



## CASE REPORT

## High-anion gap hyperchloremic acidosis mimicking diabetic ketoacidosis on initial presentation – Case report

Esmail Sangey\*, Kishan Chudasama

Emergency &amp; ICU Department, Shree Hindu Mandal Hospital, Dar es Salaam, Tanzania

## ARTICLE INFO

## Keywords:

Diabetic ketoacidosis  
Hyperchloremia  
Non-anion gap metabolic acidosis  
High-anion gap metabolic acidosis

## ABSTRACT

**Introduction:** Diabetic ketoacidosis (DKA) often becomes the primary focus and in turn masks a similar serious condition like hyperchloremic metabolic acidosis.

**Case report:** A 20 years old female with type 1 diabetes mellitus presented to the emergency department (ED) with signs and symptoms corresponding to DKA. Initial pH, HCO<sub>3</sub>, Na and Cl concentrations were 6.83, 3.6 mmol/l, 143 mmol/l and 122 mmol/l respectively; anion gap 17.4 mmol/l and absent urinary ketones. DKA regime showed no improvement in the measured parameters nor the patient. The diagnosis changed to hyperchloremic high-anion gap acidosis and treatment modifications were made by adding sodium bicarbonate infusion. There was significant improvement in the clinical status of the patient and the calculated parameters.

**Discussion:** Hyperchloremic acidosis is associated with a non-anion gap, decrease in plasma bicarbonate and increase in plasma chloride. Rarely, as with this case, it may present with a high-anion gap. The use of bicarbonate therapy has shown improvement in cases of non-anion gap acidosis however there is very little data to support its role in high-anion gap hyperchloremic metabolic acidosis.

## Introduction

Diabetic ketoacidosis (DKA) is a serious life-threatening complication of diabetes mellitus characterized with high anion gap metabolic acidosis due to excessive production of ketoacids at an expense of reduced serum bicarbonate concentration [1]. Over the past years, the limelight has been on DKA for any diabetic patient but less on hyperchloremic related acidosis. Until recent years, a raised serum chloride concentration was observed to have a clinical impact in renal impairment after administration of large quantities of chloride containing saline solutions hence causing hyperchloremic non-anion gap metabolic acidosis [2,3]. It results from raised chloride concentrations and bicarbonate loss with a normal anion gap. The identified aetiologies are gastrointestinal causes (diarrhoea), renal tubular acidosis (RTA), and exogenous causes (0.9% normal saline administration) [4]. Here we describe a case of a type 1 diabetic young woman with hyperchloremia and high-anion gap acidosis.

## Case presentation

A 20 years old female with type 1 diabetes mellitus on Mixtard insulin® 30/70 (fast/intermediate-acting insulin), presented to the emergency department with nausea, vomiting and watery diarrhoea (4

to 6 motions per day) for 3 days duration. She also had occasional spikes of fever and light-headedness. She denied history of syncope, seizures nor had any food or drug allergies.

On arrival vitals were: BP: 104/60 mmHg, HR: 124 bpm, RR: 25 breaths/min, Temp: 36.5 °C, SpO<sub>2</sub> 96% on room air, and random blood glucose: 24 mmol/l.

The physical exam revealed, she was well-nourished but dehydrated weighing about 60 kg. She was lethargic with deep laboured breathing (Kussmaul breathing) and dehydrated. She was alert and oriented to time, place and person. Abdominal exam revealed mild epigastric tenderness on superficial palpation. The rest exams were unremarkable.

Based on her history and clinical findings a diagnosis of DKA due to acute gastroenteritis was made. Two IV access with large-bore cannula were placed and a normal saline bolus of 3.5 l was given with attention to urine output, which was adequate. IV Ciprofloxacin 200 mg, Metoclopramide 10 mg and Rabeprazole 20 mg were also initiated. Thereafter, DKA management protocol was initiated.

Blood samples were taken for CBC, H. pylori antigen test, Malaria slide and Widal tests which were all unremarkable except for Leukocytosis in the CBC. Urine analysis was unremarkable including the absence of ketones. These results were obtained 2 h after her ED presentation except for venous blood gas and electrolytes which were obtained using bedside point-of-care (POC) machine at the ED and ICU

\* Corresponding author: Dr. Esmail Sangey, Emergency & ICU Department, Shree Hindu Mandal Hospital, P.O.Box 581, Dar es Salaam, Tanzania.

E-mail address: [esangey@hotmail.com](mailto:esangey@hotmail.com) (E. Sangey).

<https://doi.org/10.1016/j.afjem.2019.09.004>

Received 5 January 2019; Received in revised form 16 September 2019; Accepted 19 September 2019

Available online 17 November 2019

2211-419X/ © 2020 African Federation for Emergency Medicine. Publishing services provided by Elsevier. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**Table 1**  
Table of results.

	0 h	3 h	12 h	18 h	24 h	30 h	36 h	40 h
pH	6.83	6.82	7.05	7.10	7.20	7.33	7.32	7.37
PaCO <sub>2</sub> (mmHg)	21.9	16.7	16.9	22.7	19.8	28.8	28.5	33.9
HCO <sub>3</sub> (mmol/l)	3.6	2.7	4.7	7.1	7.7	15.2	14.7	20.8
Na (mmol/l)	143	142	139	138	145	139	142	137
K (mmol/l)	6.3	4.6	3.5	3.3	2.8	3.6	3.1	3.4
Cl (mmol/l)	122	122	114	114	117	107	110	104
Creatinine (μmol/l)	60	46	57	52	32	57	56	41
Glucose (mmol/l)	24.0	15.3	15.6	17.9	10.7	13.1	12.6	11.2
Urea (mmol/l)	5.2	4.3	2.4	2.6	2.0	3.8	4.4	4.2
Anion gap (mmol/l)	17.4	17.3	20.3	16.9	20.3	16.8	17.3	14.2

whereby she was admitted.

Serial venous blood gases and electrolytes at every 3 to 6 hour interval were done. The initial results were: pH = 6.83 (7.35–7.45), PaCO<sub>2</sub> = 21.9 mmHg (35–45 mmHg) HCO<sub>3</sub> = 3.6 mmol/l (23–28 mmol/l), Na = 143 mmol/l (135–145 mmol/l), K = 6.3 mmol/l (3.5–4.5 mmol/l), Cl = 122 mmol/l (98–109 mmol/l), Creatinine = 60 μmol/l (53–115 μmol/l), Urea = 5.2 mmol/l (2.9–8.4 mmol/l), Anion-gap = 17.4 mmol/l (8–16 mmol/l). The rest were as follows (Table 1):

From arrival up to the 2nd hour, the DKA protocol was initiated with insulin infusion at 0.1 U/kg/h and normal saline 500 ml admixed with potassium chloride 20 mmol running at 125 ml/h without the use of sodium bicarbonate infusion.

We acknowledged from the third hour of her treatment that this was not typical of DKA, as there were no clinical improvement nor any significant changes in her blood gas parameters. Thus, the diagnosis changed to hyperchloremic metabolic acidosis with high-anion gap due to acute gastroenteritis and in part, normal saline induced.

Her treatment was modified by adding sodium bicarbonate infusion, whereby HCO<sub>3</sub><sup>-</sup> deficit was calculated.

- Sodium bicarbonate 40 mmol plus potassium chloride 20 to 40 mmol admixed in 5% Dextrose water 500 ml bottle ran 125 ml/h.
- Fast acting insulin constant rate at 0.05 U/kg/h (3 U/h).

This treatment plan continued for 48 h and was stopped when pH and chloride concentration started normalising (see Table 1) and there was a significant patient improvement. Thereafter she was transferred to the general ward to resume her insulin regime and antibiotics. Later she was discharged and advised her usual diabetic clinic follow-up.

## Discussion

Anion gap is referred to as the difference of the measured cations and anions. The normal values are 8–16 mmol/l.

Hyperchloremic acidosis is a form of metabolic acidosis associated with a normal anion gap, decrease in plasma bicarbonate concentration, and an increase in plasma chloride concentration [4]. Common causes are large volume of chloride-containing saline administration, following diabetic ketoacidosis, and secondary to diarrhoea in the treatment of hypovolemia or shock. This ultimately leads to reduction in the glomerular filtration rate and then acute kidney injury [5].

Patients with diarrhoea are usually associated with normal anion-gap metabolic acidosis due to the large volume and bicarbonate losses which in-return later may lead to a rise in chloride concentration via the kidneys to maintain metabolic balance leading to high-anion gap [6], hence hyperchloremic high-anion gap acidosis.

Hyperchloremic acidosis, whether non-anion or high-anion gap, had been under-reported except for one recent study by Toledo et al., describing the prevalence of hyperchloremic high-anion gap acidosis of about 55% during the DKA presentation [7]. On the contrary, our patient had presented with hyperchloremia with high-anion gap acidosis but without urinary ketones.

Bicarbonate therapy has not shown any benefit in acute high-anion gap metabolic acidosis such as diabetic ketoacidosis, lactic acidosis and septic shock [8,9]. However in hyperchloremic non-anion gap metabolic acidosis, it had shown promising results in the clinical and biochemical improvements [10]. Bicarbonate therapy in hyperchloremic non-anion gap metabolic acidosis has been widely accepted and addressed in the past few years but to our knowledge, very little is known about this therapy in hyperchloremia with high-anion gap.

## Conclusion

Many clinicians show a limited focus on chloride anion and its clinical significance. This case and the literature review aims at creating awareness on both, non-anion gap and high-anion gap hyperchloremic metabolic acidosis. We hope to prompt further studies to take place with regards to bicarbonate therapy in a setting of high-anion gap hyperchloremic metabolic acidosis.

## Declaration of competing interest

The authors declare that they have no conflict of interest.

## References

- Kearney T, Dang C. Diabetic and endocrine emergencies. *Postgrad Med J* 2007 Feb;83(976):79–86.
- Lobo DN, Awad S. Should chloride-rich crystalloids remain the mainstay of fluid resuscitation to prevent “pre-renal” acute kidney injury?: con. *Kidney Int* 2014 Dec;86(6):1096–105.
- Barker ME. 0.9% saline induced hyperchloremic acidosis. *J Trauma Nurs Off J Soc Trauma Nurses* 2015 Apr;22(2):111–6.
- Sharma S, Aggarwal S. Hyperchloremic acidosis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018 [cited 2018 Dec 16]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK482340/>
- Toyonaga Y, Kikura M. Hyperchloremic acidosis is associated with acute kidney injury after abdominal surgery. *Nephrol Carlton Vic* 2017 Sep;22(9):720–7.
- Wang F, Butler T, Rabbani GH, Jones PK. The acidosis of cholera. Contributions of hyperproteinemia, lactic acidemia, and hyperphosphatemia to an increased serum anion gap. *N Engl J Med* 1986 Dec 18;315(25):1591–5.
- Toledo I, Wainsztein R, Mannucci C, Ferraro M, Ferreira J, Balestracci A. Impact of the hyperchloremic component of metabolic acidosis on the patient's hydration status and the treatment of diabetic ketoacidosis. *Arch Argent Pediatr*. 2018 01;116(3):e365–70.
- Duhon B, Attridge RL, Franco-Martinez AC, Maxwell PR, Hughes DW. Intravenous sodium bicarbonate therapy in severely acidotic diabetic ketoacidosis. *Ann Pharmacother* 2013 Aug;47(7–8):970–5.
- Boyd JH, Walley KR. Is there a role for sodium bicarbonate in treating lactic acidosis from shock? *Curr Opin Crit Care* 2008 Aug;14(4):379–83.
- Kraut JA, Kurtz I. Treatment of acute non-anion gap metabolic acidosis. *Clin Kidney J* 2015 Feb;8(1):93–9.