin levels cause the transfer of potassium to cellular extracts. In patients with frequent urination, potassium levels may drop due to being discharged along with urine and high urination frequency (Adeyinka & Kondamudi, 2023). In this case, the patient experienced hyperkalemia with Potassium reaching 7.9 which can be caused by the inability of the kidneys to excrete potassium in CKD patients.

In this case, it is known that the patient has comorbidities in the form of CKD stage 5 et cause DKD. Kidney Disease Improving Global Outcome (KDIGO) presents DKD is a clinical diagnosis used in CKD patients with Diabetes Mellitus, while Diabetic Nephropathy (DN) is exclusively used to describe the histological diagnosis of glomerular changes in DM patients observed from biops. Chronic hyperglycemia and glomerular hyperfiltration are the main causes of DKD, in type 2 DM there are other causal factors such as hypertension, obesity and cardiovascular disease which all cause chronic microvascular damage including the vascular system in the kidneys. There are non-modifiable risk factors such as old age, male gender, genetics, and the onset of the onset of DM in patients. On average, patients can develop DKD after 5-15 years from the onset of being diagnosed with DM (Hassan et al., 2022; Alghamdi et al., 2021; Hoogeveen, 2022). Albuminuria is a marker that is often used in the screening and diagnosis of DKD. Patients with microalbuminuria show a relatively higher risk of developing ERSD compared to patients with normoalbuminuria. Regarding the incidence of cardiovascular disease, patients with microalbuminuria have a risk of death from cardiovascular disease. In general, albuminuria describes the presence of an injury to the endothelial throughout the body, including the kidneys (Yamazaki et al., 2021). CKD management strategies include dietary adjustments, exercise, glycemic regulation and blood

pressure with pharmacotherapy, all simultaneously performed to prevent progression of CKD. In this case, the patient has a history of type 2 DM that has lasted for 20 years, and hypertension for more or less the last 10 years. The two chronic diseases above have become risk factors for CKD in patients. Urinalysis examinations performed during the patient's treatment consistently experience massive proteinuria which is a typical sign of DKD.

ACE-Inhibitors and ARBs are specifically recommended for blood pressure control in patients with comorbid CKD considering that RAAS inhibitors have renoprotective mechanisms in addition to effectively lowering blood pressure. Recent research shows Sodium-glucose cotransporter-2 (SGLT-2), and incretin such as GLP-1 are effective in improving CKD patient outcomes. SGLT-2 plays a role in reducing glomerular hyperfiltration, reducing oxidative stress, and the formation of AGE in proximal tubules, which results in a reduced risk of decreased eGFR, renal failure, and heart failure which is one of the most common causes of death in CKD patients (Akhtar et al., 2020; Tuttle et al., 2022).

The key to early treatment from HHS is fluid therapy to restore intravascular volume and hyperosmolar conditions. The choice of liquid is normal saline (0.9% NaCl) as much as 500-1000ml/hour in the first 2-4 hours. Fluid administration should pay attention to the patient's hydration status response and sodium levels. Insulin administration began with a dose of 0.1 units/kg by IV bolus and then continued with a continuous drip of 0.1 units/kg/hour. Insulin administration is lowered if blood glucose drops below 300 mg/dL. In certain cases, insulin can be administered subcutaneously. Potassium levels should be maintained at 4-5 mEq/L as insulin can cause potassium transfer into cells. Bicarbonate is not routinely administered except for pH<6.9 and the risk of hypokalemia increases in patients. Close monitoring of GDS, electrolytes, serum osmolarity, urine output, vital signs, and mental status should be observed hourly during critical periods. Therapies related to HHS triggers such as underlying infections must be adequate to improve the patient's clinical outcomes (Hassan et al., 2022; Molitch et al., 2015). In this case, patients with comorbid stage 5 CKD were given a rumatan fluid at a rate of 16 tpm, calcium gluconas, salbutamol nebulizer, ceftriaxone, subcutaneous rapid acting insulin 3 x 4 units, 6 units of long acting insulin, continuous drip furosemide, candesartan 8mg, and periodic hemodialysis (HD) and blood transfusions at HD. After being treated for 3 days, the patient did not show improvement and on the 4th day the patient died.

CONCLUSION

This case report highlights the coexistence of acute hyperosmolar hyperglycemic state (HHS) and chronic *diabetic kidney disease* (DKD) in a 61-year-old male with long-standing type 2 *diabetes mellitus*, underscoring the complex interactions between acute metabolic emergencies and chronic diabetic complications. It emphasizes the critical need for early recognition and comprehensive management of hyperglycemia, electrolyte imbalances, infections, and continuous renal monitoring to reduce morbidity and mortality. By illustrating the diagnostic and therapeutic challenges posed by overlapping acute and chronic conditions, this study calls for future larger-scale research to investigate the relationship between HHS and

DKD progression, identify predictive markers for early detection, and develop integrated treatment protocols to improve patient outcomes with multiple diabetic complications.

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