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Case Report

NRBCs associated leukopenia: alternative formula for correction of leukocytes count: a case study

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Background: White blood count is considered one of the important inflammatory markers, and its age and gender dependent, under unusual pathological conditions, which can lead to false elevation in TWBCs and should be corrected. Rare cases associated with severe hemolytic anemia and severe leukopenia have potential limitation when corrected using conventional formula.

Case presentation: A case report of 4 years old Sudanese boy patient who was hospitalized with sickle cell disease (SCD). Complete blood count (CBC) parameters were analyzed using 3PD Automated Hematology Analyzer. Peripheral blood picture (PBP) was prepared and stained using leishmen's stain. The data calculate using alternative formula as following. Corrected TWBCs = {mean white blood cells (HPF)/ mean NRBCs (HPF)} × TWBCs. The laboratory findings revealed TWBCs: $124\times10^3/\mu L$, PBP show one WBCs among each 30 NRBCs in ratio of 0.033, the corrected TWBCs: $4.09\times10^3/\mu L$. NRBCs: $119.9\times10^3/\mu L$.

Conclusion: The presence of NRBCs on ratio more than 1:1 NRBCs to WBCs must be calculated using an alternative formula for calculation of NRBCs and corrected TWBCs specially in cases of severe hemolytic anemia and megaloblastic anemia.

Keywords: *corrected TWBCs, NRBCs, alternative formula*

Introduction

The total white blood cell (WBC) count is an essential laboratory parameter that provides insight into the status of the immune system, the presence of inflammatory processes, and bone marrow function. Numerous factors, including age, sex, and underlying physiological or pathological states, can affect WBCs levels. Clinically, the total WBCs count (TWBC) is widely utilized as a diagnostic tool in the identification and monitoring of infectious diseases, hematological malignancies such as leukemia, and disorders of bone marrow origin (Bain, 2015; Hoffbrand and Steensma, 2019).

However, in specific pathological conditions: such as severe hemolytic anemia, megaloblastic anemia, and bone marrow stress nucleated red blood cells (NRBCs) may be prematurely released into the peripheral circulation. This can lead to a falsely elevated total white blood cells (TWBCs) count when measured using automated hematology analyzers, as these machines may misclassify NRBCs as leukocytes (Buttarello, 2004; Bain, 2015).

Nucleated red blood cells (NRBCs), which are immature erythroid precursors, are typically restricted to the bone marrow under normal physiological conditions. Their appearance in peripheral blood outside the neonatal period is considered abnormal and is frequently associated with serious underlying conditions, including tissue hypoxia, profound anemia, or infiltration of the bone marrow by malignant or fibrotic processes (Kuert et al., 2011; McPherson and Pincus, 2016).

Automated hematology analyzers can erroneously identify nucleated red blood cells (NRBCs) as white blood cells, potentially resulting in spurious leukocytosis. To ensure accurate interpretation of the total white blood cells count (TWBCs), especially when the NRBCs-to-WBCs ratio exceeds 1:1, it is essential to apply a correction formula that adjusts the TWBCs for NRBCs interference (de Keijzer and van der Meer, 2002; Buttarello, 2004).

The traditional correction formula used to account for nucleated red blood cells (NRBCs) in total white blood cells (TWBCs) measurements assumes a relatively low NRBCs burden. However, in severe pathological conditions where NRBCs vastly outnumber white blood cells, this method may yield inaccurate results and fail to reflect true leukocyte levels (Novis et al., 2006; Kuert et al., 2011). In such cases, the corrected WBCs count becomes essential for accurate clinical interpretation and management. This case report presents an alternative formula for TWBC correction in a Sudanese pediatric patient with sickle cell disease (SCD), who exhibited severe hemolytic anemia and an unusually high NRBC to WBC ratio. The study aims to demonstrate the limitations of the conventional approach and to validate the use of an alternative correction formula to improve diagnostic accuracy.

Case presentation

In June 2025, 4 years old Sudanese boy patient presented to the clinic with a one-month history of pallor, fatigue, fever, jaundice, chest pain and cough with history of sickle cell disease (SCD). CBC parameters were analyzed using 3PD Automated Hematology Analyzer. PBP was prepared and stained using leishmen's stain. Laboratory findings revealed normocytic normochromic moderate anemia with sickled RBCs on peripheral smear, reticulocytosis, many NRBCs, high elevation in leukocyte count (TWBCs), thrombocytosis, Elevated LDH and indirect bilirubin**.**

PBP was performed and examined 10 fields (HPF) for counting the mean NRBCs and WBCs. Applying alternative formula to calculate the percentage of NRBCs and correction of TWBCs defined as:

$$\text{Corrected TWBC} = \frac{\text{Mean WBCs per HPF}}{\text{Mean NRBCs per HPF}} \times \text{TWBC}$$

Table 1. CBC parameters

Test	Result	Test	Result
TWBCs	$124\times10^3/\mu L$	**PLT**	$785\times10^3/\mu L$
Corrected TWBCs	$4.09\times10^3/\mu L$	**Lymphocytes**	30 %
RBCs Count	$2.8\times10^3/\mu L$	**Neutrophil**	70 %
Hb g/dl	7.1 g/dl	**Mixed cells**	10 %
PCV	23.0 %	**Lymphocytes #**	$1.2\times10^3/\mu L$
MCV	83.3 fl	**Neutrophil #**	$2.8\times10^3/\mu L$
MCH	25.7 pg	**Mixed #**	$0.09\times10^3/\mu L$
MCHC	30.9 g/dl	**MPV**	8.5 fl
RDW.SD	89.7 fl	**PDW**	9.3 %
RDW.CV	33.3 %	**P.LCR**	18 %

PBP comments:

RBCs: Normocytic normochromic moderate anemia with anisopoikilocytosis, many sickle cells, target cells, polychromatic cells and NRBCs.

WBCs: Normal count and morphology.

PLTs: Marked thrombocytosis.

Diagnosis: SCD.

Table 2. Corrected TWBCs and NRBCs results

Test	Result
TWBCs	$124\times10^3/\mu L$
Corrected TWBCs	$4.09\times10^3/\mu L$
NRBCs	$119.9\times10^3/\mu L$

Discussion

The presence of nucleated red blood cells (NRBCs) in peripheral blood is a significant hematological finding, often indicative of bone marrow stress or increased erythropoietic activity. This is particularly relevant in hemolytic anemias such as sickle cell disease (SCD), where chronic hemolysis and hypoxia stimulate the premature release of immature erythroid precursors into the circulation (Carden and Little, 2019; Abboud, 2020). In the presented case, the extraordinarily high NRBC-to-WBC ratio (30:11:1) significantly distorted the total white blood cell count (TWBC) measured by the automated analyzer, yielding a grossly inflated value of $124\times10^3/\mu L$. Automated hematology analyzers may inaccurately count nucleated red blood cells (NRBCs) as white blood cells (WBCs), particularly when NRBCs are present in high numbers, potentially leading to falsely elevated leukocyte counts (spurious leukocytosis) (Buttarello, 2016; McPherson and Pincus, 2016).

The conventional method for correcting total white blood cell count (TWBC) in the presence of nucleated red blood cells (NRBCs) involves adjusting the leukocyte count based on the number of NRBCs per 100 white blood cells, under the assumption that NRBCs are present in relatively low numbers (Bain, 2015). However, this method becomes unreliable when NRBCs vastly outnumber WBCs as is evident in this case, where NRBCs constituted over 30 of the one leukocyte. This dramatic discrepancy highlights a diagnostic limitation of the conventional method and justifies the application of an alternative formula that integrates the NRBC/WBC ratio observed directly from the peripheral blood smear. In this study, the alternative correction formula, defined as:

$$\text{Corrected TWBC} = \frac{\text{Mean WBCs per HPF}}{\text{Mean NRBCs per HPF}} \times \text{TWBC}$$

This alternative correction formula offered a more realistic estimation of the leukocyte count. The corrected value, $4.09\times10^3/\mu L$, fell within the reference range, aligning more closely with the patient's clinical picture and microscopic findings. This reinforces the clinical utility of the alternative method in severe pathologic states where traditional formulas fall short. Furthermore, the peripheral blood picture (PBP) provided critical qualitative insights. The presence of numerous sickle cells, target cells, and polychromsia confirmed the diagnosis of SCD in crisis. The presence of marked anisopoikilocytosis along with a significantly elevated platelet count ($785\times10^3/\mu L$) further supports the presence of a bone marrow stress response, a common finding in hemolytic disorders (Ballas, 2018). Importantly, in resource-limited settings where access to advanced hematology platforms may be restricted, manual smear review remains indispensable. The integration of simple mathematical correction using observed smear ratios as shown in this case can significantly improve diagnostic accuracy, reduce misinterpretation, and guide appropriate clinical decision-making.

Conclusion

The findings underscore the limitations of standard WBC correction methods in extreme pathological states and advocate for the broader adoption of an alternative formulas in similar clinical scenarios. Future studies should focus on validating this approach in larger cohorts to standardize correction practices in cases of NRBC-associated leukopenia and related disorders.

Author contribution

Each author made a significant intellectual contribution, reviewed and approved the final manuscript version, and consented to take responsibility for all elements of the work.

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AI tool declaration

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Conflict of interest

The authors declare no conflict of interest. The manuscript has not been submitted for publication in other journal.

Ethical Approval

All research methods received approval from the Research and Ethics Committees (REC) of the Ministry of Health (No: 6-6-2025), Gezira State, Sudan

Informed consent

All procedures conducted in research involving human subjects adhered to the ethical guidelines set by the institutional and/or national research committees, along with the Helsinki Declaration. Written informed consent was obtained from the patient's parents.

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