

### **CASE-3: Dr. Hani Ajrina Zulkeflee, Dr Wan Nur Aimi Wan Mohd Zamri, Dr Siti Nadirah Ab Rahim, Dr Wan Nor Fazila Hafizan Wan Nik and Dr Razan Hayati Zulkeflee**

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#### Case History

A 31-year-old lady presented with infected burn injuries. Her past medical history was unremarkable. During the admission, her laboratory results showed persistent hyperkalaemia while the patient remained asymptomatic. The serial laboratory results were:



Mode of sample transportation	Date	Type of sample	Haemolysis index	Potassium concentration	Lactate dehydrogenase	Total white cell count
	Hospital A (reference range)			3.4 – 4.5 mmol/L	< 247 U/L	4.0 – 10.00 X 10 <sup>9</sup> /L
Pneumatic tube system	14/1/2023	Plasma	NIL	13.6	-	1262
	15/1/2023		NIL	7.5	1709	-
	17/1/2023		1+	19.3	2430	-
	17/1/2023	Serum	NIL	6.6	-	-
Manual transport by hand	Hospital B (reference range)			3.4 – 4.5 mmol/L	120 – 246 U/L	4.078 – 11.37 K/uL
	20/1/2023	Plasma	NIL	8.6	1291	483.7
	11/4/2023		NIL	4.2	319	18.5
	19/6/2023		NIL	3.8	255	3.4

### Questions

1. What possibilities could you offer to explain the potassium results?
2. How to investigate the results?
3. What further tests to confirm the patient's diagnosis and what is the underlying mechanism related to hyperkalaemia?
4. What is the best advice to clinicians when dealing with hyperkalaemia in this case?

### Discussion

#### Question 1

Serial potassium results showed hyperkalaemia, which is diagnosed when the potassium concentration is above 5.0 mmol/L. It is particularly concerning when the level rises above 6.5mmol/L due to its potential cardiotoxicity risks.<sup>1</sup>

The patient showed no symptoms of hyperkalaemia such as palpitation, chest pain and muscle weakness. Her electrocardiography results showed no tall and tented T wave, shortened QT interval, widened QRS complex or absent T wave. Thus, pseudo-hyperkalaemia is suspected.

Pseudo-hyperkalaemia refers to an erroneous hyperkalaemia and it poses a significant challenge in the accurate determination of potassium concentration.<sup>2</sup> Upon receiving hyperkalaemic results, the attending physicians are warranted to decide promptly, and this may result in injudicious administration of potassium-lowering therapies.

The possible causes of pseudo-hyperkalaemia include:

- Haemolysis of red blood cells (e.g. difficult venepuncture, improper specimen handling)
- In vitro leakage from other blood cells (e.g. thrombocytosis, leucocytosis)
- Potassium contamination (e.g. EDTA tube sampling, sampling at the same side of intravenous fluid).<sup>1</sup>

## Question 2

Timely identification of pseudo-hyperkalaemia is crucial to prevent the administration of inappropriate treatments. A combination of severely elevated potassium concentrations reaching levels incompatible with life and asymptomatic presentation raises the suspicion of pseudohyperkalaemia.<sup>2</sup> This shall be confirmed with a repeat sampling. Alternatively, utilizing a direct ion-selective electrode method through a blood gas analyser for the measurement of whole blood potassium offers a swift method to identify true hyperkalaemia, as it bypasses the technical processing of a patient's sample.<sup>3</sup>

Red blood cell haemolysis is the predominant preanalytical factor leading to pseudo-hyperkalaemia. Any reported potassium concentration surpassing the reference range necessitates an accompanying assessment of the haemolysis index (H-index).<sup>4</sup> Most of her results exhibited a negative haemolysis index, effectively ruling out haemolysis as the contributing factor.

Reflex testing with serum calcium, magnesium, and alkaline phosphatase (ALP) helps mitigate the risk of K<sup>2</sup>-EDTA contamination. EDTA selectively chelates divalent cations, such as calcium and magnesium, leading to hypocalcaemia and hypomagnesaemia, respectively. Indirectly, depletion of these ions renders them inaccessible for various enzymatic reactions. For instance, ALP requires magnesium and zinc as the enzyme cofactors. Thus, this elucidates the observed low concentrations of ALP in samples contaminated with EDTA.<sup>5</sup>



Simultaneous measurement of serum and plasma potassium is beneficial for further investigation of its underlying cause. Reverse pseudo-hyperkalaemia refers to an elevated plasma potassium concentration compared to the serum levels observed in the presence of significant leucocytosis.<sup>6</sup> Conversely, thrombocytosis leads to an increased measured serum potassium due to the release of potassium by platelets during the clotting process.<sup>7</sup>

Figure 1 depicts the proposed stepwise laboratory approach to hyperkalaemia, aiming for the early detection of erroneous results.

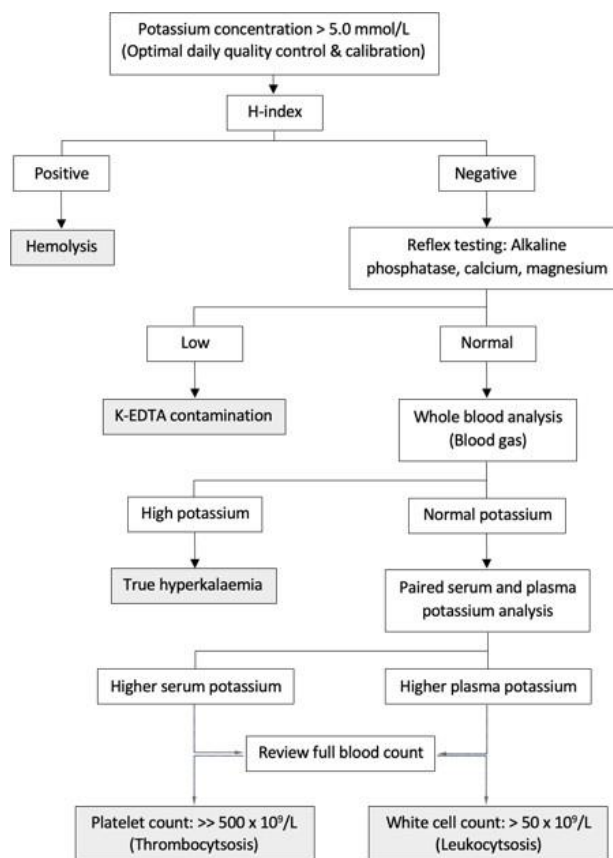


Figure 1: Diagnostic algorithm on approach to pseudohyperkalaemia

### Question 3

Urgent blood film and bone marrow biopsy confirmed a diagnosis of Chronic Lymphocytic Leukaemia (CLL).

Dysplastic leukocytes in leukaemia are easily ruptured during sample centrifugation due to an increased in the membrane fragility. CLL for example, has cytoskeletal defects on its lymphocytes and this is manifested as smudge cells on peripheral blood film. In the presence of hyperleukocytosis, in vitro lysis of CLL lymphocytes can lead to the spurious hyperkalaemia.<sup>2, 4</sup>

Serum potassium measurement yields a lower result as the fibrin clot in the serum captures and stabilizes delicate tumour cells during sample centrifugation, consequently minimizing the release of potassium from the cells.<sup>7</sup>

The pneumatic tube system is not an appropriate method for sample transport in this case due to the additional mechanical force exerted on the fragile leukemic cells. This is evident in the higher reported potassium concentration compared to the specimens transported manually by hand.

Chemotherapy was commenced, and serial laboratory results showed reduction of white blood cell count along with plasma potassium levels. This showed that the magnitude of potassium elevation is proportional to the white cell counts as we can see the normalization of plasma potassium is achieved when the white cell counts reduced.

	19/1/2023	15/2/2023	9/3/2023	11/4/2023	12/5/2023
WBC count (4.078 - 11.37 K/uL)	494.3	476.1	414.3	18.5	2.8
Plasma potassium (3.4 - 4.5 mmol/L)	7.7	5.7	4.9	4.2	3.9

#### Question 4

This case highlights the importance of recognizing pseudo-hyperkalaemia in patients with extreme hyperleukocytosis. This awareness is essential to prevent iatrogenic hypokalaemia and ensure prudent patient management. The significance of identifying pseudo-hyperkalaemia is particularly emphasized in this patient, as accurate electrolyte monitoring is crucial to assess the risk of tumour lysis syndrome during her chemotherapy treatment.<sup>2,4</sup>

The most suitable method for monitoring the patient's potassium levels is through whole blood potassium analysis using a direct ion-selective electrode method through the blood gas analyser.<sup>3,8</sup> This approach aids in distinguishing between true and erroneous hyperkalaemia. Additionally, it is imperative for clinicians to correlate blood test results with clinical findings. Effective communication between clinicians and laboratory personnel becomes essential when reported results show discrepancies.



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