MEDDOCS Open Access Publisher

ISSN: 2639-9237

Journal of Case Reports and Medical Images

Open Access | Case Report

# Persistent Acidosis in DKA Due To Covid-19 Infection despite Optimal Management

***Joby Landa[1]; Ibrahim Benshaban[2]; Tamer Shalaby[3]****

*[1]Specialist Nurse AECU at Wrexham Maelor Hospital, UK.*

*[2]GPST1 Doctor at Wrexham Maelor Hospital, UK.*

*[3]Consultant Acute and Internal Medicine at Royal Liverpool University Hospital, UK.*

***Corresponding Author(s): Tamer Shalaby**

Consultant Acute and Internal Medicine at Royal Liverpool University Hospital, UK.

Tel: +447957772597;

Email: Dr.tamershalaby@hotmail.com

Received: Dec 02, 2021

Accepted: Jan 11, 2022

Published Online: Jan 14, 2022

Journal: Journal of Case Reports and Medical Images

Publisher: MedDocs Publishers LLC

Online edition: http://meddocsonline.org/



**Keywords:** Diabetic ketoacidosis (DKA); Covid-19; Ketosis; Hyperchloremic acidosis.

## Abstract

Covid-19 has a worse prognosis on diabetic patients who can present with severe metabolic complications. We present a case of a new diagnosis likely type 1 diabetes in a middle age non-obese white female, who presented with severe Diabetic Ketoacidosis (DKA), which was resistant to treatment, and her management required slight deviation from the guidelines to improve her outcome. The patient did not show typical symptoms or signs of covid, was tested positive by Polymerase Chain Reaction (PCR) and was not given Dexamethasone. We believe this was a very difficult case of DKA to manage in a newly diagnosed diabetic patient due to the effect of Covid-19.

## Case presentation

A 54 year old non-obese white female who is fit and well presented with eight weeks history of osmotic symptoms (polyuria, polydipsia, weight loss), then she was found by her son drowsy with evidence of bilious vomiting.

She was brought by ambulance to the Resuscitation room in our A&E department and found to have a patent airway, chest examination showed equal air entry with no added sounds, oxygen saturations of 96% on room air, respiratory rate of 24 and initial ABG (Table 1) showed Severe decompensated metabolic acidosis and PO2 of 11.2 on room air and the portable chest X-ray was normal. She had cold peripheries with blood pressure of 105/62, heart rate of 108 in sinus tachycardia on ECG with normal heart sounds and lactate of 3. Glasgow coma scale (GCS) was 13 (E3, V4, M6), Capillary Blood Glucose (CBG) of 28, ketones recorded as high and no focal neurological deficit with equal and reactive pupils. She was afebrile and no evidence of rash, Deep Venous Thrombosis (DVT), no meningism and abdomen was soft and non-tender.

**Cite this article:** Landa J, Benshaban I, Shalaby T. Persistent Acidosis in DKA Due To Covid-19 Infection despite Optimal Management. J Case Rep Clin Images. 2021; 4(1): 1098.

Blood test (Table 1) showed evidence of Acute Kidney Injury (AKI) with raised inflammatory markers and raised Amylase.

CT Brain was not done due to the severity of metabolic acidosis and risk of rapid deterioration, with the subsequent improvement in GCS with treatment and the lack of history of headache or head injury or focal neurological deficit. CT abdomen later when stable did rule out intraabdominal pathology and pancreas was normal with clear lung bases.

She was started on Fixed Rate Insulin Infusion Therapy (FRII), crystalloid resuscitation then maintenance, empirical broad spectrum antibiotics after septic screen was sent and had a urethral catheter inserted for fluid balance assessment.

After 14 hours of 10 units per hour Act Rapid insulin infusion and more than five litres of Normal saline 0.9% her ketones were persistently above 7, PH below 7 and GCS of 14 (E3) while maintaining a good blood pressure and urine output with resolution of AKI after 7-8 hours.

With the advice of the Intensive care team over night and the Diabetes team in the early morning we agreed on starting Bicarbonate infusion 1.26 % due to severe and persistent acidosis and added 10% Dextrose as CBG was below 14.

VBG after one hour of the above showed marked improvement in PH to 7.13 and GCS of 15.

We noted the persistence of hyperchloremic acidosis and agreed to switch the normal saline 0.9 % to 0.18% and 4 % Dextrose with KCL, the VBG after 2 hours showed Chloride of 113 from 126 and PH of 7.3 from below 7.13.

Her SARS-CoV-2 virus PCR came back positive, her septic screen was negative and she raised inflammatory markers felt to be due to Covid infection.

Subcutaneous Insulin basal/bolus regimen initiated by the diabetes team (Daily Insulin requirement was 0.5 unit /Kg) and her HBA1C came back as 113. She made a very good recovery and left the hospital after 4 days.

**Table 1**

| | On Admission | 14 hours after FRIII and normal saline 0.9% | 1 hour After Bicarbonate infusion | 2 hours After Switch to 0.18 saline |
|---|---|---|---|---|
| PH | 6.8 (Low) | 6.9 | 7.13 | 7.3 |
| HCo3 | 3 (Low) | 5 | 8 | 11 |
| CL | 104 | 116 | 126 | 113 |
| Lactate | 3 (Hi) | 1.6 | 1.5 | |
| Glucose | 28 (Hi) | 19 | 11 | |
| Ketones | High | 7 | 6.4 | |
| K | 4.6 | 4.3 | 4 | 4.2 |
| Creatinine | 147 (Hi) | 93 | | |
| WCC | 23 (Hi) | 18 | | |
| CRP | 111 (Hi) | 107 | | |
| Amylase | 380 (Hi) | | | |

## Discussion

Diabetic Ketoacidosis (DKA) is a potentially fatal metabolic complication, which is more common in type 1 diabetes but can occur in type 2 diabetes. Criteria for diagnosing DKA are hyperglycaemia more than 11, ketones more than 3 and Acidosis with bicarbonate less than 15 or PH below 7.3 [1].

Covid-19 is caused by SARS-CoV-2 virus which can induce severe metabolic complications for patients with diabetes, including DKA and Hyperosmolar Hyperglycaemic Status (HHS) for which high doses of insulin are required with a significant increase in morbidity, mortality and hospital stay [2,3].

The virus binds to angiotensin-converting enzyme 2 receptors, which are expressed in pancreatic beta cells, adipose tissue and other organs. Causing alterations of the glucose metabolism which may lead to new mechanisms of disease and greater incidence of fasting hyperglycaemia and new onset diabetes plus a rise in ketone bodies from the effect on the adipose tissue [4,5].

A study of more than 600 patients reported that COVID-19 infection did cause ketoacidosis in non-diabetic patients and induced severe DKA for those with diabetes [6].

Ketones (β-hydroxybutyrate, acetoacetate and acetone) are formed in the liver from free fatty acids and when increased in blood due to less consumption or excess production- can be clinically evident by acidosis. Assumption now from different studies that COVID-19 might accelerate fat breakdown and induce ketosis even in non-diabetic patients [7-9].

This effect of Covid can explain why our patient was very resistant to treatment with extra doses of Insulin and crystalloid fluid therapy than what was recommended by the Joint British Diabetes Societies Inpatient Care Group guidelines [1].

More than five litres of normal saline with KCL 10 mmol/hour given in the first 14 hours with normalisation of renal function, good urine output of more than 70 mls per hour and stable blood pressure throughout with 10 units of insulin act rapid per hour (weight 69 Kg and the recommendation is 6-7 units per hour- 0.1 unit/kg/hour), and still the PH was 6.9 and the ketones persistently raised of more than 6, however, blood glucose did respond and 10% Dextrose 125 mls/hour been added as per guidelines to ensure avoiding hypoglycaemia and keep the Insulin going at this high rate to burn ketones, which is the main aim of fixed rate Insulin Infusion therapy.

Lactate was minimally raised, no risk of poisoning or alcohol as patient was teetotal and starvation ketosis was unlikely to cause such a high ketosis, which is resistant to treatment.

The aim of this case report is mainly to raise the concern of the effect of Covid-19 on blood glucose and ketone bodies; however, we have two points to raise in the management of DKA in general and will try in the next few lines to critically appraise the data available.

First, would you give bicarbonate solution in this case, the PH was 6.9 and the bicarb was 5 after adequate resuscitation for more than 14 hours?

Horng et al, performed a systematic review of several studies including three adult Randomized Controlled Trials (RCT) on bicarbonate versus no bicarbonate in DKA. Two RCTs demonstrated transient improvement in metabolic acidosis with bicarbonate treatment within the first 2 hours. No evidence of blood glucose control or clinical improvement was found. No studies involved patients with an initial pH < 6.85 [10].

**Adverse effects to expect when using bicarbonate** [11-13].

- Giving alkaline solution will reduce the hyperventilation in DKA which blows off CO2. In the hypercapnic state CO2 crosses the blood-brain barrier leading to a drop in cerebral pH and neurologic deterioration.
- Can slow ketone clearance by about 6 hours, causing a more refractory acidosis.
- Risk of hypokalaemia.

Severe metabolic acidosis carries a significant mortality of 50-60% due to inability of body enzymes to function and leads to coma, seizures, fatal arrhythmias like ventricular tachycardia and reduction of cardiac function due to less response to epinephrine which reduce the blood pressure further [14]. In 2009, the American Diabetes Association (ADA) advised for bicarbonate in DKA if PH <6.9 and to stop infusion when the PH is above 7 [15].

In summary, the use of bicarbonate in DKA remains controversial, not recommended by some experts and not included in guidelines but as many aspects in medicine the management of unwell patient lies with weighing risk versus benefit. The rationale behind the use of bicarbonate in our case was the persistent low PH below 7 after 14 hours of extra doses of fixed rate insulin infusion with crystalloid and the high risk of mortality with this persistent low PH level. When bicarbonate infusion used we stopped it when the PH rose above 7. The PH after Bicarbonate was 7.13 and K stayed around 4 and the patient started to improve clinically.

**Second point is, Hyperchloremic acidosis**

Unfortunately hyperchloremic acidosis is a Very common complication seen with the treatment of DKA by normal saline, guidelines advise the use of normal saline as it used to be the only crystalloid at least in the UK were Potassium Chloride (KCL) can be added to, which reduce the risk of hypokalaemia when Insulin is introduced and acidosis is resolved.

However, there is 154 mEq/L chloride in every litre of 0.9% saline, and expecting to give 5-7 litres in 24 hours you can appreciate why hyperchloremic acidosis is common, as when chloride rise this will be on behalf of a drop in bicarbonate level and persistent normal anion gap metabolic acidosis. We slightly deviated- again- from the guidelines and used Sodium Chloride 0.18 % and Glucose 4% Solution (plus KCL) which contains 71 mEq/L chloride, VBG 2 hours afterwards showed a rapid improvement in the hyperchloremic acidosis, of course with hourly monitoring of K as well as routine hourly ketones, blood glucose, urine output, GCS and observations.

**Learning points**

- Covid-19 can increase blood glucose level due to direct effect on pancreas as well as the stress response which increase the level of anti-insulin hormones like cortisol and glucagon.
- Covid-19 can increase the ketone level due to its effect on adipose tissue.
- We recommend checking blood glucose level in covid patients and Covid-19 PCR in patients presenting with DKA in absence of usual signs of covid.
- There could be a role for bicarbonate solution in severe metabolic acidosis <7 which is resistant to treatment, seek senior input first.
- Sodium Chloride 0.18 % and Glucose 4% Solution may be a good choice for persistent hyperchloremic acidosis with close monitoring of serum K.

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