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Review

Challenges in management of diabetic ketoacidosis in hemodialysis patients, case presentation and review of literature

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ABSTRACT

Chronic kidney disease is associated with accumulation of uremic toxins that increases insulin resistance which will lead to blunted ability to suppress hepatic gluconeogenesis and reduce peripheral utilization of insulin. CKD patients fail to increase insulin secretion in response to insulin resistance because of acidosis, 1,25 vitamin D deficiency, and secondary hyperparathyroidism. Hemodialysis causes further fluctuations in glycemic control due to alterations in insulin secretion, clearance and resistance. DKA is uncommon in hemodialysis patients because of the absence of glycosuria and osmotic diuresis which accounts for most of the fluid and electrolyte losses seen in DKA, anuric patients may be somewhat protected from dehydration and shock, although still subject to hyperkalemia and metabolic acidosis. However, substantial volume loss can still occur due to a prolonged decrease in oral intake or increased insensible water losses related to tachypnoea and fever. There is no current guidelines for the management of diabetic ketoacidosis in anuric hemodialysis patients considering their differences than general population. In this review article we reviewed the literature and came with specific recommendations for management of Ketoacidosis in patients with CKD treated by hemodialysis.

1. Background

Diabetes is leading cause of end-stage renal failure (ESRF) in developed countries accounting for 40% of new ESRF cases in the USA and 25% of incident cases in the UK. The mortality rates for dialysis patients are high [1], with 10% first-year mortality rate for patients on maintenance hemodialysis (HD) reported in UK [2]. These patients are at a particularly high-risk and the overall survival for patients with diabetes on maintenance HD is reported to be approximately halved compared to their non-diabetic peers (3.7 vs. 7 years) [2]. In adult subjects with DKA (Diabetic Ketoacidosis), the overall mortality is <1%; however, a mortality rate >5% has been reported in the elderly and in patients with concomitant life-threatening illnesses [3–5]. In such situations, death is rarely due to the metabolic complications of hyperglycaemia or ketoacidosis, but it is a consequence of the underlying precipitating illness [6,7].

Acute complications of diabetes such as Diabetic Ketoacidosis (DKA) can be encountered in ESRF. DKA in ESRF presents a diagnostic and therapeutic challenge as illustrated by the five cases described in Supplement 1. The Japanese Society for Dialysis Therapy has also published a series of 14 case reports which describe the varying clinical presentation of DKA in ESRF [8] (Table 1). The purpose of this paper is to provide recommendations for the diagnosis and treatment of DKA in ESRF with particular focus on areas where management differs from patients with preserved renal function.

2. Metabolic alterations

In DKA, the effective insulin concentration is decreased while the concentration of counter-regulatory hormones (catecholamines, cortisol, glucagon and growth hormone) is increased resulting in hyperglycemia and ketosis. Hyperglycemia occurs due

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Table 1
Case Reports published by The Japanese Soceity for Dialysis Therapy (Adapted from Ref. [8]).

No.	Age (yrs)	Gender	Type of DM	Blood Glucose level (mg/dl)	Arterial Blood pH	Serum K^+ level (mEq/L)
1	46	M	1	1467	7.09	6.6
2	63	F	1	1270	6.97	–
3	32	F	1	1912	6.76	7.2
4	65	F	–	609	7.15	–
5	36	F	–	–	–	–
6	65	M	–	–	–	–
7	71	F	2	1645	–	8.6
8	40s	M	1	1365	7.10	8.5
9	35	M	1	1686	6.54	–
10	46	M	1	1520	7.10	7.5
11	58	M	1	1363	6.84	9.6
12	45	M	1	1360	–	–
13	62	M	2	838	7.09	8.3
14	58	M	–	1001	6.81	–
Mean		52		1336	6.54	8.0
SD		13		369	0.20	1.0

SD – Standard Deviation, M – Male, F – Female, DM – Diabetes Mellitus.

to increased gluconeogenesis, accelerated glycogenolysis, and impaired glucose utilization by peripheral tissues [9–12]. This is accompanied by transient insulin resistance. Insulin deficiency combined with elevated counterregulatory hormones in DKA leads to the release of free fatty acids into the circulation from adipose tissue (lipolysis) resulting in unrestrained hepatic fatty acid oxidation in the liver to ketone bodies (β-hydroxybutyrate and acetoacetate) [13], leading to ketonemia and metabolic acidosis.

In a state of preserved renal function, hyperglycemia-induced osmotic diuresis can result in clinically significant extracellular volume deficits, dehydration and sodium depletion. The estimated fluid loss is nearly 6–10L with raised serum osmolality of 320–340mOsmol/L [14]. Hyperglycemia leads to a hypertonic state in patients with preserved renal function as well as in patients on dialysis. In dialysis patients, diuresis is absent or minimal. However, the accumulation of glucose in the extracellular space (EC) during development of hyperglycemia causes both hypertonicity and shifts of intracellular fluid into the EC resulting in what is called dialysis associated hyperglycemia (DH). In Dialysis associated hyperglycemia (DH) and DKA or Hyperosmolar Hyperglycemic State (HHS) there is extracellular volume expansion resulting in edematous patients having greater hypertonicity and extracellular hypervolemia than euvolemic or hypovolemic subjects with the same degree of hyperglycemia [15,16].

It is important to distinguish between tonicity and osmolality to understand the hyperglycemic changes in body fluids and solutes. Osmolality and tonicity are related but not synonymous. Serum osmolality is the sum of all solutes in the serum (intracellular and extracellular), while tonicity (or effective osmolality) is the part of total osmolality contributed by extracellular solutes having difficulty crossing cell membranes, therefore resulting in steady-state fluid shifts between extracellular compartment and intracellular compartment [15,16]. A high urea concentration is usually encountered in these situations, but it does not contribute to tonicity.

The parameter of interest in DH patients and its management is tonicity because it is the source of changes in cell volume and can cause neurological manifestations in hyperglycemia [17]. Tonicity or effective plasma osmolality (Posm in mosmol/kg) can be estimated from either of the following equations:

$$\text{Effective Posm} = [2 \times \text{Na (meq/L)}] + [\text{glucose (mg/dL)} \div 18], \textbf{or}$$

$$\text{Effective Posm} = \text{Measured Posm} - [\text{BUN (mg/dL)} \div 28]$$

[where Na is the serum sodium concentration, the multiple 2 accounts for the osmotic contribution of the anions accompanying sodium (primarily chloride and bicarbonate), and 18 and 28 are conversion factors from units of mg/dL into mmol/L respectively [16–18]].

Interestingly, reports of DH and DKA are more frequently seen with patients on hemodialysis (HD) as compared to peritoneal dialysis (PD) [19–21]. No difference in serum sodium concentration or tonicity was found between the two dialysis modalities for a comparable degree of hyperglycemia.

The solute and fluid disturbances seen in patients with DH is different from the changes caused by hyperglycemia in patients with preserved renal function as it is not complicated by osmotic diuresis. The presence of hyperglycemia should lead to the development of a hypertonic state in patients on dialysis and in those with preserved renal function. However, DH results in extracellular volume expansion while severe hyperglycemia in preserved renal function causes a clinically significant extracellular volume deficit. In DH baseline extracellular volume is theoretically an important determinant of the degree of hypertonicity and extracellular volume expansion in edematous patients is expected to result in greater hypertonicity and greater extracellular hypervolemia compared to euvolemic or hypovolemic subjects with the same degree of hyperglycemia.

3. Diagnosis

Recommendation 1: DKA in patients with ESRD on HD is a rare clinical presentation and difficult to diagnose. Since ESRD is a state of persistent chronic metabolic acidosis, DKA should be suspected in patients with diabetes (specially type 1) who are unwell with an acidosis that is greater than would normally be (persistent). In such case measurement of Serum β-hydroxybutyrate is a useful tool in establishing diagnosis of DKA in patients with ESRD on HD.

Diagnostic criteria for DKA include presence of blood glucose >250 mg/dl, arterial pH of ≤7.30, bicarbonate level of ≤18 mEq/L, and adjusted for albumin anion gap of >10–12 [22]. There is also an increase in the blood ketone concentration. The accumulation of ketoacids is culpable for the raised anion gap metabolic acidosis. In patients with CKD stage 4–5, the diagnosis of DKA can be challenging due to the presence of concomitant underlying chronic metabolic acidosis or mixed acid-base disorders. Anion gap of >20 usually supports the diagnosis of DKA in these patients [23]. Assessment of augmented ketonemia is usually performed by the nitroprusside reaction, which provides a semi-quantitative

estimation of acetoacetate and acetone levels. Although the nitroprusside test (both in urine and in serum) is highly sensitive, it can underestimate the severity of ketoacidosis because this assay does not recognize the presence of β-hydroxybutyrate, the main metabolic product in ketoacidosis [6,9]. If available, serum β-hydroxybutyrate should be measured to establish diagnosis [24].

On admission, leucocytosis with cell counts in the 10,000–15,000 mm^3 range may be present and is not necessarily indicative of an infectious process. In ketoacidosis, leucocytosis is attributed to stress and maybe correlated to elevated levels of cortisol and norepinephrine [25]. However, leucocytosis with cell counts >25,000 mm^3 may designate infection and require further evaluation [26].

Serum sodium is usually low because of the osmotic flux of water from the intracellular to the extracellular space in the presence of hyperglycemia. An increased or even normal serum sodium concentration in the presence of hyperglycemia indicates a profound degree of free water loss. To assess the severity of sodium and water deficit, serum sodium may be corrected by adding 1.6 mg/dl to the measured serum sodium for each 100 mg/dl of glucose above 100 mg/dl [6,9].

Studies on serum osmolality and mental alteration have established a positive linear relationship between osmolality and mental obtundation [27,28]. The occurrence of stupor or coma in a diabetic patient in the absence of definitive elevation of effective osmolality (≥320 mOsm/kg) demands immediate consideration of other causes of mental status change. In the calculation of effective osmolality, [sodium ion (mEq/l) × 2 + glucose (mg/dl)/18], the urea concentration is not considered because it is freely permeable, and its accumulation does not induce major changes in intracellular volume or osmotic gradient across the cell membrane [6].

Serum potassium concentration may be elevated because of an extracellular shift of potassium caused by insulin deficiency, hypertonicity, and acidemia [29]. Patients with low normal or low serum potassium concentration on admission have severe total-body potassium deficiency and require careful cardiac monitoring. However, patients with ESRD can have hyperkalaemia at presentation. Serum phosphate concentration at the time of admission, like serum potassium, is usually elevated and does not reflect an actual body deficit that uniformly exists due to shifts of intracellular phosphate to the extracellular space [9,30,31]. Insulin deficiency, hypertonicity, and increased catabolism all contribute to the movement of phosphate out of cells.

4. Principles of management

4.1. Hyperosmolar state

Recommendation 2: Gradual correction of the hyperosmolar state is important to avoid fatal complications such as cerebral edema and pontine myelinolysis. Anuric patients with DKA rarely present with dehydration and shock due to hyperglycemia-induced osmotic diuresis. Majority of the patients have hypertonicity with low serum sodium concentration at presentation. These patients improve with insulin infusion. Close monitoring of volume status, serum glucose and electrolytes is required. The recommended target rate for reduction in serum glucose is 50–75 mg⁄dl⁄hr during treatment. Emergency hemodialysis should be recommended with caution in patients with extreme hyperglycemia, hypertonicity and low serum sodium concentration as change in tonicity may be quite rapid.

Approach to the management of the hyperosmolar state in patients on dialysis is the same as in patients with preserved renal function. Inaccurate fluid resuscitation can cause an elevation in serum sodium concentration, thereby increasing the plasma osmolality, which can lead to pontine myelinolysis [32]. Conversely, a sudden drop in serum sodium can result in cerebral edema. The highest risk for cerebral edema is during the first 8–12 h. To avoid fatal complications such as pontine myelinolysis and cerebral edema, it is important to gradually correct hyperglycemia and serum osmolality using isotonic or hypotonic saline, as indicated, based upon the serum sodium levels and hemodynamic status [33]. Patients on maintenance HD are less likely to be volume depleted and, in most cases, the extracellular volume would be expected to expand compared to baseline.

There are three possible combinations of tonicity and serum sodium concentration in DH. First, increased tonicity with high or normal serum sodium. This is commonly seen in HHS, but not in DH. It reflects a large water deficit and highlights the need for water administration. Katz's formula Δ[Na]/Δ[Glu] can be used to estimate serum sodium concentration after correction of hyperglycemia. Total water deficit can then be calculated from the difference between this estimate and the desired (normal) serum sodium concentration, and from an estimate of total body water based on body weight [34]. Careful hydration is mandatory to avoid fluid overload. In most patients a bolus of 250–500 mL will suffice, which should be administered carefully with clinical evaluation of volume status after each bolus [15]. Second, tonicity at presentation is normal or low and serum sodium concentration is low. This is also an unusual combination and indicates relative water excess, which can be managed with dialysis during or after correction of hyperglycemia with insulin. Third, tonicity at presentation is high and serum sodium concentration is low. This is commonly seen in DH. Water deficit or excess is small in this case and does not require special treatment apart from insulin therapy alone [16].

Dehydration and shock due to hyperglycemia-induced osmotic diuresis are unlikely at presentation in anuric patients with DKA. Therefore, management of hyperglycemia is simpler in comparison to patients with preserved renal function. The only treatment needed in majority of the patients is insulin infusion with close monitoring of volume status, serum glucose and electrolytes. Insulin infusion alone can correct hypertonicity [16]. The preferred rate of decline in serum glucose during treatment is 100–125 mg⁄dl ⁄hr. To avoid fatal neurologic complications from rapid changes in brain cell volume, current guidelines suggest that the decline in serum tonicity during treatment of severe hyperglycemia should not exceed 3 mOsm⁄kg⁄hour [35].

Emergency hemodialysis in a patient with hyperglycemia and low serum sodium concentration can cause diffusion of glucose from blood into the dialysate and diffusion of sodium from the dialysate into the blood. The rate of change in serum tonicity depends on the transfer coefficients and the concentration gradients for glucose and sodium across the dialysis membrane. In patients with extreme hyperglycemia, the change in tonicity may be quite rapid during dialysis. In one study the rate of decline of tonicity was reported as 14.5 mOsm/kg/hr [19], almost five times higher than the rate of change in tonicity that is considered safe [35]. A safe approach would be to avoid rapid changes.

Development of depressed level of consciousness is an important indicator of cerebral edema. A CT Brain scan should be obtained immediately to rule out other causes of coma. Thereafter, osmotherapy with hypertonic saline 3–5 ml/kg, even in case of hypernatremia, should be given. In case of non-availability of hypertonic saline, Mannitol 20% can be used at 0.5–2.5 ml/kg. A rapid response can be expected within 10–15 min of administering hypertonic saline. In case of a positive response, the dose of hypertonic saline can be repeated 2–3 times as required. However, if there is no response to osmotherapy, then intubation and mechanical ventilation should be considered with target pCO_2 of 4-4.5Kpa to avoid further cerebral ischemia from hypocapneic

vasoconstriction.

4.2. Fluid management

Recommendation 3: In patients with DKA and ESRD on HD, fluid resuscitation with boluses of 250–500 ml should be used guided by continuous re-evaluation of volume status.

The most important initial step in management is fluid replacement followed by insulin administration with the goals of treatment being correction of hypotension, clearance of ketones and correction of electrolyte imbalances. In DKA, patients are expected to have a total body water deficit of approximately 5–8L, correction of which results in significant metabolic improvement. Fluid resuscitation with isotonic saline (0.9% NaCl) at 15–20 ml/kg/h for the first hour is recommended for all patients. Fluid replacement should be guided by volume, cardiac and renal status.

In patients with hypovolemic shock, infusion of 0.9% NaCl should be continued and the addition of a plasma expander should be considered. When hypovolemia is mild (i.e., BP is stable and urine output is adequate) fluid should be selected based on the serum sodium concentration. Low serum sodium requires 0.9% NaCl at a rate of 4–14 mL/kg/hr. If serum sodium levels are normal to high, changing to a lower salt content solution, such as 0.45% NaCl at 4–14 mL/kg/hr is recommended. The aim is to correct the total body water deficit in the first 24 h. This is crucial as rehydration will lower plasma glucose and osmolality. When blood glucose falls to below 250 mg/dl, 5% dextrose should be added to the NaCl infusion to prevent iatrogenic hypoglycemia. Dextrose supplementation to maintain blood glucose concentration between 150 and 250 mg/dl should continue as long as insulin infusion is required to treat acidosis. To avoid complications of rapid fluid shifts, the change in osmolality should be no greater than 3 mOsm/kg of free water per hour, and sodium changes should not exceed 1 mmol/h [36].

In case of ESRD careful rehydration is required. If fluid overload occurs, it should be managed with immediate hemodialysis. It is important to be aware of cardiac function and oxygen requirement in these patients, and the treating physician must have a high index of suspicion for MI in these patients. Dialysis dependent patients in DKA may not be volume depleted. It is important to replace fluid through small boluses of 250–500 ml guided by continuous re-evaluation with repeat boluses based on hemodynamic status. Intravenous fluid drips should be avoided in anuric patients unless indicated.

4.3. Insulin therapy

Recommendation 4: Insulin therapy is the mainstay of treatment in patients with DKA and ESRD on HD.

Insulin therapy is the mainstay of DKA management as it suppresses ketone body synthesis, reduces blood glucose and corrects electrolyte imbalances, particularly hyperkalemia. It has been established that insulin is an effective therapy regardless of the route of administration, however insulin infusion is preferred to subcutaneous administration as it has a shorter half-life and can be easily titrated [28,31,37]. Kitabchi et al. demonstrated that bolus doses of insulin are not necessary if the patient has received insulin through infusion at 0.14 units/kg/hr. However, insulin infusion at <0.1unit/kg/hr without a bolus dose would result in subtherapeutic levels of insulin and might not suppress ketogenesis [38].

Hence, as per the most recent recommendation from the Joint British Diabetes Societies, insulin infusion should be started at 0.1unit/kg/hr without a bolus dose provided the infusion is started immediately [39]. Patients with ESRD are considered a high-risk group requiring special attention. In these patients, the recommendation is to start insulin infusion at 0.05–0.07unit/kg/hr to prevent sudden changes in osmolality and hypoglycemia. The goal of treatment should be reduction of plasma ketones by 0.5 mmol/h, bicarbonate by 3 mmol/h and capillary blood glucose by 50–75 mg/dl per hour. The infusion rate should be adjusted based on the attainment of these targets [39].

4.4. Electrolyte disturbances

The electrolyte abnormalities encountered in these patients differs from patients with preserved renal function where mainly disturbance in concentrations of sodium, potassium, phosphate and magnesium is seen.

4.4.1. Potassium

Recommendation 5: Patients with DKA and ESRD on HD do not require routine potassium replacement as these patients usually have hyperkalemia at presentation. In the presence of biochemical hypokalemia, total body stores of potassium may be raised due to poor excretion. Cardiac monitoring is important in patients with hyperkalemia.

Hyperosmolality in DKA causes a shift of potassium from within the cell to the extracellular space resulting in hyperkalemia. Rohrscheib et al. analysed abnormalities in serum potassium in 40 episodes of DKA; 6 episodes in peritoneal dialysis (PD) and 34 episodes in hemodialysis (HD), and in 245 episodes of non-ketotic hyperglycemia (NKH)—70 episodes in PD and 175 episodes in HD. In HD patients the episodes of ketoacidosis were associated with higher mean serum glucose concentration (934 vs. 682 mg/dl) and tonicity (307 vs. 297 mOsm/kg) compared to episodes of NKH. The authors found that HD patients are more prone to DKA with hyperkalemia compared to patients on PD. However, the frequency of hyperkalemia was higher in ketoacidosis than in non-ketotic hyperglycemia in both dialysis modalities [40]. Additionally, Blickrer reported that DKA aggravates hyperkalemia in more than 50% of cases in dialysis patients [41].

Since dialysis dependent patients are usually hyperkalemic, they should not receive routine potassium supplementation. Even in the presence of biochemical hypokalemia, total body potassium stores may be high as these patients are unable to excrete excess potassium load. Serum potassium levels can vary at presentation. In case of high potassium levels (>5.5 mmol/l) cardiac monitoring is important and, these patients require emergency hemodialysis in addition to treatment with insulin [42]. Conversely, patients with low serum potassium (<3.5 mmol/l) levels are at a risk for cardiac arrhythmias and muscle weakness. The recommendation in such cases is correction with 40 mmol/l of potassium chloride until serum potassium is more than 3.5 mmol/l [43]. In the presence of normokalemia, acidosis should be corrected prior to initiation of potassium supplementation [41]. Initiating potassium replacement in the absence of laboratory assessment in patients with compromised renal function can be fatal [44].

4.4.2. Phosphate and magnesium

Recommendation 6: Serum phosphate concentration can very at presentation with hyperphosphatemia being more common in ESRD. Insulin therapy lowers serum phosphate. In case of hypophosphatemia, prompt recognition and replacement are important. Prophylactic replacement of phosphate is not required.

The second electrolyte which is altered in DKA is phosphate. Dialysis dependent patients can have hyperphosphatemia (due to excessive protein intake of insufficient dialysis) or hypophosphatemia (due to poor oral intake, malnutrition or inappropriate use of phosphate binders). In case of hyperphosphatemia at

presentation, institution of insulin therapy lowers serum phosphate. Hypophosphatemia can cause muscular weakness and neurological dysfunction. If present, it should be corrected carefully as excessive replacement of phosphate can lead to hypocalcemia [32] and hamper oxygen delivery to peripheral tissues [45].

Prophylactic phosphate repletion is unnecessary; however, prompt recognition and replacement of deficit is important. Intravenous phosphate replacement may be indicated if serum phosphate is less than 1–1.5 mg/dl, while oral replacement is adequate for mild hypophosphatemia. To prevent hypocalcemia, serum calcium and magnesium levels should be carefully monitored [30,46]. Finally, disturbance in serum magnesium may also be observed in these patients. Chronic magnesium deficiency has been reported in uncontrolled diabetes and can contribute to insulin resistance. However, research has yet to show any benefits in the administration of magnesium in diabetic emergencies [32].

4.5. Metabolic acidosis

Recommendation 7: In anuric patients, severe and persistent metabolic acidosis may be seen at presentation. The recommended treatment for correction of severe metabolic is emergency hemodialysis. Bicarbonate administration is not recommended for correction of acidosis.

Development of DKA involves a series of closely interrelated derangements of intermediary metabolism and of body fluid volume and composition [47]. A key component of the diagnostic criteria for DKA is raised anion gap metabolic acidosis due to accumulation of beta-hydroxybutyrate and acetoacetate. One of the factors influencing severity of metabolic acidosis is the rate of acid excretion in urine. Acid excretion is markedly increased in patients with preserved renal function thereby minimizing the severity of acidosis [48]. This mechanism is significantly impaired in patients with anuria resulting in persistent and severe metabolic acidosis. Additionally, pulmonary dysfunction due to volume overload or pre-existing pathology (i.e., obstructive or restrictive airway disease, infection, etc.) can impair ventilatory compensation to metabolic acidosis [41].

In DKA patients with preserved renal function, aggressive fluid resuscitation can partially correct metabolic acidosis by increasing renal blood flow and hence acid excretion, however, this approach is not applicable in dialysis-dependent patients [49]. Bicarbonate administration is rarely of value in DKA and is not routinely recommended. The recommended treatment for correction severe metabolic acidosis is HD.

If ketoacidosis is present in a patient with DH, emergency hemodialysis using bicarbonate dialysate can lead to a rapid rise in serum bicarbonate and blood pH. Adverse effects associated with the rapid correction of metabolic acidosis are not known as they have not been studied adequately. Therefore, conventional hemodialysis is best avoided in treating patients with DH, and emergency HD may be considered only if there is severe pulmonary edema, profound metabolic acidosis and/or severe hyperkalemia with ECG manifestations [50]. Peritoneal dialysis has lower solute transfer rates than hemodialysis and can be continued during treatment of severe DH [50]. Though supporting evidence is lacking, Continuous

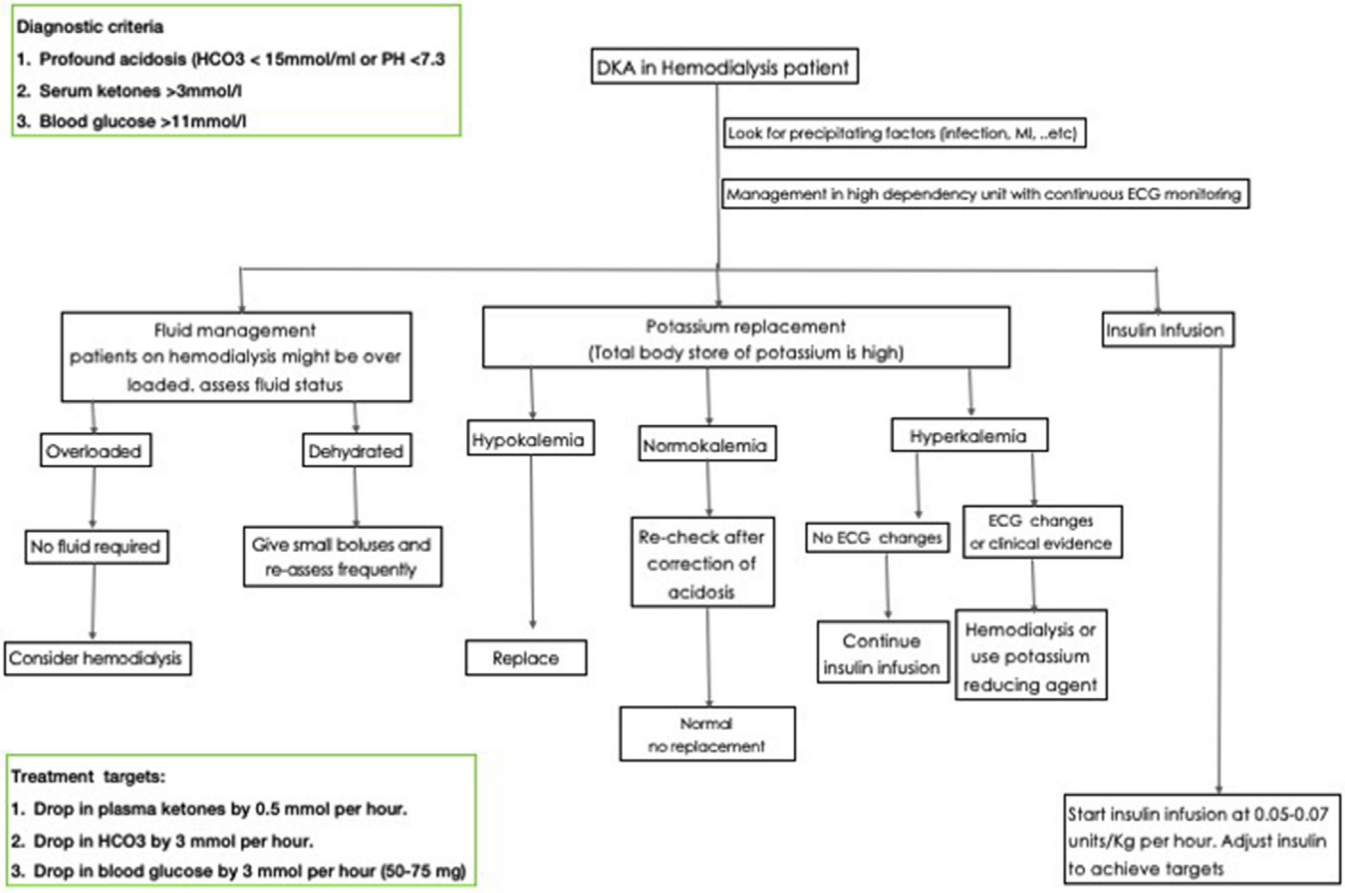

Fig. 1. Algorithm for management of DKA in patients with CKD V on Hemodialysis.

renal replacement therapy (CRRT) can be a better option for patients with profound metabolic acidosis since it provides a slower correction and slow solute clearance per unit time as compared with intermittent hemodialysis therapy. This definitely will be more appropriate for patients with hemodynamic instability [51,52].

In summary, the diagnosis and management of DKA in ESRF is challenging. DKA in patients with ESRF on HD should be suspected in case of severe and persistent raised anion gap metabolic acidosis. Insulin therapy and emergency hemodialysis in case of life-threatening hyperkalemia and severe metabolic acidosis are the most important modalities of treatment resulting in resolution of DKA. Based upon our experience from a single tertiary-care centre, we have formulated an algorithm to guide identification and treatment of DKA in patients with ESRF on HD (Fig. 1).

5. Summary of recommendations

Recommendation 1: DKA in patients with ESRD on HD is a rare clinical presentation and difficult to diagnose. Since ESRD is a state of persistent chronic metabolic acidosis, DKA should be suspected in case of persisting metabolic acidosis despite optimal renal replacement therapy. Measurement of Serum β-hydroxybutyrate is a useful tool in establishing diagnosis of DKA in patients with ESRD on HD.

Recommendation 2: Gradual correction of the hyperosmolar state is important to avoid fatal complications such as cerebral edema and pontine myelinolysis. Anuric patients with DKA rarely present with dehydration and shock due to hyperglycemia-induced osmotic diuresis. Majority of the patients have hypertonicity with low serum sodium concentration at presentation. These patients improve with insulin infusion. Close monitoring of volume status, serum glucose and electrolytes is required. The recommended target rate for reduction in serum glucose is 50–75 mg⁄dl⁄hr during treatment. Emergency hemodialysis should be recommended with caution in patients with extreme hyperglycemia, hypertonicity and low serum sodium concentration as change in tonicity may be quite rapid. Continuous renal replacement therapy (CRRT) might be appropriate for patients with profound metabolic acidosis.

Recommendation 3: In patients with DKA and ESRD on HD, fluid resuscitation with boluses of 250–500 ml should be used guided by continuous re-evaluation of volume status.

Recommendation 4: Insulin therapy is the mainstay of treatment in patients with DKA and ESRD on HD.

Recommendation 5: Patients with DKA and ESRD on HD do not require routine potassium replacement as these patients usually have hyperkalemia at presentation. In the presence of biochemical hypokalemia, total body stores of potassium may be raised due to poor excretion. Cardiac monitoring is important in patients with hyperkalemia.

Recommendation 6: Serum phosphate concentration can very at presentation with hyperphosphatemia being more common in ESRD. Insulin therapy lowers serum phosphate. In case of hypophosphatemia, prompt recognition and replacement are important. Prophylactic replacement of phosphate is not required.

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Conflicts of interest

All authors have no conflicts of interest.

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