AJMB
Avicenna Journal of Medical Biochemistry
Avicenna J Med Biochem, 2023; 11(1):98-99. doi:10.34172/ajmb.2023.2407
http://ajmb.umsha.ac.ir

Letter to Editor

Reverse Pseudohyperkalemia: A Biochemist's Perspective

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Received: December 28, 2022 **Revised:** January 20, 2023 **Accepted:** January 20, 2023 **ePublished:** March 18, 2023

Please cite this article as follows: Balasundararaj D. Reverse pseudohyperkalemia: a biochemist's perspective. Avicenna J Med Biochem. 2023; 11(1):98-99. doi:10.34172/ajmb.2023.2407

To Editor,

Hyperkalemia is a life-threatening condition as it leads to a disturbance in the electrical conductivity of the heart and causes arrhythmias. This electrolyte abnormality is commonly seen in hematological malignancies due to tumor lysis. Hence, monitoring of potassium levels is often required in patients with these types of malignancies. The often disregarded problem during the estimation of potassium is reverse pseudohyperkalemia. It is a condition where the potassium levels are falsely elevated in plasma but are within the normal reference range in serum. This is in contrast to pseudohyperkalemia where the potassium levels are normal in plasma but falsely elevated in serum (1).

Reverse pseudohyperkalemia is mostly observed in chronic lymphocytic leukemia patients with elevated white blood cell (WBC) count when a blood sample is collected in heparin tubes for potassium estimation (2). However, we encountered a scenario in our laboratory where there was a spurious elevation in potassium levels in the plasma sample of a 62–year-old male diagnosed with mantle cell lymphoma with a WBC count of 401.4×10^3/uL. As the patient was ambulatory and stable without the clinical signs of hyperkalemia, to exclude interference due to preanalytical causes, a second sample was analyzed for potassium, the level of which was found to be spuriously elevated (Table 1).

One of the common causes of elevated potassium often encountered in laboratories is hemolysis (3). In our scenario, both samples were free from hemolysis after centrifugation at 3500 rpm for 10 minutes. Nevertheless, both samples were sent to the laboratory through a pneumatic tube in lithium heparin vacutainers. To substantiate that hyperkalemia was caused by WBC lysis, blood samples were drawn from the patient in both lithium heparin and serum tubes and manually transported to the laboratory. During analysis, the serum potassium level was within the normal reference range, but the plasma potassium level, even though elevated, was not to the extent of the previous sample (Table 1). This ascertained that hyperkalemia could occur due to fragile WBCs in hematological malignancies, which are vulnerable to lysis due to mechanical stress in the form of pneumatic tube transfer and the centrifugation of the sample (4). Unlike plasma, the degree of WBC lysis in serum drastically reduced as the fibrin meshwork entrapped the WBCs and provided a cushioning effect during centrifugation (5). Moreover, the heparin present in the plasma tube also increased the fragility of the WBC membrane and promoted lysis (6). In many clinical chemistry laboratories, plasma tubes are preferred for sample collection to decrease the turnaround time. However, it is necessary for laboratories to reconsider their decision before switching over to plasma tubes completely because of the potential problem of reverse pseudohyperkalemia in hematological malignancies.

As biochemists, we routinely come across falsely elevated potassium levels due to preanalytical factors such as traumatic venipuncture, forceful transfer of blood sample from the syringe to a vacutainer, and vigorous shaking of sample tubes. Reverse pseudohyperkalemia as a cause of elevated potassium is seldom encountered in clinical laboratories. The undue elevation of potassium levels in our patient's heparin sample prompted us to investigate further and enabled us to come to an appropriate diagnosis, which would have been overlooked if the elevation in potassium was mild. Hence, from the experience we had in our laboratory, the following

Table 1. Potassium Values Obtained during Analysis for Various Samples

Sample 1 (Heparin Tube) - Pneumatic Transfer	Sample 2 (Heparin Tube) - Pneumatic Transfer	Sample 3 (Heparin Tube)- Manual Transfer	Sample 4 (Red Top Vacutainer) - Manual Transfer
17.36 mmol/L	16.33 mmol/L	9.54 mmol/L	5.25 mmol/L

Note. All analytical values were cross verified by analysing in two different analysers. The estimation of potassium was done in blood gas and electrolyte analyzers based on direct ion selective electrode method.

recommendations are proposed.

- Laboratories should formulate a policy to collect samples for potassium estimation in serum tubes from patients with hematological malignancies to avoid inappropriate treatment measures.
- Laboratories must re-evaluate, before completely replacing serum tubes with plasma tubes to improve the turnaround time of the tests.
- Medical laboratory technicians must be educated regarding the prevalence of such a rare phenomenon at regular intervals.

Competing Interests

The author declares that there is no conflict of interests to declare.

Ethical Approval

None to be declared.

Funding

No funding was received.

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