Case Report

Lipemia-Induced Hemoglobin Overestimation and Correction by Plasma Replacement in a Pediatric Acute Lymphoblastic Leukemia Patient

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Keywords

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Abstract

Background: Pre-analytical and analytical errors in laboratory testing can lead to clinical misinterpretation. This case highlights a falsely elevated hemoglobin level due to lipemia and the corrective laboratory intervention.

Case: A 3-year-7-month-old girl with acute lymphoblastic leukemia underwent a follow-up complete blood count which reported a hemoglobin level of 16.9 g/dL. The hemoglobin result was inconsistent with previous clinical findings and hematocrit. A simultaneously drawn venous blood gas sample showed a hemoglobin value of 9.2 g/dL. The biochemistry sample showed visible lipemia, with a lipemia index of 3041. The same sample revealed a triglyceride level of 8042 mg/dL (1:50 dilution) and total cholesterol of 492.2 mg/dL. These findings indicated a falsely elevated hemoglobin due to lipemia. The patient was not on parenteral nutrition. Pediatric endocrinology consultation attributed lipemia to L-asparaginase and corticosteroids in the treatment regimen. To eliminate lipemic interference, the EDTA blood sample was centrifuged at 1000 x g for 10 minutes, and the lipemic plasma was replaced with an equal volume of 0.9% NaCl solution. The sample was gently mixed to restore whole blood integrity. After this plasma replacement procedure, hemoglobin was measured as 10.2 g/dL, consistent with the blood gas result and clinical picture.

Conclusion: This case emphasizes the need to correlate laboratory results with clinical and biochemical data. In lipemic samples, plasma replacement may provide a practical correction method for falsely elevated hemoglobin values when resampling is not feasible. Recognition and prompt correction of lipemia-induced errors are crucial to avoid inappropriate clinical decisions.

Introduction

In laboratory medicine, pre-analytical and analytical errors can significantly compromise the accuracy of test results, potentially leading to misdiagnosis, delayed treatment, or inappropriate clinical decisions. The reliability of laboratory findings is particularly critical in guiding the diagnosis, monitoring, and management of patients. Ensuring analytical precision is therefore essential for optimal patient outcomes [1].

Lipemia refers to visible turbidity of serum or plasma caused by an elevated concentration of large lipoprotein particles, especially chylomicrons and very low-density lipoproteins (VLDL). This accumulation causes visible turbidity which interferes with optical measurement techniques commonly used in clinical chemistry and hematology analyzers. Spectrophotometric readings can be affected by light scattering, and automated cell counters may also be influenced by changes in the sample's refractive index, leading to potential errors in test results [1,2]. In the context of complete blood count (CBC) testing, lipemia can cause false elevation of hemoglobin (Hb) values. Since mean corpuscular hemoglobin concentration (MCHC) and mean corpuscular hemoglobin (MCH) are calculated parameters derived in part from Hb, such interference can lead to inaccurate red blood cell indices as well [3].

Case Presentation

A 3-year-7-month-old girl diagnosed with acute lymphoblastic leukemia (ALL) was undergoing induction chemotherapy according to Protocol 1A, which included dexamethasone, vincristine, daunorubicin, and L-asparaginase. She was also receiving multiple supportive medications, including piperacillin-tazobactam, amikacin sulfate, pantoprazole, azithromycin, fluconazole, calcimax, and vitamin D.

During routine follow-up, a CBC analyzed using the Sysmex XN-1000 showed a Hb value of 16.9 g/dL, which was markedly inconsistent with the clinical picture and with previous hematologic data. Two days earlier, Hb had been reported as 10.7 g/dL. The discrepancy was confirmed during specialist validation approximately two hours after sampling. A simultaneously drawn venous blood gas sample, analyzed on the ABL90 FLEX, showed a Hb value of 9.2 g/dL, further supporting the suspicion of analytical interference.

Biochemistry analysis on the Roche Cobas C702 revealed visible lipemia, with a lipemia index of 3041. Triglycerides were markedly elevated at 8042 mg/dL (measured with a 1:50 dilution), and total cholesterol was 492.2 mg/dL. These findings indicated a falsely elevated Hb due to lipemia.

Subsequent biochemistry, coagulation, and CBC samples also appeared lipemic. The patient was not receiving parenteral nutrition. Pediatric endocrinology was consulted, and it was suggested that the hyperlipidemia might be related to the chemotherapy agents, particularly L-asparaginase and corticosteroids. Initiation of fenofibrate treatment was recommended.

Comparison of hematological parameters with those obtained two days earlier is shown in Table 1. Hb, MCH and MCHC were markedly increased, while other parameters remained relatively stable.

Table 1: Hematologic Parameters: Two Days Prior vs Current.

Parameter	WBC	RBC	PLT	Hb (g/dL)	Hct (%)	MCV (fL)	MCH (pg)	MCHC(g/dL)
Two Days Prior	0.38	3.09	72	10.7	26.6	86.1	34.6	40.2
Current	0.5	3.01	171	16.9	25.6	85	56.1	66

To correct the lipemia related interference, the EDTA whole blood sample was centrifuged at 1000 x g for 10 minutes. The lipemic plasma was carefully removed and replaced with an equal volume of isotonic NaCl solution, without disturbing the buffy coat layer. The sample was gently mixed to restore whole blood integrity. After this plasma replacement procedure, Hb was measured as 10.2 g/dL, consistent with the blood gas result and clinical picture. Changes in other parameters were also observed, most notably MCH, which returned toward reference ranges following plasma replacement. These changes are summarized in Table 2.

Table 2: Plasma Replacement Effect on CBC Parameters.

Parameter	WBC	RBC	PLT	Hb (g/dL)	Hct (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)
Before Replacement	0.5	3.01	171	16.9	25.6	85	56.1	66
After Replacement	0.36	3.13	173	10.2	19.1	61	32.6	53.4

Discussion

Accurate laboratory results are essential for appropriate diagnosis and treatment, especially in hematology and oncology patients. In this case, a grossly lipemic sample led to a falsely elevated Hb value in a pediatric patient with ALL, raising concerns of analytical interference. The discrepancy between the CBC and venous blood gas Hb values, along with the visibly lipemic serum and extremely high lipemia index of 3041, prompted further investigation.

Lipemia is a well-known interferent in photometric analyses. It increases sample turbidity, which causes light scattering and affects absorbance-based measurements. Hematology analyzers, such as the Sysmex XN-1000, estimate Hb via spectrophotometry after chemical lysis of red cells. In contrast, co-oximetry-based blood gas analyzers like the ABL90 FLEX measure Hb at multiple wavelengths and are less affected by lipemia [3-5]. This may account for the more reliable 9.2 g/dL Hb reading obtained from the blood gas analyzer.

The falsely elevated Hb level on CBC also results in spurious increases in calculated indices, such as MCH and MCHC [3-5]. In this case, the falsely elevated Hb (16.9 g/dL) also caused artificial increases in MCH (56.1 pg) and MCHC (66 g/dL). After plasma replacement, MCH decreased to 32.6 pg, returning to the normal reference range, while MCHC dropped to 53.4 g/dL but remained above normal. This persistent elevation in MCHC may be attributed to the influence of hematocrit (Hct) values on its calculation, as MCHC is derived from Hb and Hct. The post-replacement Hct (19.1%) decreased, possibly contributing to continued MCHC overestimation.

The observed reduction in mean corpuscular volume (MCV) and Hct values after plasma replacement may be explained by using 0.9% NaCl solution instead of the analyzer's proprietary diluent, which aligns with one of the implementation methods outlined by Gulati et al. [3].

According to established recommendations, the CBC results obtained after plasma replacement can be considered reliable if white blood cell (WBC), red blood cell (RBC), and platelet (PLT) values remain within the expected between-run reproducibility limits when compared to the initial run. In cases where discrepancies exist between initial and rerun counts, it is acceptable to report the original WBC, RBC, PLT, Hct, MCV, and red cell distribution width (RDW) values, while incorporating the corrected Hb, MCH, and MCHC from the post-replacement measurement [3]. In our case, the close agreement of WBC, RBC, and PLT values before and after replacement provided confidence in the validity of the rerun Hb and MCH result. To clearly report the correction and assist interpretation, we added the following note to the laboratory report, as recommended in the literature: "Lipemic sample was treated with isovolumetric replacement to reduce interference. The affected results were corrected after treatment" [2].

Various methods such as high-speed centrifugation and lipid extraction have been suggested to reduce lipemia-related interference in serum or plasma samples. However, these approaches are not applicable to CBC testing, which requires whole blood [2].

Several practical strategies have been proposed to address Hb interference due to lipemia in CBC analysis. Another approach is to measure lipemic plasma Hb and apply a correction formula to derive accurate Hb, MCH, and MCHC values [3,6]. Additionally, dilution with isotonic diluent followed by correction for dilution factor has been suggested. Point-of-care devices, which are less affected by lipemia, may also serve as an alternative for reliable Hb measurement. If none of these methods can be applied, reporting only the unaffected parameters (WBC, RBC, PLT, Hct, MCV, RDW) with an interpretive comment noting that Hb, MCH, and MCHC values could not be reliably obtained due to lipemia [3].

In our case, pediatric endocrinology consultation was requested due to the absence of parenteral nutrition and the extreme degree of hypertriglyceridemia. The patient was receiving both L-asparaginase and dexamethasone as part of her ALL-induction protocol. These agents, while essential in the treatment of ALL, are known to significantly disrupt lipid homeostasis. L-asparaginase has been shown to elevate serum triglyceride levels by increasing endogenous synthesis of VLDLs [7,8]. Concurrently, glucocorticoids such as dexamethasone can further exacerbate this effect by activating lipoprotein lipase, stimulating hepatic cholesterol synthesis, and enhancing de novo lipogenesis [7,9]. The combined influence of these agents leads to the rapid accumulation of lipoproteins in circulation, with diminished clearance capacity, resulting in transient but marked hyperlipidemia [7]. Although typically self-limiting, this biochemical derangement may significantly interfere with laboratory testing, as observed in our patient's falsely elevated Hb and derived parameters.

In addition to analytical inaccuracy, lipemia and other preanalytical interferences may also incur hidden costs by necessitating repeat testing, delaying clinical decisions, and prompting unnecessary investigations [10]. Therefore, implementing corrective measures and standardized protocols is of dual importance-not only to safeguard patient safety but also to enhance healthcare cost-effectiveness. Despite growing recognition of lipemia-induced errors in CBCs, standardized guidelines for whole blood analysis remain limited, underscoring the need for institutional protocols and further collaborative efforts.

Conclusion

Lipemia must be recognized as a critical source of analytical interference in CBC interpretation, especially due to its potential to cause falsely elevated Hb levels. This case highlights the importance of correlating analytical results with the clinical and biochemical context to avoid misinterpretation. Plasma replacement with isotonic NaCl solution may serve as a simple and effective technique to correct lipemia related errors when immediate resampling is not feasible. Timely identification and correction of such interferences improve

test result accuracy and support appropriate clinical decision-making.

Conflict of Interest Statement
None declared.

Ethical Approval
This case report was conducted in accordance with the Declaration of Helsinki. Informed written consent was obtained from the patient. Ethical committee approval was not required according to institutional policy for single anonymized case reports.

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Data Availability
All data generated or analyzed during this study are included in this published article.

Author Contributions
ZŞE conceptualized the study, curated the data, and prepared the initial draft. KTU contributed to validation, visualization, and writing – review and editing. Both authors revised the manuscript for intellectual content, and all authors read and approved the final version of the manuscript.

Abbreviations
ALL: Acute Lymphoblastic Leukemia
CBC: Complete Blood Count
Hb: Hemoglobin
Hct: Hematocrit
MCH: Mean Corpuscular Hemoglobin
MCHC: Mean Corpuscular Hemoglobin Concentration
MCV: Mean Corpuscular Volume
RBC: Red Blood Cell
RDW: Red cell Distribution Width
WBC: White Blood Cell
VLDL: Very Low-Density Lipoproteins

References
1. Rifai N, Chiu RWK, Young I, Burnham CD, Wittwer CT, editors. Tietz textbook of laboratory medicine. 7th ed. St. Louis: Elsevier; 2023. p. 91–94.
2. Fernández Prendes C, Castro Castro MJ, Sánchez Navarro L, Rapún Mas L, Morales Indiano C, Arrobas Velilla T. Handling of lipemic samples in the clinical laboratory. Adv Lab Med. 2023;4(1):5–27. doi:10.1515/almed-2023-0003.
3. Gulati G, Uppal G, Gong J. Unreliable automated complete blood count results: causes, recognition, and resolution. Ann Lab Med. 2022;42(5):515–530. doi:10.3343/alm.2022.42.5.515.
4. Radišić Biljak V, Dolovčak L, Bakarić I, Nikler A, Saračević A, Grdić Rajković M. How to handle lipemic CBC samples on Sysmex hematology analyzers? Adv Lab Med. 2025;6(2):166–172. doi:10.1515/almed-2024-0206.
5. Zandecki M, Genevieve F, Gerard J, Godon A. Spurious counts and spurious results on haematology analysers: a review. Part II: white blood cells, red blood cells, haemoglobin, red cell indices and reticulocytes. Int J Lab Hematol. 2007;29(1):21–41. doi:10.1111/j.1365-2257.2006.00871.x.
6. Zeng SG, Zeng TT, Jiang H, Wang LL, Tang SQ, Sun YM, et al. A simple, fast correction method of triglyceride interference in blood hemoglobin automated measurement. J Clin Lab Anal. 2013;27(5):341–345. doi:10.1002/jcla.21568.
7. Laumann RD, Pedersen LL, Andrés-Jensen L, Mølgaard C, Schmiegelow K, Frandsen TL, et al. Hyperlipidemia in children and adolescents with acute lymphoblastic leukemia: a systematic review and meta-analysis. Pediatr Blood Cancer. 2023;70(12):e30683. doi:10.1002/pbc.30683.
8. Parsons SK, Skapek SX, Neufeld EJ, Kuhlman C, Young ML, Donnelly M, et al. Asparaginase-associated lipid abnormalities in children with acute lymphoblastic leukemia. Blood. 1997;89(6):1886–1895.
9. Magomedova L, Cummins CL. Glucocorticoids and metabolic control. Handb Exp Pharmacol. 2016;233:73–93. doi:10.1007/164_2015_1.
10. Lippi G. Unveiling the hidden clinical and economic impact of preanalytical errors. Turk J Biochem 2025;50(3): 331-338. doi: 10.1515/tjb-2025-0196.