

Interpretation of Arterial blood gases

Part II, Normal Anion Gap or Hyperchloremic Metabolic Acidosis

Moazzum Khurshid, FCPS. Asim Noor, FCPS. Jawed Abubaker, MD, FCCP.
Department of Medicine
Liaquat National Hospital

.....

The normal anionic gap metabolic acidosis is characterized by a primary decrease in bicarbonate concentration associated with hyperchloremia. In this disorder, plasma bicarbonate decreases and is replaced by chloride to maintain electroneutrality. Consequently, these disorders are also referred to as hyperchloremic metabolic acidosis¹.

Normal anion-gap metabolic acidosis occurs from the loss of bicarbonate through the kidneys or through the gut, or from the addition of an acid with chloride as the accompanying anion.

A step-wise conventional approach to interpret the acid-base data is as follows:

Case # 1:

A 72 year old woman was admitted to the hospital with a one week history of diarrhea and fever.

Labs:

Na 133mEq/l; K 2.5 mEq/l; pH 7.12; PaCO₂16mmHg; PaO₂94mmHg
Cl 118mEq/l; HCO₃ 5 mEq/l; S.Albumin 3.8mg%

- Is the data internally consistent?
>Yes
- What is the acid base disorder?
>Acidemia
- What is the primary acid base disorder?
>Metabolic acidosis

- What type of metabolic acidosis?
>Normal anion gap or hyperchloremic metabolic acidosis. (The anion gap is 10).
- Is the compensation adequate for the primary disturbance?
>Yes

Final diagnosis please....

Clinical condition please.....

Case # 2:

A 20 year old man without any comorbid presents with short history of shortness of breath and weakness and now also started to have bone pains.

Labs: ABG: pH 7.28 PaCO₂ 30 mmHg PaO₂ 88 mmHg HCO₃ 14 mEq/l
Na 142 mEq/l Cl 114 mEq/l K 2.6 mEq/l Urea 25mg% BSR 85 mg%
urine dipstick ++ to glucose.

- Is the data internally consistent?
>Yes
- What is the acid base disorder?
>Acidemia
- What is the primary acid base disorder?
>Metabolic Acidosis
- What type of metabolic acidosis?
>Normal anion gap acidosis. (Anion gap is 14)
- Is the compensation adequate?

>Yes; expected PaCO₂ by winter's formula is 29 ± 2.

- Primary condition.....

This is normal anion gap acidosis or hyperchloremic acidosis with low potassium

The causes of hyperchloremic metabolic acidosis can be divided into four main types² and with each type having different causes of their own as shown in the following (Table 1):

CAUSES OF HYPERCHLOREMIC METABOLIC ACIDOSIS

TYPE	CAUSES
Renal with hypokalemia	Proximal RTA, type 2
	Distal RTA, type 1
Renal with hyperkalemia	Type 4 RTA; hyporenin-hypoaldosteronism
Nonrenal with hypokalemia	Diarrhea
	Urinary diversions, pancreatic fistula
Nonrenal with hyperkalemia	Parenteral Therapy with, NaCl, KCl, NH ⁴ Cl, CaCl ₂ , ArgHCl, LysHCl
RTA = renal tubular acidosis.	

THE URINARY ANION GAP IN HYPERCHLOREMIC METABOLIC ACIDOSIS

An important means of distinguishing between renal tubular acidosis and extra renal bicarbonate loss, for example from diarrhea, is to look at the urinary anion gap³⁻⁶. In normal individuals with normal acid base milieu it is usually between 0-2.

Since the normal renal response to metabolic acidosis is an increase in ammonia genesis, (the mechanism through which kidney loses acid from ammonia to ammonium NH_3 to NH_4) the urine in the case of diarrhea should normally contain large amounts of NH_4Cl while the kidney retains sodium and potassium. The urinary anion gap, which is $(\text{Na}^+ + \text{K}^+) - \text{Cl}^-$, should then be strongly negative because of the unmeasured NH_4^+ . This test is superior to measurement of urine pH, since decreased Na^+ delivery to the distal nephron in the Na^+ avid state of diarrhea may impair urinary acidification and pH will not be maximally acid³⁻⁶.

In renal diseases in which there is either a failure of ammonia genesis or the excretion of sodium plus potassium with bicarbonate, the urinary anion gap will be zero or positive. That is characteristic of distal renal tubular acidosis^{3,5}.

When other unmeasured anions such as ketoacids and lactate are present in the urine, a positive urinary anion gap does not indicate renal tubular acidosis. These situations are usually associated with an elevated serum anion gap but on occasion prompt renal excretion of organic anions with sodium and potassium may minimize an increase in the serum gap. This is particularly possible in cases of DKA and D-lactic acidosis, as D-lactate is not absorbed by the renal tubule. In the metabolic acidosis of glue-sniffers, hippurate, a product of toluene, is excreted, giving the appearance of a non-gap metabolic acidosis with positive urinary anion gap.

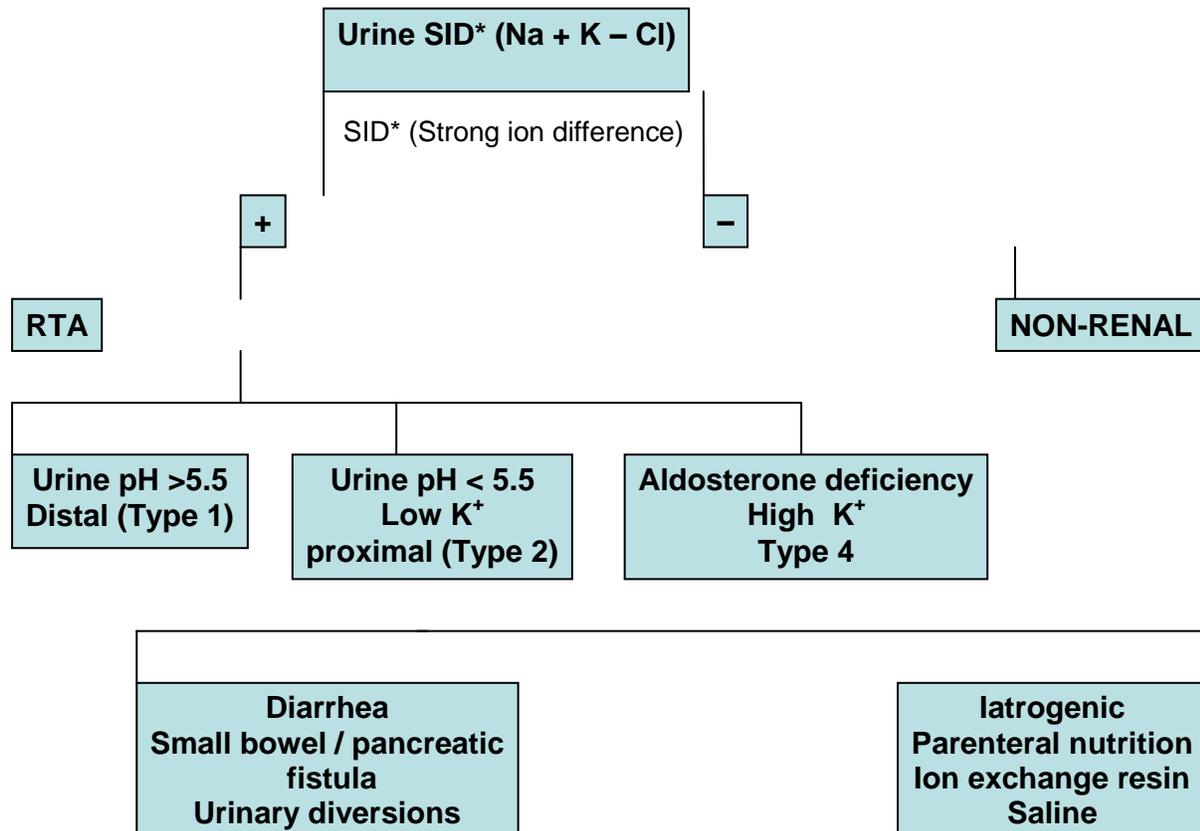
Fractional excretion of Na^+ FENa:

In addition to the UAG, the **fractional excretion of Na^+** (FENa) may be helpful and would be expected to be low (less than 1% to 2%) in patients with HCO_3^- loss from the gastrointestinal tract, whereas it usually exceeds 2% to 3% in RTA⁷. FENa is calculated by the following formula

$$\text{FENa} = \text{urine Na} \div \text{serum Na} \times \text{serum creatinine} \div \text{urine creatinine} \times 100$$

Remember that the urine anion gap and FENa are only useful when the renal function is normal.

A **useful algorithm**⁸ to evaluate the causes of normal anion gap or hyperchloremic acidosis is suggested below,



CASES REVIEWED

In Case 1, the urinary electrolytes were sent and they showed the following results;

Urine Na 20, K 10, Cl 40

Now let's calculate the Urine anion gap i.e.

$$\text{Na} + \text{K} - \text{Cl} = -10$$

Thus, verifying that normal anion gap acidosis is caused by diarrhea.

Similarly the urine anion gap in Case 2 was 12 i.e.

$$\text{Na} + \text{K} - \text{Cl} = 22 + 20 - 30 = 12$$

Thus, verifying that this normal anion gap acidosis is caused by renal tubular acidosis.

SUMMARIZING HYPERCHLOREMIC METABOLIC ACIDOSIS⁹

	Renal defect	Serum potassium	Urine pH	Urine Anion Gap	Treatment
Gastrointestinal losses of HCO_3	None	Low	<5.3	Negative	Na,K, HCO_3 as required
Type1 RTA (Distal)	Distal H^+ secretion	Low	>5.3	Positive	NaHCO_3 1-3meq/kg/d K or Na citrate in Ca stone disease

Type 2 RTA (Proximal)	Proximal reabsorption of HCO ₃	Low	<5.3	Positive	NaHCO ₃ or K-citrate (10-15meq/kg/d), Thiazide
Type 4 RTA	Distal Na reabsorption, K secretion and H secretion	High	<5.3	Positive	*Fludrocortisone (0.1-0.5mg/dl), dietary K restriction, furosemide, NaHCO ₃

* Patient should not be hypertensive or volume overloaded.

REFERENCES:

- 1) Mcphee, Papadakis, Tierney. Fluid and Electrolyte Disorders. Current Medical Diagnosis and Treatment. 46th ed: 910-913
- 2) Goldman. Acid base disorders. Cecil Textbook of Medicine. 22nd ed.W.B.Saunders; 2004.
- 3) Battle, DC, Hizon, M, Cohen, E, et al. The use of the urine anion gap in the diagnosis of hyperchloremic metabolic acidosis. N Engl J Med 1988; 318:594.
- 4) Halperin, ML, Vasuvattakul, S, Bayoumi, A. A modified classification of metabolic acidosis. A pathophysiologic approach. Nephron 1992; 60:129.
- 5) Rose, BD, Post, TW, Clinical Physiology of Acid-Base and Electrolyte Disorders, 5th Ed, McGraw-Hill, New York, 2001, pp. 590-592.
- 6) Oh, M, Carroll, HJ. Value and determinants of urine anion gap. Nephron 2002; 90:252.
- 7) Brenner. Acid Base Disorders. Brenner & Rector's. The Kidney. 7th ed. 2004. Saunders
- 8) Hall, Schmidt, Wood. Acid Base Balance. Principles of Critical Care. 3rd Ed, 2005.McGraw- Hill, 1205-1206.

- 9) Cogan MG: Fluid and electrolytes: Physiology and Pathophysiology. McGraw-Hill, 1991.