Received: 1 May 2024 | Accepted: 25 June 2024

DOI: 10.1111/dme.15405

DIABETIC Medicine

INVITED REVIEW

Special Issue: From Bench to Bedside

Management of diabetes-related hyperglycaemic emergencies in advanced chronic kidney disease: Review of the literature and recommendations

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Abstract

Aims: Despite the substantial progress in the management of diabetes mellitus (DM), chronic kidney disease (CKD) remains one of the most common complications. Although uncommon, diabetic emergencies [diabetic ketoacidosis (DKA), hyperosmolar hyperglycaemic state (HHS)] can still occur in stage 4 and 5 CKD, at times with less typical clinical manifestations due to the altered pathophysiology, presence of chronic metabolic acidosis and effect of haemodialysis on glycaemic control and metabolic parameters. The purpose of this article is to review the current literature and provide recommendations for the diagnosis and treatment of DKA, euglycaemic DKA and HHS in people with advanced CKD.

Methods and Results: Guidance on the management of diabetes-related emergencies mainly focuses on individuals with preserved renal function or early-stage CKD. Existing literature is limited, and recommendations are based on expert opinions and case reports. Given the clinical need for amended guidelines for this population, we are proposing a management algorithm for DKA and HHS based on clinical and metabolic parameters.

Conclusions: In this review article, we propose treatment algorithms for diabetes-related hyperglycaemic emergencies in people with advanced CKD. Further research is needed to validate our proposed algorithms.

KEYWORDS

diabetes, emergencies, hyperosmolar hyperglycaemic state, ketoacidosis

1 | INTRODUCTION

Despite the advances in the management of diabetes mellitus (DM), chronic kidney disease (CKD) remains one of the major complications, with end-stage renal disease (ESRD) presenting in up to 31.3% of the cases.[1,2] Even though declining renal function is associated with impaired gluconeogenesis and lower insulin degradation, and thus reduced insulin requirements, people with advanced CKD can still present with diabetic ketoacidosis (DKA), euglycaemic DKA and very rarely with hyperosmolar hyperglycaemic state (HHS) with similar underlying precipitating factors.[3] The prevalence of DKA in people with ESRD was estimated at 3.74% in a retrospective study conducted in the USA.[4]

Current guidelines on the management of diabetes-related emergencies mainly focus on individuals with preserved renal function or early-stage CKD, while recommendations on advanced CKD rely on case reports and expert opinions.[3] However, the differences in clinical and biochemical parameters in this population potentially create the need for a different therapeutic approach to

ensure patient safety and optimal management. The purpose of this article is to review the current literature and provide recommendations for the diagnosis and treatment of DKA, euglycaemic DKA and HHS in people with CKD stage 4 and 5.

What's new?

- We propose customized treatment algorithms for DKA and HHS in people with advanced CKD.
- Careful assessment of volume status is key in the management of DKA in stage 4 or 5 CKD.
- In HHS, initial fluid resuscitation with frequent reassessment of volume status should be considered.

1.1 | DKA in advanced CKD

1.1.1 | Pathophysiology

DKA results from the reduced action of circulating insulin in the presence of increased counter-regulatory stress hormones such as glucagon, cortisol and norepinephrine. These changes lead to increased gluconeogenesis, glycogenolysis, reduced oxidation along with decreased uptake and use of glucose by the peripheral tissues and concomitant insulin resistance. Gluconeogenic substrates such as glycerol, lactate and gluconeogenic amino acids are elevated as a result of protein catabolism, muscle glycogenolysis and increased lipolysis (Figure 1).[5–7] Mild hyperglycaemia is noted in the early stages of DKA in people with preserved kidney function, but as hyperglycaemia worsens, osmotic diuresis leads to volume depletion and a reduction in glomerular filtration, which slows down glucose excretion. Trigger factors, such as infections, also precipitate DKA by enhancing hyperglycaemia through the release of counter-regulatory hormones and creating a pro-inflammatory state.[6]

Counter-regulatory hormones activate hormone-sensitive lipase in the adipose tissue, which promotes the production of non-esterified fatty acids (NEFA). With insulin being absent or not working, NEFA continue to be oxidized into ketone bodies in the liver. Furthermore, decreased renal clearance leads to their accumulation. Supply of extracellular and cellular buffers including bicarbonates becomes exhausted and is no longer able to compensate for the ketoacids resulting in a high anion gap metabolic acidosis. People with better preservation of renal function are able to excrete ketone bodies and therefore have greater ketonuria, with lower ketonaemia, anion gap and hypertonicity.[8]

The osmotic diuresis resulting from hyperglycaemia and high concentrations of ketone bodies leads to volume depletion, decreased glomerular filtration rate and promotes the net loss of electrolytes. Hypovolaemia leads to hypoperfusion, which in turn increases lactic acid levels aggravating acidaemia and further deterioration of high anion gap acidosis.[6]

Insulin drives potassium from the extracellular to the intracellular compartment and thus insulin deficiency initially results in hyperkalaemia.[3] In the presence of osmotic diuresis, potassium is excreted through the urine leading to reduced total body potassium despite the concurrent serum hyperkalaemia. This is further enhanced by plasma hypertonicity that drives intracellular water and potassium into the extracellular space.[3] As acidaemia progresses and bicarbonate is consumed, extracellular hydrogen ions from ketone bodies are exchanged for intracellular potassium ions in an effort to continue the buffering process. Moreover, the renin-angiotensin-aldosterone system (RAAS) is activated by hypovolaemia increasing aldosterone concentrations, leading to further potassium excretion. All the above mechanisms contribute to potassium loss, which is eventually reflected in reduced serum potassium.[6]

People in early CKD stages may present with similar pathophysiology; however, declining renal function negatively affects water excretion, and thus, osmotic diuresis and subsequent dehydration are not as prominent in individuals with impaired renal function and they are absent in those with anuria. However, polydipsia is still present due to the hypertonicity leading to increased water intake, which in turn results in increased interstitial and intravascular volume.[3] Furthermore, in the presence of impaired kidney function, increased extracellular potassium cannot be excreted leading to hyperkalaemia without a change in total body potassium. Chronic metabolic acidosis is common in advanced CKD due to decreased acid excretion and high daily endogenous and exogenous acid loads[9] (Table 1). Acidosis deteriorates rapidly in the presence of an underlying cause (Table 2). However, clinically distinguishing between DKA and acidosis of uraemia remains challenging, especially considering similar symptomatology.[3] Hence, ketone measurements are key.

1.1.2 | Diagnosis of DKA

People with normal renal function or CKD stages 1–3

DKA is confirmed when blood glucose concentration is ≥11.1 mmol/L or patient is known to have diabetes, capillary or blood ketone concentration ≥3.0 mmol/L or significant ketonuria (2+ or more on standard urine sticks)

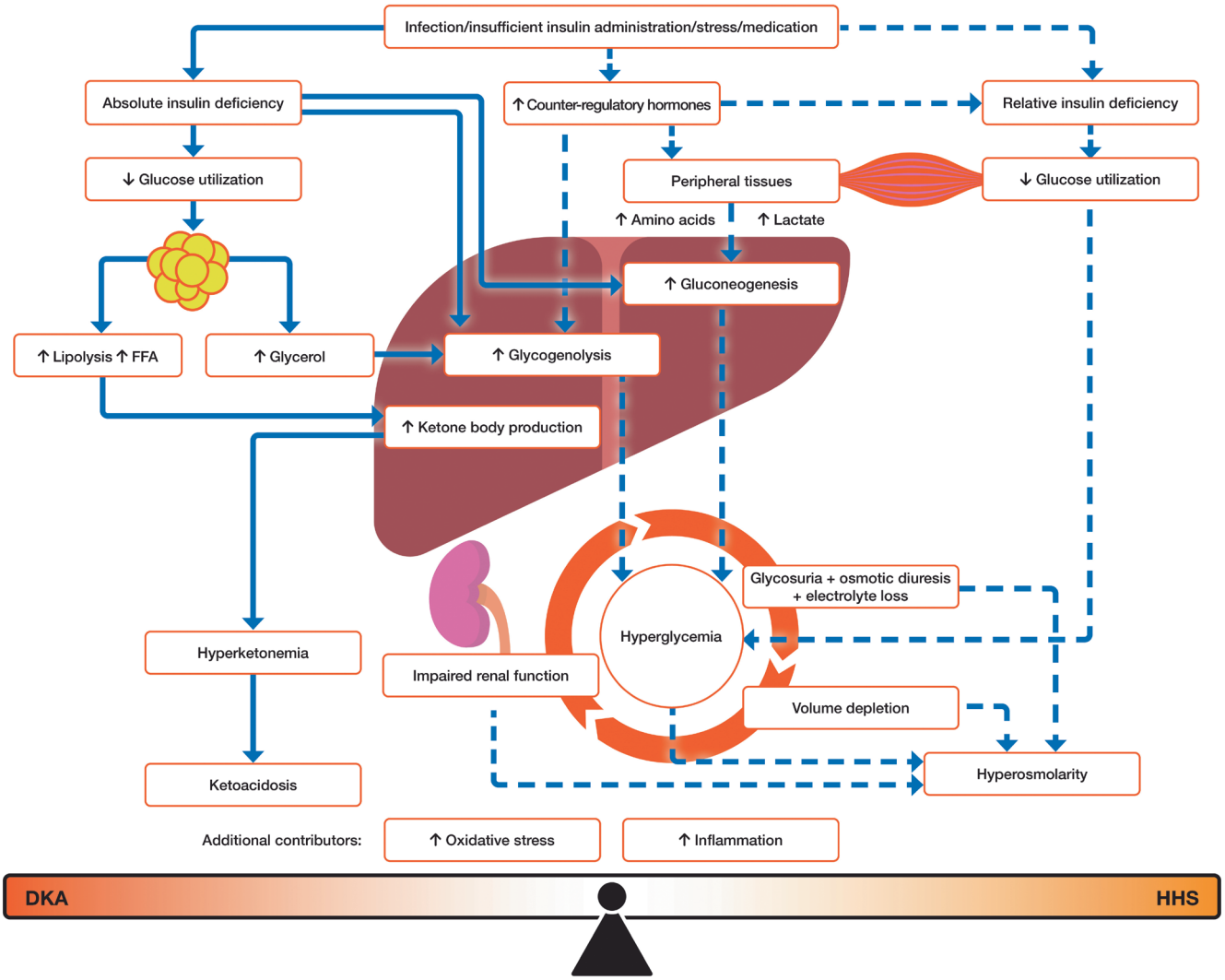

FIGURE 1 Pathogenesis of DKA and HHS (reproduced with permission).

TABLE 1 Pathophysiological changes in DKA depending on the degree of renal function.

	Normal renal function	CKD stages 1–3	CKD stages 4 and 5	ESRD
Insulin degradation	Normal	Normal	Decreased	Decreased
Ketone body formation	Mild to severe	Mild to severe	Moderate to severe	Moderate to severe
Ketonuria	Moderate to severe	Moderate to severe	Mild to moderate	Non-existent to mild depending on ability to form urine
Acidosis	Mild to severe	Mild to severe	Moderate to severe	Depends on timing of latest dialysis session
Hypertonicity	Mild to severe	Mild to severe	Moderate to severe	Depends on timing of latest dialysis session
Potassium (K^+) levels	Hyperkalaemia with total body K^+ deficit	Hyperkalaemia with total body K^+ deficit	Hyperkalaemia with normal total body K^+	Depends on timing of latest dialysis session

and bicarbonate concentration is ≤18.0 mmol/L and/or venous pH ≤7.3.[7,10] All three criteria must be present to establish diagnosis. In euglycaemic DKA, pH is ≤7.3 or serum bicarbonate <18 mmol/L, ketones are ≥3.0 mmol/L with either normal plasma glucose or a milder degree of hyperglycaemia (11–14 mmol/L).[7,11]

TABLE 2 Differential diagnosis of metabolic acidosis with raised anion gap.

Diabetic ketoacidosis
Starvation ketoacidosis
Alcoholic ketoacidosis
Ethanol/methanol overuse
Uraemia—chronic kidney failure
Lactic acidosis
Salicylates/paracetamol overdose
Carbon monoxide/cyanide poisoning

People with CKD stage 4 or 5

In people with advanced CKD, chronic metabolic acidosis can mask the diagnosis of DKA. Even though diagnostic criteria remain the same, it should be considered that other factors, such as renal impairment, lactic acidosis secondary to dehydration and use of metformin, can also lead to high anion gap metabolic acidosis. A markedly elevated anion gap (>20) however should raise suspicion and urge clinicians to check for blood ketones in particular serum β-hydroxybutyrate.[12] There are conflicting data on diagnostic ketone thresholds in patients with advanced CKD; significant metabolic differences have been observed in people with DKA at different levels of renal function. An observational study reported lower mean ß-hydroxybutyrate level, but higher glucose, anion gap and osmolality in ESRD compared to people with moderate renal failure or preserved renal function. However, the recommended diagnostic threshold remained a ß-hydroxybutyrate level of more than 3 mmol/L.[13]

Other findings include hyperkalaemia as well as hyponatraemia resulting from the osmotic shift of water from the intracellular to the extracellular space due to the underlying hyperglycaemia. The presence of hypo- or normo-kalaemia indicates severe total body potassium deficiency.[12,14]

Clinical manifestations may vary significantly depending on the stage of renal impairment. Volume status is typically reduced in people with adequate diuresis and is additionally affected by extra renal losses such as vomiting and diarrhoea. In people with reduced diuresis or anuria on the other hand, volume status may be expanded and present with signs of fluid overload such as shortness of breath, raised jugular venous pressure, peripheral oedema, hypertension and pulmonary oedema.[3]

People on dialysis

For those on dialysis, it is important to note that dialysis solutions often contain glucose to prevent hypoglycaemia during the sessions, but the concentration of glucose in the dialysate is lower than the plasma resulting in a net negative glucose balance and lower glucose post-dialysis. Hyperkalaemia and acidosis are also corrected with dialysis; however, ketogenesis is likely to continue in view of insufficient insulin. Therefore, the timing of the latest dialysis session, the amount of fluid removed, the presence of vomiting, diarrhoea or excessive insensible losses affect the above parameters making the diagnosis more challenging. Overall, dialysis will improve hyperglycaemia (a 36% decrease in blood glucose 2 h after dialysis has been reported) and metabolic acidosis.[15] For this reason, some authors suggest checking capillary ketone and lactate levels in all people with ESRD and metabolic acidosis.[16] It is worth noting that dialysis improves insulin sensitivity and clearance; therefore, more conservative insulin rates should be considered for the management of DKA in this group.[17]

Recommendations:

1. When a person with advanced CKD presents with nausea, vomiting and/or abdominal pain, symptoms should not be attributed to uraemia alone without excluding other causes.
2. Assess volume status: fluid overload can be manifested with shortness of breath, pulmonary oedema and/or hypertension. For those on dialysis, comparison of post-dialysis weight and weight at presentation can assist with diagnosis and management.
3. Blood ketone and lactate levels should be included in the investigations when people with advanced CKD present with high anion gap metabolic acidosis.
4. Dialysis might improve serum glucose levels, hyperkalaemia and acidosis, but ketogenesis can continue to deteriorate so a lower threshold for ketone testing is recommended for this special population.

1.1.3 | Management of DKA

Management priorities in DKA vary depending on the stage of the kidney disease, and this is linked to fluid status and insulin requirements. Joint British Diabetes Societies for Inpatient Care group (JBDS-IP) and International consensus on the management of diabetic emergencies recommend starting with a fixed rate intravenous insulin infusion rate of 0.1 unit/kg/h.[7,10] Since insulin requirements are lower in ESRD, an initial lower dose at a rate of 0.05 units/kg/h is suggested.[18] Blood glucose and ketones should be monitored hourly. The insulin infusion rate is adjusted by assessing response to treatment with plasma ketones (aiming for an hourly reduction of 0.5 mmol/L), blood glucose (hourly reduction of 3–5 mmol/L) and serum bicarbonate (hourly increase by 3 mmol/L). Since a degree of hypertonicity often co-exists in people with ESRD, it should be noted that the reduction of effective osmolality, as calculated by $(2\times Na^{+})+$blood glucose, should not exceed 8 mOsm/kg/h to minimize the risk of cerebral osmotic demyelination.

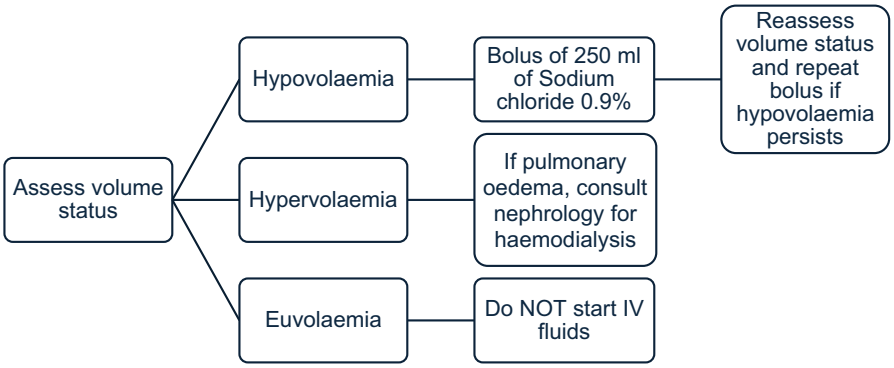

FIGURE 2 Management of fluids in DKA and advanced CKD.

If the initial assessment reveals increased volume status, intravenous fluids are not required unless there is hypotension or other signs of volume depletion. If volume overload is noted, an insulin infusion on its own, without accompanying fluids may suffice except for significant fluid overload presenting with pulmonary oedema, when dialysis will be required.[3] This decision however should be made carefully in conjunction with the renal team; hyperglycaemia and increased osmolality of the extracellular compartment can lead to a massive fluid shift from the intracellular compartment to the vascular compartment, which can be corrected with insulin alone, whereas concomitant dialysis and insulin administration may lead to intravascular volume depletion and hypotension during dialysis.[19] Occasionally, accurate estimation of volume status is challenging, and in this case, central pressure monitoring could be considered.

If there is evidence of volume depletion (vomiting, diarrhoea, excessive insensible losses, dry mucous membranes, reduced skin turgor, hypotension, weight at or below their post-dialysis weight), careful administration of boluses of 250 mL of sodium chloride 0.9% with frequent monitoring of clinical and laboratory parameters is recommended. In people on dialysis, pre-dialysis weight should be targeted.[3,14]

Serum electrolytes should be monitored closely, and potassium supplementation should be restricted to those with hypokalaemia. Serum potassium concentration is usually elevated as described above. Hyperkalaemia is usually more severe in people on dialysis compared to those not on dialysis for the same level of hyperglycaemia.[20] In either case, it is expected to improve with administration of intravenous insulin. Continuous cardiac monitoring is advised when potassium is above 5.5 mmol/L. Correction with 40 mmol/L of potassium chloride is recommended when serum potassium is below 3.5 mmol/L.[12]

Emergency haemodialysis should be considered in extreme hyperglycaemia, significant hypertonicity with often co-existent severe hyponatraemia, severe metabolic acidosis in people with anuria and persistent hyperkalaemia that does not respond to insulin administration. Attention should be given to avoid rapid correction of blood glucose levels and plasma osmolality as a sudden decrease can lead to cerebral oedema.[19] Bicarbonate supplements are often used in clinical practice when serum bicarbonate levels are less than 22 mmol/L and reversible causes have been excluded.[21] Increased risk of cerebral oedema and prolonged admission with the administration of intravenous bicarbonate in DKA have been reported in children, which, along with the lack of evidence for their effectiveness, have led to limited use in severe metabolic acidosis (pH <6.9).[22] However, considering bicarbonate regeneration is insufficient in advanced CKD, their use can be considered when pH <7.2.

Recommendations (Class IIa): Proposed algorithm for managing DKA in advanced CKD[10,23]:

Assessment and diagnosis

- ABCDE approach
- Evaluate the clinical condition, including vital signs, mental status and laboratory findings (blood glucose, electrolytes, renal function, blood ketones, pH)
- Confirm the diagnosis of DKA based on the presence of hyperglycaemia (blood glucose >11 mmol/L), ketonaemia (≥3 mmol/L) and metabolic acidosis (pH ≤7.3, bicarbonate ≤18 mmol/L)
- Additional investigations: Blood cultures, ECG, CXR, midstream urine test (MSU), dialysis line/peritoneal dialysis catheter infection/sepsis. Pregnancy test is recommended in women of childbearing age

Identify underlying causes

Determine the precipitating factors leading to DKA, such as infection, non-adherence with insulin therapy or other stressors and treat accordingly

Initial management

- Administer oxygen therapy if the individual is hypoxic (sat O_2 < 92%)
- Establish intravenous access. If intravenous access cannot be obtained request critical care support immediately
- Assess volume status
    - If hypovolaemia, give a bolus of sodium chloride 0.9% (250 mL) bolus and reassess
    - In euvolaemia, do not start IV fluids

- Hypervolaemia, do not start IV fluids and if severe fluid overload, urgent renal consultation is recommended for consideration of dialysis (Figure 2)

- Involve the critical care team

Insulin therapy

- Commence a fixed rate intravenous insulin infusion (FRIII) at 0.1 unit/kg/h. 50 units short acting insulin (e.g. Actrapid® or Humulin S®) made up to 50 mL with 0.9% sodium chloride solution. If patient normally takes long-acting insulin analogue (such as glargine, detemir and degludec), continue at usual dose
- In people with ESRD, start with a lower insulin infusion rate (e.g. 0.05 units/kg/h) and adjust based on blood glucose levels to achieve a gradual reduction (target: 3–5 mmol/L decrease in blood glucose per hour)

Initial monitoring

- Hourly capillary blood glucose
- Hourly capillary ketone measurement
- Venous bicarbonate, pH and potassium at 60 min, 2 h and every 2 h thereafter
- 4 h plasma electrolytes

Electrolyte management

- Do not replace potassium unless serum potassium is below 3.5 mmol/L
- Hyperkalaemia is common and is expected to improve with insulin administration
- Continuous cardiac monitoring is advised when potassium is above 5.5 mmol/L
- If potassium >6.5 mmol/L, coordinate with nephrology for appropriate renal replacement therapy

Bicarbonate therapy

- As bicarbonate regeneration is insufficient in advanced CKD, bicarbonate supplementation can be considered when pH <7.2
- Renal consultation is advisable in severe metabolic acidosis (pH <7.2)

Reassess response to treatment

- Insulin infusion rate may need to be adjusted if capillary ketones are not falling by at least 0.5 mmol/L/h, venous bicarbonate is not rising by at least 3 mmol/L/h or plasma glucose not falling by at least 3 mmol/L/h
- Continue FRIII until ketones less than 0.6 mmol/L, venous pH >7.3 and/or venous bicarbonate over 18 mmol/L
- If ketones and glucose are not falling as expected, check if the insulin infusion pump is working
- If insulin infusion is working but response to treatment is inadequate, increase insulin infusion rate by 0.5–1 unit/h increments hourly until targets achieved
- *Consider halving the rate of intravenous insulin infusion when blood glucose ≤ 14 mmol/L*

Resolution of DKA

- Resolution of DKA is defined as ketones <0.6 mmol/L and venous pH >7.3
- If DKA is not resolved, review insulin infusion
- If ketonaemia has cleared and patient is not eating or drinking, move to a variable rate intravenous insulin infusion (VRIII) as per JBDS-IP or local guidelines
- If patient is eating and drinking normally and DKA has resolved, start subcutaneous insulin

1.2 | Euglycaemic DKA in advanced CKD

Euglycaemic DKA typically occurs in the setting of relative or absolute insulin deficiency, leading to increased lipolysis, ketogenesis and subsequent ketone body accumulation. The hallmark hyperglycaemia seen in classical DKA may be absent or minimal in euglycaemic DKA. The clinical presentation however is similar to classical DKA and may include symptoms such as nausea, vomiting, abdominal pain and altered mental status.[24] The majority of those affected have type 2 diabetes are treated with SGLT-2 inhibitors and have an evident trigger factor such as an infection, major surgery, dehydration, reduced oral intake or prolonged fasting.

Despite their efficacy and cardiovascular benefits, SGLT-2 inhibitors have been associated with an increased risk of euglycaemic DKA, potentially due to glycosuria leading to decreased plasma glucose levels and decreased insulin release. Decreased insulin levels in conjunction with increased glucagon promote lipolysis and ketogenesis.[25] Management of euglycaemic DKA is identical to classic DKA; however, since initial blood glucose is below 14 mmol/L, glucose 10% infusion should be started immediately alongside the FRIII.[10]

Euglycaemic ketosis can also present during continuous renal replacement (CRRT) with glucose free solutions and low caloric intake. During CRRT, glucose is removed from the blood (from 30 to 160 g per day depending on glycaemia and hemofiltration rate) and glycogen stores are depleted within 2–3 days when glucose free solutions are used.[26] This leads to elevation of glucagon and increased gluconeogenesis and ketogenesis, resulting in euglycaemic ketoacidosis. It can present even in the absence of diabetes.[27] A high anion gap metabolic acidosis with improving lactate levels in people on CRRT should raise suspicion and prompt ketone testing. Ketosis is managed by raising the daily caloric intake (some authors suggest 25 kcal/kg/day) with a supplemental dextrose infusion along with insulin administration. Glucose-containing CRRT solutions should also be considered.[26,27]

1.3 | HHS in advanced CKD

1.3.1 | Diagnosis of HHS

HHS is a serious and potentially life-threatening condition characterized by extremely high blood glucose levels and severe dehydration. It is most commonly seen in people with type 2 diabetes. Residual insulin production is present, but not adequate to counteract insulin resistance; therefore, glucose cannot be sufficiently used by peripheral tissues, which in turn leads to the release of counter-regulatory hormones such as

glucagon, growth hormone and cortisol, that promote gluconeogenesis and glycogenolysis. These further exacerbate hyperglycaemia given that glucose is not utilized by peripheral tissues. Serum osmolality increases significantly, and free water and electrolytes are excreted in the urine leading to moderate or severe dehydration (Figure 1).[7,28] Contrary to DKA, ketone body formation is minimal due to residual insulin secretion suppressing ketogenesis. HHS is rare in people with advanced CKD, who do not tend to develop significant diuresis, but a mixed HHS/DKA picture can be seen considering that glucose accumulates in the extracellular space leading to increased effective osmolality and significant hyperglycaemia[29] (Table 3).

Diagnostic criteria include hypovolaemia, raised plasma osmolality (>320 mOsm/kg), marked hyperglycaemia (>30.0 mmol/L) without significant ketonaemia (<3.0 mmol/L) or acidosis (pH >7.3) and bicarbonate (>15.0 mmol/L). In mixed HHS/DKA, pH is below 7.3, bicarbonate is less than 15 mmol/L and ketone more than 3 mmol/L.[30] Since urea is often raised in advanced in CKD, effective osmolality is more useful for both diagnosis and assessing response to treatment.

1.3.2 | Management of HHS

Mixed DKA/HHS should be managed as DKA. There are no evidence-based recommendations on the management of HHS in people with advanced CKD. Aggressive fluid resuscitation with 30 mL/kg crystalloid fluid is recommended for people on dialysis on other occasions such as hypotension in the context of sepsis with data from retrospective studies supporting its safety.[31,32] Since people with HHS are usually significantly dehydrated, a similar initial approach with frequent assessment of fluid responsiveness and volume status could be considered.

Recommendations (class IIb): Proposed algorithm for managing HHS in advanced CKD[30]:

Assessment and diagnosis

- ABCDE approach
- Evaluate the clinical condition, including vital signs, mental status and laboratory findings (blood glucose, electrolytes, renal function, blood ketones, pH)
- Confirm the diagnosis of HHS on the basis of hypovolaemia, raised plasma osmolality (>320 mOsm/kg), marked hyperglycaemia (>30.0 mmol/L) without significant hyperketonaemia (<3.0 mmol/L) or acidosis (pH >7.3) and bicarbonate (>15.0 mmol/L)
- Additional investigations: Blood cultures, ECG, CXR, MSU, dialysis line/peritoneal dialysis catheter infection/sepsis. Pregnancy test is recommended in women of childbearing age

TABLE 3 Expected pathophysiological changes in HHS depending on the degree of renal function.

	Normal renal function	CKD stages 1–3	CKD stages 4 and 5	ESRD
Hypovolaemia	Severe	Severe	Moderate to severe	If residual urine production, moderate to severe
Urine output	Significantly increased	Significantly increased	Variable	Variable
Osmolality	Moderately to significantly increased	Moderately to significantly increased	Significantly increased	Significantly increased
Effective osmolality	Moderately to significantly increased	Moderately to significantly increased	Moderately to significantly increased	Moderately to significantly increased
Hyperglycaemia	Severe	Severe	Severe	Severe

Identify underlying causes

Determine the precipitating factors leading to HHS, such as infection, non-adherence with insulin therapy or other stressors and treat accordingly

Initial management

- Administer oxygen therapy if the individual is hypoxic (sat $O_2 < 92\%$)
- Establish intravenous access. If intravenous access cannot be obtained, request critical care support immediately
- Administer 1 L isotonic saline (0.9% NaCl) over 1 h for volume expansion and correction of dehydration. Consider a slower rate in people with congestive heart failure
- Monitor fluid balance hourly
- Involve the critical care team
- If severe hypertonicity (>350 mOsm/kg), urgent renal consultation is recommended

Electrolyte management

- Hypo-and hyper-kalaemia are not as common in HHS
- Do not replace potassium unless serum potassium is below 3.5 mmol/L
- Continuous cardiac monitoring is advised when potassium is above 5.5 mmol/L
- If potassium >6.5 mmol/L, coordinate with nephrology for appropriate renal replacement therapy

Reassess response to treatment:

- Hourly blood glucose, Na^+, K^+, urea and effective osmolality for the first 6 h, then 2 h
- Aim for an hourly osmolality drop of 3.0–8.0 mOsm/kg
- Assess volume status every 30–60 min and consider an infusion rate of 20–25 mL/kg/h for IV fluids as recommended by NICE.[33]
- If plasma Na^+ is increasing but osmolality is declining at appropriate rate, continue 0.9% sodium chloride
- If plasma Na^+ is increasing and osmolality increasing or declining at a slower than recommended rate, check fluid balance. If positive balance is inadequate, then increase the rate of infusion of 0.9% sodium chloride solution. If the osmolality is increasing and fluid balance adequate, then consider switching to 0.45% sodium chloride at same infusion rate
- If osmolality falls at rate >8.0 mOsm/kg/h, consider reducing infusion rate of fluids
- If glucose is dropping less than 5.0 mmol/L per hour, check fluid balance. If positive balance is inadequate, increase rate of 0.9% sodium chloride. If fluid replacement is adequate and glucose is not falling, start an IV insulin FRIII at 0.05 units/kg/h. In people with ESRD, start with a lower insulin infusion rate at 0.02 units/kg/h

Resolution of HHS

- Measured or calculated serum osmolality falls to less than 320 mosm/kg.
- Renal function has returned to baseline
- Hyperglycaemia has been corrected (<13.9 mmol/L)
- Cognitive status has improved

2 | CONCLUSIONS

Taking into account the altered pathophysiology and clinical manifestations of diabetic emergencies in people with stage 4 and 5 CKD and ESRD on dialysis, an amended treatment approach is needed. In this review article, we propose customized algorithms for DKA, euDKA and HHS in advanced CKD. Even though further research is needed to validate the above recommendations, we believe the proposed guidance could consist of a useful tool in decision-making when managing diabetic emergencies in this challenging population.

FUNDING INFORMATION

This article was not supported by any funder.

CONFLICT OF INTEREST STATEMENT

There is no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analysed in this study.

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How to cite this article: Stathi D, Dhatariya KK, Mustafa OG. Management of diabetes-related hyperglycaemic emergencies in advanced chronic kidney disease: Review of the literature and recommendations. *Diabet Med*. 2025;42:e15405. doi:10.1111/dme.15405