Pseudohypobicarbonatemia Associated with Hypertriglyceridemia-Induced Acute Pancreatitis: A Case Report

Lutfun Nahar Nizhu[1], Ahmad Mursel Anam[2], Raihan Rabbani[3]

[1.] Specialist, Acute Medicine & HDU, Square Hospitals Ltd.
[2.] Associate Consultant, Acute Medicine & Critical Care, Square Hospitals Ltd.
[3.] Senior Consultant, ICU, Square Hospitals Ltd.

Case Report

Received: September 09, 2024
Revised: October 07, 2024
Accepted: December 12, 2024

*Corresponding Author:

Dr. Lutfun Nahar Nizhu
Specialist
Acute Medicine and HDU
Square Hospitals Ltd.
18/F Qazi Nuruzzaman Sarak, Dhaka 1205, Bangladesh.
E-mail: oporajita84@gmail.com

ABSTRACT:

Pseudohypobicarbonatemia or factitious low serum bicarbonate level caused by an interfering substance is rare. We describe a patient who presented with severe hypobicarbonatemia along with high anion gap. She also had profound hyperlipidemia. A reanalysis of blood samples after lipid removal using the dilution method showed marked improvement in the bicarbonate level. The light scattering effect of hyperlipidemia interfered with the photometric analysis by the automatic analyzer of the laboratory causing this factitious phenomenon.

Key words: Pseudohypobicarbonatemia, Hypertriglyceridemia-induced acute pancreatitis, Metabolic acidosis

INTRODUCTION:

Hypobicarbonatemia with an elevated anion gap on a metabolic panel is often the first sign of a life-threatening condition.[1] Lipemia may cause factitiously low serum bicarbonate levels with high anion gap.

Here we present a case where a patient had a very low serum bicarbonate level, but normal in ABG. The discrepancy between the acidosis observed in the metabolic panel and the ABG was due to the fact that high levels of lipids in the blood may disrupt the accurate measurement of bicarbonate levels, leading to falsely low results.[2] Most laboratories measure bicarbonate levels using either an enzymatic/spectrophotometric or an indirect ion-selective electrode method, both of which can be affected by the light-scattering effect of hyperlipidemia. However, the ABG analyzer uses a direct ion-selective electrode method, which isn't susceptible to the errors associated with a photometric analyzer.

Understanding the impact of conditions like hypertriglyceridemia on electrolytes measurement is crucial in clinical practice, helping to avoid unnecessary investigations and interventions.

CASE REPORT:

A 44-year-old female, a known case of diabetes mellitus and dyslipidemia was admitted with severe abdominal pain and vomiting for one day. On admission, the patient was tachycardic (111 beats/min), normotensive and afebrile. Abdominal examination revealed epigastric tenderness Grading 4. Laboratory investigations revealed elevated lipase (6558 U/L, normal range 23-300 U/L). The patient's blood sample is lipemic and her lipid panel showed a very high triglyceride level (35890mg/dL). USG showed a swollen pancreas. She was diagnosed with hypertriglyceridemia-induced acute pancreatitis. The bicarbonate level measured as electrolytes (TCO_2) was undetectable (<5mmol/L), but the bicarbonate (HCO_3) levels on arterial blood gases were normal at 23 mmol/L.

We treated her with intravenous normal saline at 125 – 250 mL/hour and intravenous insulin at 0.2 units/kg/hour[3,4]. However, her metabolic derangements were puzzling, since the TCO_2 was undetectable on serum electrolytes, but the HCO_3 was normal on the blood gas

analysis. In the absence of any apparent explanation for a decrease in serum bicarbonate with a high anion gap, despite extensive work-up, we doubted the validity of the laboratory testing.

Our collaboration with laboratory scientists and extensive literature search revealed that hypertriglyceridemia can affect bicarbonate measurement using the laboratory's spectrophotometric analysis method by auto analyzer even using the most upgraded machine, VITROS XT 7600. Conditions like hypertriglyceridemia may cause a light-scattering effect, leading to falsely low bicarbonate readings which is also called pseudohypobicarbonatemia.

The patient's condition worsened, and she developed shock and ARDS. As a result, she was transferred to the ICU and placed on mechanical ventilation. A CT of the abdomen revealed necrotizing pancreatitis. Plasma exchange was initiated to lower her triglyceride levels. Additionally, she developed acute kidney injury (AKI) with anuria and severe metabolic acidosis, necessitating hemodialysis. Unfortunately, the patient passed away seven days after being admitted to the hospital.

DISCUSSION:

Three mechanisms are involved in lipemia interference when analyzing blood samples: light scattering, volume displacement effect, and lack of sample homogenization.[5,6]

Light scattering by lipoproteins

Lipemia interferes with electrolyte measurements by causing light scattering due to lipoproteins, particularly chylomicrons and very low-density lipoprotein (VLDL). The interference in spectrophotometric methods depends on the method used and the wavelength at which absorbance is measured. As a result, interference from lipemia may not be the same between different analytical methods.[7,8]

Volume displacement effect

This mechanism has a strong impact on the determination of electrolytes. Most auto analyzers measure electrolytes concentrations using indirect ion-selective electrodes. The result is calculated based on the serum or plasma matrix composition, which is 92% aqueous phase and 8% solid phase. In samples with high-fat content, the aqueous phase decreases, leading to an underestimation of constituents like electrolytes distributed in this phase. This effect is referred to as the "volume displacement effect". [9-11]

Lack of sample homogenization

This effect is caused by the difference in density of particles in serum or plasma samples. When centrifuged, chylomicrons and VLDL will be found at the top of the tube due to their low density, while the rest of the components will distribute based on their polarity. Hydrophobic components will be in the lipid phase at the top of the tube, while hydrophilic components will be in the aqueous phase at the bottom of the tube. Analyzers use sensors to ensure that the needle does not penetrate too deeply into the tube to obtain a sample from the upper part of the tube, as this could lead to a falsely decreased concentration of hydrophobic electrolytes.[5,6]

Lipemia removal methods

Centrifugation methods

Serum/plasma centrifugation is the method of choice for removing lipemia. Sample ultracentrifugation (100,000–2,000,000×g) removes lipids effectively and facilitates analyte determination.[12,13] However, large lipoproteins (chylomicrons) can be separated in serum/plasma by high-speed centrifugation (10,000–15,000×g).[14,15] When lipemia is caused by VLDL accumulation, the procedure is less effective. After high-speed centrifugation, a lipid layer forms in the upper part, and the infranatant is collected using a glass pipette with care not to contaminate the sample with the lipid layer. Biochemical quantities are measured in the infranatant. This method is not appropriate for hydrophobic substances (hormones and drugs, among others), since they would distribute across the lipid layer and measurement in the infranatant would give falsely low results.

Dilution or replacement methods

To reduce or eliminate the concentrations of an interferent in serum or plasma, especially in lipophilic components that can diffuse significantly in the lipid phase, the sample should be diluted. This will reduce the interference from lipemia to below the relevant limit but not excessively to keep the component concentration within the limit of quantification. A useful strategy to reduce interference in blood samples is to replace plasma with an equal volume of isosmotic dilutant. However, it's important to note that this method may lead to misleading results due to possible cell loss during replacement.

At our hospital, we utilize the VITROS XT 7600 for biochemical analysis. This system employs the latest microslide technology and utilizes the spectrophotometric method for biochemical analysis. It includes a spreading layer designed to remove triglycerides from lipemic samples; however, in cases of highly turbid samples, a viscosity error may occur. In severe hypertriglyceridemia to ensure accurate reporting of triglyceride and electrolyte levels, our lab technicians employ the dilution method.

CONCLUSION:

The case demonstrates the importance of understanding a laboratory error that occurs with certain analyzers. It emphasizes the need for physicians to be aware that high triglycerides can cause artificially low bicarbonate levels, potentially leading to misdiagnosis and unnecessary treatment with side effects. This factor should be considered when low bicarbonate levels have no clear explanation and when there is a difference between bicarbonate levels measured on metabolic panels and those calculated by arterial blood gas tests.

ACKNOWLEDGMENT:

We would like to express our gratitude to Md. Maksuduzzaman, the laboratory coordinator of Square Hospitals, for his collaborative efforts in analyzing lipemic samples and providing detailed information about the technology of the analyzer machine. His expertise has significantly helped us.

REFERENCES:

1. Garg D, Chatterjee T: A case of profound hypertriglyceridemia causing pseudohypobicarbonatemia. Cureus. 2023, 15: e37489. 10.7759/cureus.37489
2. Rifkin SI, Shaub B: Factitious hypobicarbonatemia associated with profound hyperlipidemia. Ren Fail. 2014, 36:1155-7. 10.3109/0886022X.2014.917945
3. Marić N, Mačković M, Bakula M, et al. Hypertriglyceridemia-induced pancreatitis treated with continuous insulin infusion-Case series. Clin Endocrinol (Oxf) 2022; 96:139.
4. Rawla P, Sunkara T, Thandra KC, Gaduputi V. Hypertriglyceridemia-induced pancreatitis: updated review of current treatment and preventive strategies. Clin J Gastroenterol 2018; 11:441.
5. Prendes CF, Castro MJ, Navarro LS, Mas LR Indiano CM, Velilla TA. Handling of lipemic samples in the clinical laboratory. Advances in Laboratory Medicine, (2023) 4(1), 5-15. https:// doi.org/10.1515/ almed-2023-0003
6. Farrell CJ, Carter AC. Serum indices: managing assay interference. Ann Clin Biochem 2016; 53:527–38.
7. Nikolac N. Lipemia: causes, interference mechanisms, detection and management. Biochem Med 2014; 24:57–67.
8. Kroll M. Evaluating interference caused by lipemia. Clin Chem 2004;50: 1968–9.
9. McCarron EP, Murray E, McKeeman GC, Coward SM, Hamilton P, Connolly G, et al. Investigating the effects of endogenous lipaemia on the measurement of sodium by indirect ion specific electrode potentiometry. Ann Clin Biochem 2022; 59:324–9.
10. Goyal B, Datta SK, Mir AA, Ikkurthi S, Prasad R, Pal A. Increasing glucose concentrations interfere with estimation of electrolytes by indirect ion selective electrode method. Indian J Clin Biochem 2016; 31:224–30.
11. Koch CD, Vera MA, Messina J, Price N, Durant TJS, El-Khoury JM. Preventing pseudohyponatremia: intralipid®-based lipemia cutoffs for sodium are inappropriate. Clin Chim Acta 2021; 520:63–6.
12. Calmarza P, Cordero J. Lipemia interferences in routine clinical biochemical tests. Biochem Med 2011; 21:160–6.
13. Soh SX, Loh TP, Sethi SK, Ong L. Methods to reduce lipemic interference in clinical chemistry tests: a systematic review and recommendations. Clin Chem Lab Med 2021; 60:152–61.
14. Dimeski G, Jones BW. Lipaemic samples: effective process for lipid reduction using high speed centrifugation compared with ultracentrifugation. Biochem Med 2011; 21:86–92.
15. Castro-Castro MJ, Candás-Estébanez B, Esteban-Salán M, Calmarza P, Arrobas-Velilla T, Romero-Román C, et al. Removing lipemia in serum/plasma samples: a multicenter study. Ann Lab Med 2018;38: 518–23.