Changes of the Platelet Count and Red Cell Distribution Width during Induction Treatment are Predictors of Induction Failure in Pediatric Acute Lymphoblastic Leukemia

Abdelhafiz AS[1,2], Ali A[3,4,5], Alfarouk A[2], Ibrahim A[2], Galeb F[2], Elzembely MM[6,7]

[1] Department of Clinical Pathology, National Cancer Institute, Cairo University, Cairo, Egypt.
[2] Department of Clinical Pathology, Shefa Alorman Oncology Hospital, Luxor, Egypt
[3] Department of Laboratory Medicine, School of Medicine, Jiangsu University, Zhenjiang 212013, P. R. China
[4] Department of Pulmonary Medicine, Abbassia Chest Hospital, EMOH, Cairo, Egypt
[5] Department of Respiratory allergy, Al-Rashid Allergy Center, KMOH, Kuwait
[6] Pediatric Oncology Department, South Egypt Cancer Institute, Assiut University,
[7] Pediatric Oncology Department, Shefa Al-Orman Children Cancer Hospital, Luxor

Received: 10 June 2025
Accepted: 7 August 2025

Authors Information:
Ahmed Samir Abdelhafiz
Department of Clinical Pathology, National Cancer Institute, Cairo University, Cairo, Egypt.
Department of Clinical Pathology, Shefa Alorman Oncology Hospital, Luxor, Egypt
email:drahmedsamir83@gmail.com

Asmaa Ali
Department of Laboratory Medicine, School of Medicine, Jiangsu University, Zhenjiang 212013, P. R. China
Department of Pulmonary Medicine, Abbassia Chest Hospital, EMOH, Cairo, Egypt
Department of Respiratory allergy, Al-Rashid Allergy Center, KMOH, Kuwait
email:asmaa.ali81@yahoo.com

Ahmed Alfarouk
Clinical Pathology Department, Shefa Alorman Oncology Hospital, Luxor, Egypt
email:Ahmedalfarouk91@gmail.com

Asmaa Ibrahim
Clinical Pathology Department, Shefa Alorman Oncology Hospital, Luxor, Egypt
email:asmaa.biotechnology@gmail.com

Fayek Galeb
Clinical Pathology Department, Shefa Alorman Oncology Hospital, Luxor, Egypt
email:fayek.ghaleb@shefaorman.org

Mahmoud Motaz Elzembely
Pediatric Oncology Department, South Egypt Cancer Institute, Assiut University,
Pediatric Oncology Department, Shefa Al-Orman Children Cancer Hospital, Luxor
email: elzimbily@aun.edu.eg

Corresponding Author:
Mahmoud Motaz Elzembely
Pediatric Oncology Department, South Egypt Cancer Institute, Assiut University,
Pediatric Oncology Department, Shefa Al-Orman Children Cancer Hospital, Luxor
email: elzimbily@aun.edu.eg

Abstract:

Background: Acute lymphoblastic leukemia (ALL) is the most common cancer during childhood. The goal of this study is to evaluate the value of different peripheral blood parameters in the prediction of induction remission in these patients.

Methods: Our study included 100 children with ALL who were admitted to Shefa Al-Orman Children's Cancer Hospital between January 2022 and January 2024. Data about complete blood counts (CBC) and bone marrow parameters at days 0, 8, 19, and 42 of induction chemotherapy were collected and analyzed.

Results: B-ALL cases represented 75% of cases. Ninety-four patients achieved complete remission (CR) by the end of induction. A significant decrease in both platelets (PLT) and red cell distribution width (RDW) was found to increase the likelihood of induction failure ($p = 0.03$ and 0.05, respectively). The ROC curve revealed that only PLT had significant discrimination ability between successful and failed induction, with an AUC of 0.64 ($p = 0.03$).

Conclusion: We concluded that a decrease in platelet count and RDW was associated with induction failure. Long-term follow-up is needed to evaluate the effect of these parameters on disease-free survival and overall survival.

Keywords: Acute Lymphoblastic Leukemia; Peripheral Blood; Platelets; Red Cell Distribution Width; Induction

Introduction:

Acute lymphoblastic leukemia (ALL) is the most common type of childhood cancer and accounts for 20 to 25% of childhood malignancies [1,2]. Over the past fifty years, the survival rates for pediatric ALL have significantly improved from 10% to more than 80%. However, relapse still occurs in about 20% of the cases [1,3].

Several clinical, genetic, and immunophenotypic criteria are used to predict response to treatment and risk of relapse in pediatric ALL. These include age, sex, total leucocytic count, molecular, cytogenetic criteria, and minimal residual disease (MRD). Based on these criteria, patients are stratified to apply the most effective treatment protocols [3].

Recovery of the hematopoietic system and different hematological parameters during and after induction chemotherapy is one of the prognostic factors for overall survival in hematological malignancies. It has been reported that platelet count and time to platelet recovery after induction therapy were associated with remission rates after induction chemotherapy in different types of acute leukemia [4-6]. High Absolute lymphocyte count (ALS) is another parameter that was associated with improved survival in childhood ALL [7]. Neutrophil to lymphocyte ratio (NLR) and lymphocyte to monocyte ratio (LMR) also have a well-established prognostic role in diffuse large B-cell lymphoma (DLBCL), Hodgkin lymphoma (HL), and multiple myeloma (MM). However, this role has not been well established in leukemia [8].

Red blood cell distribution width (RDW), a measure of the variability in the size of red blood cells (RBCs), has also been found to be a potential prognostic marker in different hematological malignancies, including Acute Myeloid Leukemia, Chronic Lymphocytic Leukemia, Chronic Myeloid Leukemia, and Hodgkin Lymphoma [9-11].

In limited resource settings, the application of advanced molecular and flow cytometry tests for the detection of minimal residual disease (MRD) is not feasible. Therefore, it is important to find new biomarkers that can be used for the prediction of the success of treatment. Herein, we aimed to evaluate the value of different peripheral blood parameters as predictors of induction remission in children with ALL admitted to Shefa Al-Orman Children Cancer Hospital (SOCCH).

Patients and Methods:

The medical records of children with ALL who were diagnosed and treated at SOCCH between January 2022 and January 2024 were retrospectively reviewed. Eligible patients for this analysis were between 1 year and 18 years of age, diagnosed with ALL according to the 2016 World Health Organization (WHO) classification of hematopoietic and lymphoid tumors and were treated according to the St. Jude Total Therapy XV protocol [11,12]. It is important to note that while primary diagnoses were made according to the 2016 WHO classification, the immunophenotypic sub-classifications for B- and T-ALL presented in Table 1 are based on a widely accepted maturation-based scheme consistent with the broad principles applied in earlier WHO versions (such as the 2008 WHO classification and its clinical application at the time), and were utilized for initial patient stratification and analysis within our available data [13]. Patients who received their induction chemotherapy elsewhere or patients with mixed phenotypic acute leukemia were excluded from the study. Medical records were reviewed for complete blood count parameters at days 0, 8, 19, and 42 of induction chemotherapy. In cases of blood or platelet transfusion, CBCs were recorded 48 hours after the transfusion to minimize the transient rise in blood counts due to the transfusion itself. Initial immunophenotyping (IPT) data, cytogenetics & molecular studies, initial bone marrow aspirate (BMA), subsequent BMA, MRD using flow cytometry at days 19 and 42, and median number of packed RBCs and platelet transfusions between D1 and D19 and from D19 to D42. Induction failure was defined as blast percentage > 5% with persistently elevated MRD > 1%.

Statistical analysis

The statistical analysis for this study was performed using Minitab 17.1.0.0 for Windows (Minitab Inc., 2013, Pennsylvania, USA). The normality of the data was assessed through the Shapiro-Wilk test. Continuous data were represented as medians and interquartile ranges or ranges, while categorical data were presented as numbers and proportions. The paired t-test and chi-square test were utilized to evaluate the changes in variables before and after induction therapy. Logistic regression analysis was used to find potential predictors of induction failure, and Receiver operating characteristics were applied to determine the suitable cutoff value of the most independent predictors of induction failure. All tests were two-tailed and a p-value of less than 0.05 was considered statistically significant.

Results:

Patient Characteristics

The study included 100 eligible children with ALL who were diagnosed and treated at SOCCH during the study period (January 2022 to January 2024). The age of eligible participants ranged from 1 year to 16 years, with a mean (SD) age of 7 (4) years. Fifty-five percent (n=55) were male, and 45% (n=45) were female. B-ALL constituted the majority of cases at 77% (n=77), with common B-ALL being the most frequent subtype (58.4% of B-ALL cases). T-ALL accounted for 23% (n=23) of the cohort. Lymphadenopathy and hepatosplenomegaly were common clinical presentations, observed in 53% and 61% of patients, respectively. Molecular and cytogenetic findings included t(12;21) in 8% of patients, MLL gene rearrangements in 6%, t(9;22) in 4%, and t(1;19) in 5%. At the end of induction, 94% (n=94) of children achieved complete remission, while 6% (n=6) had persistent minimal residual disease (MRD) ≥1% at D42, classifying them into a very high-risk group according

to the St. Jude Total Therapy XV protocol. Details about the patients' characteristics are found in Table 1.

Table 1: Demographic and clinical patients' characteristics

Patient Characteristics	Frequency (%)
Sex	
Male	55 (55%)
Female	45 (45%)
Subtype	
B-ALL	77 (77%)
Pro B-ALL	3 (4%)
Common B-ALL	45 (58.4%)
Pre-B ALL	29 (37.6%)
T-ALL	23 (23%)
Early T-ALL	11 (47.8%)
Intermediate T-ALL	7 (30.5%)
Late T-ALL	5 (21.7%)
Clinical Presentation	
Lymphadenopathy	53 (53%)
Hepatosplenomegaly	61 (61%)
Molecular /Cytogenetics findings	
t(12;21) (p13;q22)	8 (8%)
MLL gene rearrangements	6 (6%)
(t9;22) (q34; q11)	4 (4%)
t(1;19) (q23;p13)	5 (5%)
Response to induction	
Remission	94 (94%)
Failure of remission	6 (6%)

Changes in CBC Parameters During Induction

During the induction phase of chemotherapy, significant dynamic changes were observed in several complete blood count (CBC) parameters (Table 2).

Hemoglobin (HB) levels showed a significant increase from a median baseline of 8.70 g/dL (Q1-Q3: 6.90-10.08) on day 0 to a median of 9.35 g/dL (Q1-Q3: 8.60-10.18) by day 8 (p=0.001). This elevation was sustained, with a median of 9.20 g/dL (Q1-Q3: 8.30-10.10) on day 19 (p=0.01 vs. baseline) and 9.45 g/dL (Q1-Q3: 8.40-10.60) by day 42 (p=0.001).

Total Leukocytic Count (TLC) significantly decreased from a median of 12.50 x 109/L (Q1-Q3: 4.70-64.50) at baseline to 2.70 x 109/L (Q1-Q3: 1.40-5.25) by day 8 (p<0.001), and further to 1.30 x 109/L (Q1-Q3: 0.60-2.00) by day 19 (p<0.001 vs. baseline). The median TLC on day 42 was 3.45 x 109/L (Q1-Q3: 2.20-5.60), still significantly lower than baseline (p<0.001).

Platelet (PLT) count showed a substantial increase by day 42. The median PLT count was 47.00 x 109/L (Q1-Q3: 20.50-96.50) at baseline, showing no significant change by day 8 (median 40.00 x 109/L, p=0.79) or day 19 (median 53.00 x 109/L, p=0.19). However, by day 42, the median PLT count significantly increased to 191.50 x 109/L (Q1-Q3: 80.30-314.30) (p<0.001 vs. baseline, D8, and D19).

Red Cell Distribution Width (RDW) exhibited a significant decrease by day 19. From a median baseline of 16.70% (Q1-Q3: 15.00-18.70), RDW significantly dropped to 15.80% (Q1-Q3: 14.90-17.35) by day 19 (p=0.01 vs. baseline) before returning to baseline levels by day 42 (median 16.80%, Q1-Q3: 14.90-19.70; p=0.88 vs. baseline).

Neutrophil-to-lymphocyte ratio (NLR) and lymphocyte-to-monocyte ratio (LMR) also showed significant changes. Both NLR (baseline median 0.25; Q1-Q3: 0.09-0.70) and LMR (baseline median 9.50; Q1-Q3: 3.87-28.43) significantly decreased by day 42 (NLR median 1.13; Q1-Q3: 0.55-2.79, p<0.001; LMR median 2.00; Q1-Q3: 1.25-4.00, p<0.001).

Changes in BMA Parameters During Induction

Bone marrow aspirate (BMA) parameters demonstrated significant blast reduction during the induction phase (Table 3). A substantial decrease in blast cells was observed from a median of 90% (Q1-Q3: 78-93) at baseline to 1.00% (Q1-Q3: 1-4) by day 19 (p<0.001). This significant reduction continued until day 42, where the median blast percentage remained 1.00% (Q1-Q3: 1-2) (p<0.001 vs. baseline; p=0.03 vs. D19). Bone marrow cellularity also changed, with a shift from predominantly hypercellular at baseline (82%) to hypocellular (81%) by day 19, and then a recovery towards normocellularity by day 42 (55%).

Blood Transfusion During the Induction Phase

The median number of packed red blood cell (RBC) transfusions between D1 and D19 was 5 times, which was significantly higher than the median of 2 times of packed RBC transfusions administered between D19 and D42 (p<0.001). Similarly, the median number of platelet transfusions between D1 and D19 was 6 times, significantly higher than the median of 2 times between D19 and D42 (p<0.001).

Predictors of induction failure:

Six percent of children failed induction as determined by blast cells > 5% and MRD > 1% at D42. The utility of CBC indices for predicting this high-risk MRD status was assessed using multiple logistic regression models, as shown in Table 4.

A significant decrease in Platelet count at D42 was found to increase the likelihood of persistent MRD (OR = 0.99, 95% CI: 0.9841-1.0009, p=0.03). This indicates that for every unit decrease in platelet count at D42, the odds of persistent MRD slightly increased. Similarly, a significant decrease in RDW at D19 was also found to be associated with an increased likelihood of persistent MRD (OR = 0.79, 95% CI: 0.6054-1.0246, p=0.05). In contrast, Hemoglobin (p=0.12) and Lymphocyte count (p=0.78) at D42 did not show a statistically significant prediction for persistent MRD in this model.

The Receiver Operating Characteristic (ROC) curve analysis revealed that only Platelet count at D42 had significant discrimination ability between successful induction (MRD < 1%) and persistent MRD (MRD ≥1%), with an Area Under the Curve (AUC) of 0.64 (p=0.03; Fig. 1). At a cutoff value of <57.5 x 10^9/L, the Platelet count had a sensitivity of 80% and a specificity of 52% in predicting persistent MRD, as shown in Table 5.

.

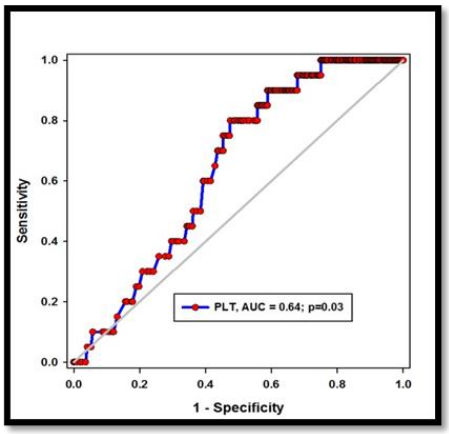

Fig.1: Predictive power of platelets in induction failure
AUC: area under the curve, p<0.05 considered significant

Table 2: Changes in the different CBC indices during induction phase of chemotherapy

		HB	TLC	PLT	BLAST	RDW	N	L	M	NLR	LMR
Baseline CBC	Median	8.70	12.50	47.00	22.50	16.70	1.50	4.45	0.20	0.25	9.50
	Q1	6.90	4.70	20.50	0.00	15.00	0.50	2.65	0.10	0.09	3.87
	Q3	10.08	64.50	96.50	76.50	18.70	4.63	9.72	1.25	0.70	28.43
Day-8	Median	9.35	2.70	40.00	0.00	16.60	0.60	1.50	0.00	0.35	9.75
	Q1	8.60	1.40	20.00	0.00	15.00	0.30	0.90	0.00	0.16	3.00
	Q3	10.18	5.25	75.00	0.00	18.45	1.40	2.87	0.20	1.16	23.00
	p1	0.001	<0.001	0.79	<0.001	0.41	0.31	0.01	0.01	0.09	0.73
Day-19	Median	9.20	1.30	53.00		15.80	0.20	1.10	0.00	0.14	8.75
	Q1	8.30	0.60	28.00		14.90	0.00	0.50	0.00	0.00	2.94
	Q3	10.10	2.00	119.00		17.35	0.80	2.20	0.10	0.70	22.13
	p2	0.01	<0.001	0.19		0.01	0.38	0.09	0.13	0.45	0.61
	p3	0.37	0.06	0.26		<0.001	0.32	0.46	0.99	0.09	0.23
Day-42	Median	9.45	3.45	191.50		16.80	1.50	1.20	0.45	1.13	2.00
	Q1	8.40	2.20	80.30		14.90	0.80	0.70	0.12	0.55	1.25
	Q3	10.60	5.60	314.30		19.70	3.25	2.23	0.83	2.79	4.00
	p4	0.001	<0.001	<0.001		0.88	0.25	0.001	0.41	<0.001	<0.001
	p5	0.81	0.28	<0.001		0.32	0.71	0.04	0.21	<0.001	<0.001
	p6	0.44	0.001	<0.001		0.001	0.18	0.02	0.11	<0.001	0.01

The data presented as median and inter quartile range (Q1-Q3), the test of significant: Mann Whitney test, p<0.05 considered significant. P1: Baseline Vs: day-8, P2: Baseline Vs Day-19, P3: Day-8 Vs Day-19, P4: Baseline Vs Day-42, P5: Day-8 Vs Day-42, P6: Day-19 Vs Day-42, HB; hemoglobin, TLC; total leuckocytic count, PLT; platelets, RDW; red cell distribution width, N; neutrophil, M;monocytes, L; lymphocytes, NLR; neutrophil-to-lymphocyte ratio, LMR; lymphocyte-to-monocyte ratio.

Table 3: Bone marrow changes during induction phase of chemotherapy.

	Baseline		Day-19			Day-42			
	Median	Q1-Q3	Median	Q1-Q3	*P1*	Median	Q1-Q3	P2	P3
BM-blast	90	(78-93)	1.00	(1-4)	<0.001	1.00	(1-2)	<0.001	0.03
Cellularity	N	%	N	%		N	%		
Hypercellular	82	82	7	7	-	10	10	-	-
Hypocellular	11	11	81	81		35	35		
Normocellular	7	7	12	12		55	55		

*The categorical data presented as number and percentage, and numerical data as median and inter quartile range (Q1-Q3), the test of significant: Mann Whitney test, p<0.05 considered significant. P1: Baseline Vs: day-19, P2: Baseline Vs Day-42, P3: Day-19 Vs Day-42.

Table 4: Predictors of induction failure.

Factors	Coefficient	OR	95% CI	P
HB	0.22	1.25	(0.9438,1.6429)	0.12
PLT	-0.01	0.99	(0.9841,1.0009)	0.03
RDW	-0.24	0.79	(0.6054,1.0246)	0.05
L	0.02	1.00	(0.9853,1.0203)	0.78

OR: odd ratio, CI: confidence interval, The test of fitness: Hosmer-Lemeshow test, X^2= 4.6, p=0.79, the test of significant: Multiple regression analysis, p< 0.05 considered significant, HB; hemoglobin, PLT; platelets, RDW; red cell distribution width, L; lymphocytes

Table 5: Sensitivity and specificity of platelets in discriminating induction failure.

Cutoff	Sensitivity	95% CI	Specificity	95% CI	PV +	PV -
57.5	80%	0.5634 to 0.9427	52%	0.4720 to 0.5770	27%	92%

CI: confidence interval, PV+: positive predictive value, PV-: negative predictive value

Discussion:

Although the survival of pediatric ALL has improved dramatically in the past few decades, thanks to the improved risk stratification and treatment protocols [14], the situation may not be the same in limited resource settings [15]. Detection of remission-minimal residual disease- in ALL is generally evaluated using flow cytometry and/or molecular studies [5]. However, these techniques are expensive and need specific training, which may not be available in many low/and middle-income countries, except in a few centers. Evaluation of the dynamics of CBC during the early treatment phases can be tested as a potential alternative for follow-up of ALL patients in situations where resources are limited. Here, we evaluated the value of different CBC parameters in the prediction of induction remission in children with ALL. We found that a significant reduction of the platelet counts and RDW during induction can be useful markers for the prediction of induction failure.

Platelet recovery and time to this recovery have been identified as predictors of outcome in different types of acute leukemia. In a study that included 249 ALL patients, Faderl et al. found that shorter time to platelet recovery could predict longer disease-free survival and overall survival in this group of patients [15]. In a large adult study that included 932 patients with acute myeloid leukemia, Yanada et al. found that higher platelets count at the end of induction is an independent predictor of longer relapse free survival [5].

In our study, we did not only detect the changes in the platelet counts during induction but also identified a cutoff value (57.5 cells/m^3), which can be used to predict induction failure. This result is quite similar to the results by Grunnan et al. who found that partial and complete recoveries of the platelets during induction were associated with lower morbidity and better response to chemotherapy, and that this recovery occurs earlier than recovery of other elements, such as neutrophil count [16].

During and after chemotherapy, platelet recovery occurs mainly from megakaryocytes derived from the hematopoietic stem cells (HSCs) in the bone marrow (BM). As 94% of the cases developed complete remission by the end of induction, we assume that efficient platelet recovery during induction chemotherapy is associated with the presence of healthy stem cells and bone marrow environment and could be an early indication for the success of this phase of treatment.

In our analysis, lymphocyte count (L) at D42 showed no statistically significant association with induction failure in our logistic regression model. One possible explanation for this lack of significant prediction could be the profound and often prolonged myelosuppression induced by induction chemotherapy in ALL. Lymphocytes are highly sensitive to cytotoxic agents, and their counts typically drop significantly during this phase. While absolute lymphocyte count (ALC) recovery has been noted as a prognostic factor in some studies [7], the timing and dynamics of lymphocyte recovery in our specific cohort, coupled with the varied individual responses to intense chemotherapy, may have rendered it less discriminatory for early induction failure compared to platelet count and RDW. Additionally, factors such as prophylactic antimicrobial usage, presence of infections, or even the type and duration of supportive care could influence lymphocyte counts independent of bone marrow recovery specific to leukemia remission. In contrast, platelet recovery is more directly reflective of megakaryopoiesis and the overall health and proliferative capacity of the bone marrow. Similarly, RDW changes appear to capture subtle alterations in erythropoiesis related to marrow function and inflammatory states linked to treatment response. It is plausible that while lymphocytes play a critical role in immune surveillance and host defense, their changes during induction might be more indicative of overall immune suppression and recovery rather than being a direct, early marker of the efficacy of blast clearance, particularly in a limited-resource setting where detailed immune monitoring may not be feasible. Further studies with larger cohorts and more granular tracking of different lymphocyte subsets might reveal specific prognostic roles that were not evident in our broad peripheral lymphocyte count analysis.

In addition to platelet count, changes of RDW were also predictors for the results of induction treatment. RDW is an easy-to-measure parameter that has been widely used to discriminate between different types of anemia [17], and it reflects the heterogeneity in the volume of RBCs [18]. Several studies investigated the role of RDW as a prognostic marker in different pathological conditions, such as inflammation [19], cardiovascular disease [20], as well as solid tumors [21-23], and hematologic malignancies.

A significant reduction of RDW was associated with the failure of induction treatment in our patients. A meta-analysis that investigated the Prognostic role of RDW in hematological malignancies, including lymphoma, myeloma, and CML, has shown that patients with higher RDW potentially have a poorer prognosis compared to those with lower RDW [17]. High RDW at diagnosis has also been associated with poor outcomes for patients with AML and CML [24,25]. However, these studies have evaluated RDW at diagnosis only. In our study, we evaluated the trend of RDW values rather than the detection of a single measurement.

Hospitalized patients usually develop a type of anemia called anemia of chronic disease or anemia of inflammation [26]. In general, this type of anemia is usually normocytic, normochromic anemia, and it occurs due to limited production of RBCs, being a type of hypo-proliferative anemia [27]. We assume that the transition to this type of anemia in patients who failed to achieve complete remission was associated with reduction of RDW, where the limited proliferative ability of the bone marrow led to the production of uniform cells, with limited variability in size.

Our study is limited in being a retrospective study that included cases from a single center. However, we assume that the data generated from this work could be interesting and useful, since our main goal was to find easy and simple markers among the routine laboratory tests and measurements for prediction of the outcome of induction treatment in pediatric ALL patients. We acknowledge that the small number of (failure) events (n=6) in our cohort represents a limitation, particularly when assessing the robustness of our predictive model. Our study is a single-center, retrospective analysis from a specific resource-limited setting, and the incidence of induction failure (or persistent high-risk MRD) in pediatric ALL remains relatively low due to advancements in treatment protocols. This inherent low-event rate, while positive for patient outcomes, presents a challenge for statistical modeling aimed at predicting these rarer events. This exploratory study aimed to identify simple, accessible peripheral blood biomarkers (HB, PLT, RDW, L) for early treatment response in resource-limited settings where advanced MRD testing is unavailable. Despite a small event count and a limited regression model (four variables for six events, raising overfitting concerns), the findings align with established literature, particularly on platelet recovery and RDW's prognostic role in hematologic malignancies. While the results are biologically plausible, the study acknowledges its preliminary nature and emphasizes the need for validation in larger, multi-center cohorts to confirm the predictive potential of PLT and RDW, framing the work as hypothesis-generating for future research.

Conclusion and recommendations:

We identified two parameters from the peripheral blood that can be used to predict the outcome of induction treatment in children with ALL. Low platelets count at the end of induction was an important predictor of failure of induction treatment and could be one of the early indicators of inability of the bone marrow stem cells to replenish the peripheral blood. A drop in the RDW was another predictor of induction failure, probably due to the development of anemia of chronic disease and limited proliferative ability of the bone marrow. Long-term follow-up is needed to evaluate the effect of these parameters on disease-free survival and overall survival in patients in whom induction was successful or failed to achieve complete remission.

Authors' Contributions:

Dr. Mahmoud M. Elzembely, as the corresponding author, & Dr. Fayek Ghaleb played a pivotal role in the conceptualization, study design, drafting of the manuscript and overall supervision. Dr. Ahmed Samir Abdelhafiz, played a pivotal role in laboratory data analysis and interpretation, potentially contributing to the conceptualization, data curation, and drafting of the manuscript. The contributions of Asmaa Ali, Ahmed Alfarouk and Asmaa Ibrahim played pivotal role in data collection, analysis, and manuscript preparation.

References:

1. Bhojwani D, Yang JJ, Pui CH. Biology of childhood acute lymphoblastic leukemia. Pediatr Clin North Am. 2015;62(1):47-60.
2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin. 2020;70(1):7-30.
3. Chen X, Newell LF, Xie H, et al. Low platelet count reduces subsequent complete remission rate despite marrow with <5% blasts after AML induction therapy. Leukemia 2015;29:1779–80.
4. Zeidler L, Zimmermann M, Möricke A, et al. Low platelet counts after induction therapy for childhood acute lymphoblastic leukemia are strongly associated with poor early response to treatment as measured by minimal residual disease and are prognostic for treatment outcome. Haematologica. 2012;97(3):402-409.
5. Yanada M, Borthakur G, Garcia-Manero G, et al. Blood counts at time of complete remission provide additional independent prognostic information in acute myeloid leukemia. Leuk Res. 2008;32(10):1505-1509.
6. Rabin KR, Gramatges MM, Borowitz MJ, et al.. Absolute lymphocyte counts refine minimal residual disease-based risk stratification in childhood acute lymphoblastic leukemia. Pediatr Blood Cancer 2012;59:468–74.
7. Stefaniuk P, Szymczyk A, Podhorecka M. The Neutrophil to Lymphocyte and Lymphocyte to Monocyte Ratios as New Prognostic Factors in Hematological Malignancies - A Narrative Review. Cancer Manag Res. 2020;12:2961-2977.
8. Podhorecka M, Halicka D, Szymczyk A, et al. Assessment of red blood cell distribution width as a prognostic marker in chronic lymphocytic leukemia. Oncotarget. 2016;7(22):32846-32853.
9. Li T, Li X, Chen H, et al. Higher Red Blood Cell Distribution Width is a Poor Prognostic Factor for Patients with Chronic Myeloid Leukemia. Cancer Manag Res. 2021;13:1233-1243.
10. Herraez I, Bento L, Del Campo R, et al. Prognostic Role of the Red Blood Cell Distribution Width (RDW) in Hodgkin Lymphoma. Cancers (Basel). 2020;12(11):3262.
11. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood. 2016;127(20):2375-2390.
12. Pui CH, Relling MV, Sandlund JT, Downing JR, Campana D, Evans WE. Rational and design of total therapy study XV for newly diagnosed childhood acute lymphoblastic leukemia. Ann Hematol. 2004;83 Suppl 1:S124-6
13. Campo, E., Swerdlow, S. H., Harris, N. L., Pileri, S., Stein, H., & Jaffe, E. S. (2011). The 2008 WHO classification of lymphoid neoplasms and beyond: evolving concepts and practical applications. Blood, The Journal of the American Society of Hematology, 117(19), 5019-5032.
14. Ali A, El-Hefedy A, Sayed, D., Osman, A. Clinicolaboratory Characteristics and Outcome of Pediatric Acute Lymphoblastic Leukemia in a Resource-Limited Setting: A Study from South Egypt', Research in Oncology, 202218(2), pp. 61-68.
15. Faderl S, Thall PF, Kantarjian HM, Estrov Z. Time to platelet recovery predicts outcome of patients with de novo acute lymphoblastic leukaemia who have achieved a complete remission [published correction appears in Br J Haematol. 2003 Oct;123(1):186]. Br J Haematol. 2002;117(4):869-874.
16. Grunnan JD, Rosthøj S. Time course of peripheral blood count recovery during induction chemotherapy for childhood acute lymphoblastic leukemia. Hematology. 2019;24(1):467-472.
17. Ai, L., Mu, S. & Hu, Y. Prognostic role of RDW in hematological malignancies: a systematic review and meta-analysis. Cancer Cell Int 18, 61 (2018).
18. Owoicho O, Tapela K, Olwal CO, Djomkam Zune AL, Nganyewo NN, Quaye O. Red blood cell distribution width as a prognostic biomarker for viral infections: prospects and challenges. Biomark Med. 2022;16(1):41-50.
19. Yeşil A, Senateş E, Bayoğlu IV, Erdem ED, Demirtunç R, Kurdaş Övünç AO. Red cell distribution width: a novel marker of activity in inflammatory bowel disease. Gut Liver. 2011;5(4):460-467.
20. Arbel Y, Weitzman D, Raz R, et al. Red blood cell distribution width and the risk of cardiovascular morbidity and all-cause mortality. A population-based study. Thromb Haemost. 2014;111(2):300-307.
21. Koma Y, Onishi A, Matsuoka H, et al. Increased red

blood cell distribution width associates with cancer stage and prognosis in patients with lung cancer. PLoS One. 2013;8(11):e80240. Published 2013 Nov 11.

22. Ay S, Eryilmaz MA, Aksoy N, Okus A, Unlu Y, Sevinc B. Is early detection of colon cancer possible with red blood cell distribution width?. Asian Pac J Cancer Prev. 2015;16(2):753-756.
23. Albayrak S, Zengin K, Tanik S, Bakirtas H, Imamoglu A, Gurdal M. Red cell distribution width as a predictor of prostate cancer progression. Asian Pac J Cancer Prev. 2014;15(18):7781-7784.
24. Vucinic V, Ruhnke L, Sockel K, et al. The diagnostic red blood cell distribution width as a prognostic factor in acute myeloid leukemia. Blood Adv. 2021;5(24):5584-5587.
25. Li T, Li X, Chen H, et al. Higher Red Blood Cell Distribution Width is a Poor Prognostic Factor for Patients with Chronic Myeloid Leukemia. Cancer Manag Res. 2021;13:1233-1243. Published 2021 Feb 10.
26. Fraenkel PG. Understanding anemia of chronic disease. Hematology Am Soc Hematol Educ Program. 2015;2015:14-18.
27. Adamson JW. The anemia of inflammation/malignancy: mechanisms and management. Hematology Am Soc Hematol Educ Program. 2008;159-165.