CASE REPORT

Normokalemia in Grossly Haemolysed Samples

Salbiah Isa[1], Norizati Razali[2], Mohd Jamsani Mat Salleh[2]

[1] Life Style Science Cluster, Advanced Medical and Dental Institute (IPPT), Universiti Sains Malaysia, 13200 Kepala Batas, Pulau Pinang, Malaysia.
[2] Department of Pathology, Hospital Pulau Pinang, Jalan Residensi, 10990 Georgetown, Pulau Pinang, Malaysia.

ABSTRACT

Haemolysis interferes with many test results through release of red blood cell (RBC) intracellular contents or via specific analytical interferences. In grossly haemolysed sample, potassium level can be raised considerably dependent on the degree of haemolysis and may exceed the critical limit value. In this case report, the potassium level from a grossly haemolysed sample taken after haemodialysis remains within normal range, and this has led to unnecessary repeated blood samplings hence delay the diagnosis. With the persistently high haemolytic index (HI) of ≥ 400mg/dL and normal potassium levels in sequences of samples taken post haemodialysis should raise a high suspicion of in vivo haemodialysis related-haemolysis. An effective communication between laboratory and clinician, and a proper, well-designed protocol or guideline on the management of sample haemolysis in clinical laboratory therefore is very essential to ensure all clinically important but rare case of in vivo haemolysis can be identified early and the potential unwanted serious outcomes can be prevented accordingly.

Keywords: Haemolysed, Haemolysis, in vivo, Haemodialysis, Haemolytic index

Corresponding Author:
Salbiah Isa, M.PATH
Email: salbiahisa@usm.my
Tel: +604-5622291

INTRODUCTION

Haemolysis (or hemolysis) is recognised as the most common cause of sample rejection in many clinical laboratories. Haemolysis interferes with many test results through release of RBC intracellular contents or via specific analytical interferences such as through chemical or spectrophotometric interference, causing inaccurate measurement of some analytes (1).

Based on the concentration of free haemoglobin in the sample, haemolysis is usually graded as mild, moderate and gross. Historically, the degree of haemolysis is determined by manual inspection of the density of red colour changes of the plasma or serum sample. However, with the advance in technology, a more efficient quantitative measurement of free haemoglobin by automation became available and has been practiced in some clinical laboratories.

The type of analytes affected, and the extent of interferences are determined by the degree of haemolysis. However, the cut off or the range of free haemoglobin concentration in different categories of haemolysis can vary among laboratories due to different in the instruments and laboratory protocol used.

One of the analytes which has considerable clinical impact by the haemolysis is potassium. Based on the laboratory's method (Roche Cobas e702 ISE), potassium result can be affected even with mild haemolysis (defined as HI of ≥ 90 mg/dL). Therefore, in grossly haemolysed sample with HI ≥ 400 mg/dL, the level of potassium is expected be considerably raised, sometimes can be up to critical limit values.

In this case report, we highlight a case of end stage renal failure (ESRF) patient, whose potassium results were remained within normal range despite of grossly haemolysed samples.

CASE REPORT

A 73-year-old gentleman with ESRF on regular haemodialysis and underlying multiple medical illness (diabetes mellitus, hypertension, dyslipidaemia and benign prostate hyperplasia) presented with lethargy, vomiting, and diarrhea. He also complained of dark colored urine and facial and body redness. His last haemodialysis session was 4 hours prior to his presentation. Physical examination revealed systolic hypertension, hyperthermia, facial and body flushing

(described as 'lobster appearance') and there was also an infected scalp sebaceous cyst. The first blood sample for biochemistry tests sent from hospital emergency department was noted to be grossly haemolysed with HI of 3386 mg/dL. As according to the laboratory's protocol, the sample was rejected, therefore no result was generated. However, a suggestion to repeat the test with a new blood sample and a brief guideline on the correct phlebotomy technique were included in the laboratory report.

The second (repeat) blood sample was also noted to be grossly haemolysed. Similar outcome was observed for subsequent samples received from the wards. Within 24 hours of admission, the patient had a total of 7 blood takings for biochemistry tests and all were rejected and not reported due to gross haemolysis. In view of persistent gross haemolysis and unreportable results, the case was referred to the pathologist in charged whereby the blood withdrawal was instructed to be withheld until the next day.

On the next day (after 24 hours admission), the 8th and subsequent blood samples showed better quality with reducing HI (Figure 1). Upon improvement of the HI, biochemistry test results were then reported to clinician as requested. Patient's biochemistry results (potassium, LDH, Bilirubin), respective HI and Hb level of the first 10 consecutive samples are tabulated in Table I.

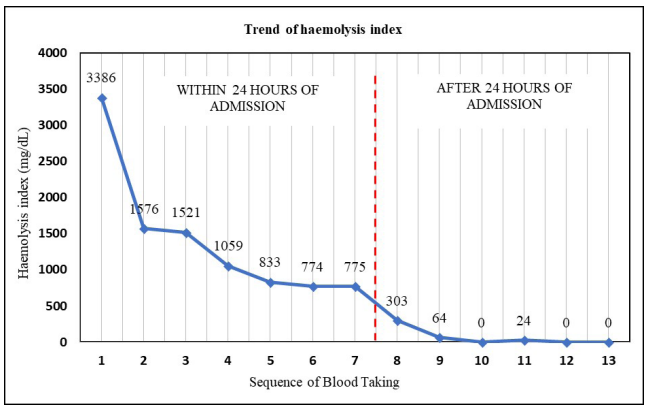

Figure 1: Trend of Haemolytic Index (HI) in Sequences of Blood Samples

Despite of raised LDH and Bilirubin, and low Hb level, the patient's reticulocytes count was within the normal range i.e. 2.65% (Ref range: 0.5 – 25.5%). Full blood picture (FBP) showed evidence of infection or inflammation with no fragmented cells. The Direct Antiglobulin Test (DAT) was weakly positive.

Based on the patient's presentation and his blood tests results, a diagnosis of haemodialysis related-haemolysis was made to explain the patient's 'lobster appearance' and persistent grossly haemolysed samples. He was closely monitored for any potential complication of haemodialysis related-haemolysis and underwent his pre-scheduled haemodialysis sessions in the hospital's haemodialysis unit with close observation. The infected sebaceous cyst over the scalp was treated with antibiotics. His hospitalization course was uneventful, and his symptoms were gradually improved. An investigation was carried out to find the possible factor that induced the haemodialysis related-haemolysis, however the detail report was still in progress at the time the patient was discharged from the hospital on the tenth day of admission.

DISCUSSION

Haemolysis is the most common cause of compromised sample encountered in laboratory. As according to World Health Organization (WHO) recommendation, most laboratories opt to reject grossly haemolysed samples to avoid inaccurate result being reported to clinician. However, not all haemolysed samples encountered in clinical laboratory are related to improper phlebotomy technique. A small number of cases can be attributed by a more serious and fatal in vivo haemolysis, which contribute to about 3.2% of all haemolysed samples received in the laboratory (1). Therefore, it is important to be aware that simply rejecting grossly haemolysed samples are not appropriate in some cases.

In vivo haemolysis is usually characterized by a significant raise of LDH, reduced haptoglobin, evidence in FBP, reticulocytosis and persistent hemolysis in multiple samples taken at different collection times and tubes. Among the identified cause include medical conditions with antigen-antibody reaction, haemolytic

Table I: Biochemistry, haemolysis index and Hb results of the first 10 consecutive samples

Analyte	Unit	Reference range	Sequence of blood taking									
			1	2	3	4	5	6	7	8	9	10
K	mmol/L	3.5 – 5.1	3.8	3.3	3.5	3.7	3.3	3.3	3.6	3.1	2.9	3.2
T. BILI	µmol/L	0 – 24	-	-	90	-	217	216	220	148	73	-
D.BILI	µmol/L	< 5	-	-	14	-	61	63	62	62	44	-
LDH	U/L	135 – 225	-	-	-	3636	3668	3701	3335	2947	2558	-
Hb	g/dL	13 – 17	11.7	9.9	10.8	9.2	9.3	8.0	8.2	-	-	8.4
HI	mg/dL	<15	3386	1576	1521	1059	833	774	775	303	64	0

K=Potassium, T.Bili=Total Bilirubin, D.Bili=Direct Bilirubin, LDH=Lactate Dehydrogenase, Hb=Haemoglobin, HI=Haemolytic index

anaemia, drugs, toxins, and mechanical RBC rupture due to artificial heart valve, haemodialysis, and use of heart-lung bypass machine (2). In our case, as the patient developed haemolysis after haemodialysis session, the persistently gross haemolysis with characteristic pattern of biochemistry and haematology test results should raise a high suspicion of haemodialysis-related in vivo haemolysis.

However, despite of having HI > 400 mg/dl, raised LDH and bilirubin and low Hb levels, the suspicion of in vivo haemolysis in this case was attenuated by the patient's normal potassium levels. In some cases of in vivo haemolysis, the efficiency of potassium-regulating system in the body may quickly normalize serum potassium to prevent hyperkalemia (3). However, it is uncertain if the cause for the normal potassium level seen in the patient throughout the hospital stay can be explained by the above mechanism in view of the patient's compromised renal regulatory status. As the patient had vomiting and diarrhoea, potassium loss might has occurred, and this can be part of the cause a 'normal' potassium level. Other contrary finding seen in this case concerning in vivo haemolysis is normal reticulocytes count. This probably could be due to inadequacy of compensatory reticulocytosis in the presence of infection and iron deficiency in the setting of end stage renal failure (4).

Haemolysis related-haemodialysis is a rare life-threatening condition. Most patients usually presented with non-specific signs and symptoms i.e. nausea, pain (abdominal, chest, back), shortness of breath and hypertension (5). Its low prevalence of occurrence and non-specificity of the patient's clinical presentations may also be the factors which contributed to the difficulty and delay in its detection such as seen in our case. This was further complicated by lack of effective communication between the laboratory and the clinicians that lead to unnecessary, time consuming and distressing repetitive blood takings and unreportable laboratory results.

To ensure all the clinically important haemolytic disorders such as haemodialysis related-haemolysis to be identified early, a systematic and well-designed approach in the management of haemolysed sample is therefore required in clinical laboratories. Until a standard guideline is available, the protocol can be established locally through consensus between the laboratory and the clinicians. Effective communication and good liaison between the laboratory and the clinicians will also ensure all clinically important haemolysis cases are promptly discovered and the relevant laboratory results are appropriately reported for the best of the patient care.

CONCLUSION

Sample haemolysis is commonly encountered problem in medical laboratory and contribute to the most common cause of sample rejection. A proper and standard guideline in the management of haemolysed sample is therefore required for efficient detection of serious case of in vivo haemolysis, consequently prevent the risk of unnecessary intervention and possible life-threatening complications to the patient.

ACKNOWLEDGEMENT

All those involved in writing of this case report.

REFERENCES

1. Thomas L. Haemolysis as influence and interference factor. eJIFCC vol 13 no 4. Available from http://www.ifcc.org/ejifcc/vol13no4/130401002.htm.
2. Effects of Haemolysis on Clinical Specimens. Calgary Lab Services.Com. Available from http://www.calgarylabservices.com/lab-services-guide/specimen-collection/hemolysis.aspx.
3. Mary M. Barrett, Y. Victoria Zhang. Clinical Normal Potassium in the Presence of Gross Hemolysis. Chemistry. 2015;61 (8):1114-15.
4. Barcellini W, Fattizzo B. Clinical Applications of Hemolytic Markers in the Differential Diagnosis and Management of Hemolytic Anemia. Disease Markers. 2015;2015. 635670. Available from, DOI: 10.1155/2015/635670
5. Tharmaraj, D. and Kerr, P. G. Haemolysis in haemodialysis. Nephrology. 2017;22(11) 838-47.