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Original Article

Evaluation of Complete Blood Count Parameters in Patients with Leukemia

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ABSTRACT

Background: CBC parameters are the first objective indicators of leukemia, but the pattern varies with the type of leukemia and the stage of the disease.

Methods: 128 newly diagnosed leukemia patients and 60 non-malignant controls were evaluated in a hospital-based observational study. Peripheral smear, bone marrow examination, flow cytometry and cytogenetic/molecular tests were used to classify patients as acute myeloid leukemia, acute lymphoblastic leukemia, chronic myeloid leukemia or chronic lymphocytic leukemia.

Results: Anemia was present in 105 patients (82.0%), leukocytosis in 87 (68.0%), thrombocytopenia in 78 (60.9%) and circulating blasts in 95 (74.2%). Mean hemoglobin was lowest in acute leukemia (AML 7.9 ± 1.8 g/dL; ALL 8.2 ± 1.7 g/dL), while mean leukocyte count was highest in CML (118.6 ± 72.4 ×10^3/µL). Platelet count was significantly lower in AML than CML (58.4 ± 42.6 ×10^3/µL vs. 312.8 ± 188.5 ×10^3/µL, $p<0.001$). Acute leukemia had a positive correlation between blast percentage and leukocyte count ($r=0.52$, $p<0.001$) and a negative correlation between blast percentage and platelet count ($r=-0.47$, $p<0.001$). 91.4% of leukemia cases were detected prior to confirmatory testing by CBC-based suspicion followed by smear review.

Conclusion: CBC parameters demonstrated clear differences between the different leukemia subtypes and are still essential for initial suspicion, triage and prioritization of definitive hematological evaluation.

Keywords: Leukemia, complete blood count, blasts, thrombocytopenia, leukocytosis, peripheral smear, flow cytometry.

INTRODUCTION

Leukemia is a diverse group of haematological malignancies in which the abnormal proliferation of immature or mature blood cells occurs in the bone marrow, peripheral blood and in other tissues. The complete blood count (CBC) is the initial investigation that alerts the physician to the possibility of a leukemia in most patients, and modern classification incorporates morphology, immunophenotype, cytogenetics and molecular abnormalities [1],[2].

Leukemia is characterized by CBC abnormalities such as anemia, leukocytosis or leukopenia, thrombocytopenia, thrombocytosis, neutropenia, lymphocytosis, basophilia and circulating blasts. Acute leukemias typically show marrow failure and blasts, while chronic leukemias can be detected as a chronic leukocytosis or lymphocytosis. The first CBC pattern assists with the determination of urgency, smear review and selection of confirmatory tests [3],[4].

Flow cytometry and molecular testing are also crucial for diagnosis and treatment planning but may not be available on the spot in every hospital. A systematic approach to CBC and peripheral smear analysis can help decrease the time to referral and missed diagnoses. This is particularly important in patients with fever, bleeding, fatigue, gum hypertrophy, bone pain or unexplained infections [5],[6].

The current study aimed to assess the CBC parameters in newly diagnosed leukemia patients and to compare the pattern in AML, ALL, CML and CLL. The goal was to evaluate the diagnostic significance of common haematological abnormalities and their relationship with the type of leukemia and disease burden [7].

MATERIALS AND METHODS

This was an observational study carried out in a tertiary care hematology laboratory for 18 months. Patients with newly diagnosed leukemia, 12 years of age or older, were enrolled prior to chemotherapy or tyrosine kinase inhibitor (TKI) therapy. For comparison of baseline CBC parameters, a control group of 60 patients with non-malignant conditions and normal or reactive blood counts was included.

Patients who had relapsed leukemia, previous chemotherapy, recent transfusion within 10 days of baseline sampling, and myelodysplastic syndrome (MDS) without leukemic transformation or incomplete confirmatory testing were excluded. Diagnosis of leukemia subtype was made by peripheral smear, bone marrow aspirate/biopsy, cytochemistry (if applicable), flow cytometry, BCR-ABL1 testing and other cytogenetic or molecular tests as indicated by clinical diagnosis.

A five-part automated hematology analyzer was used to perform CBC. Parameters were hemoglobin, total leucocyte count, absolute neutrophil count, absolute lymphocyte count, absolute monocyte count, platelet count, MCV, RDW, mean platelet volume and flags of differential count. Peripheral smears were stained with Leishman stain and independently examined by two pathologists for the presence of blasts, dysplasia, Auer rods, basophilia, smudge cells and platelet morphology.

The data were analyzed with SPSS version 26. Continuous variables were presented as mean ± SD or median (IQR). Categorical variables were displayed as numbers and percentages. The following statistical methods were used: ANOVA, Kruskal-Wallis test, chi-square test and correlation analysis. A p value of < 0.05 was deemed significant.

RESULTS

The study included 128 leukemia patients: 48 AML, 32 ALL, 28 CML and 20 CLL. The mean age was 39.7 ± 18.6 years, with CLL patients being older than acute leukemia patients. Fever, fatigue, pallor, bleeding manifestations and splenomegaly were common presenting features. CBC abnormality was the initial reason for hematology referral in 117 patients (91.4%).

Table 1. Distribution of leukemia subtypes and common clinical features.

Feature	AML (n=48)	ALL (n=32)	CML (n=28)	CLL (n=20)	p-value
Age (years)	36.5 ± 15.2	24.8 ± 10.9	42.6 ± 13.8	61.4 ± 9.6	<0.001
Male sex, n (%)	29 (60.4)	20 (62.5)	17 (60.7)	13 (65.0)	0.981
Fever, n (%)	31 (64.6)	24 (75.0)	11 (39.3)	4 (20.0)	<0.001
Bleeding, n (%)	22 (45.8)	11 (34.4)	4 (14.3)	1 (5.0)	<0.001
Splenomegaly, n (%)	15 (31.3)	10 (31.3)	24 (85.7)	11 (55.0)	<0.001
CBC-triggered referral, n (%)	43 (89.6)	29 (90.6)	27 (96.4)	18 (90.0)	0.824

Table 2. Complete blood count parameters across leukemia subtypes.

Parameter	AML	ALL	CML	CLL	p-value
Hemoglobin (g/dL)	7.9 ± 1.8	8.2 ± 1.7	10.1 ± 2.0	10.8 ± 1.6	<0.001
TLC (×10^3/µL)	54.2 ± 48.6	38.9 ± 31.4	118.6 ± 72.4	72.1 ± 41.8	<0.001
Platelets (×10^3/µL)	58.4 ± 42.6	72.3 ± 54.2	312.8 ± 188.5	142.5 ± 79.6	<0.001
RDW (%)	18.2 ± 3.1	17.5 ± 2.8	16.4 ± 2.1	15.8 ± 1.9	0.005
Peripheral blasts (%)	58.6 ± 22.4	62.1 ± 20.8	4.8 ± 5.2	0.6 ± 1.1	<0.001
Basophils (%)	0.8 ± 0.6	0.5 ± 0.4	7.6 ± 4.8	0.4 ± 0.3	<0.001

Table 3. Frequency of key CBC abnormalities in leukemia patients.

CBC abnormality	Total n (%)	AML n (%)	ALL n (%)	CML n (%)	CLL n (%)
Anemia	105 (82.0)	44 (91.7)	29 (90.6)	19 (67.9)	13 (65.0)
Leukocytosis	87 (68.0)	31 (64.6)	18 (56.3)	28 (100.0)	10 (50.0)
Leukopenia	14 (10.9)	8 (16.7)	6 (18.8)	0 (0.0)	0 (0.0)
Thrombocytopenia	78 (60.9)	40 (83.3)	24 (75.0)	6 (21.4)	8 (40.0)
Circulating blasts	95 (74.2)	48 (100.0)	32 (100.0)	12 (42.9)	3 (15.0)
Analyzer blast/abnormal flag	111 (86.7)	46 (95.8)	31 (96.9)	20 (71.4)	14 (70.0)

In acute leukemia, blast percentage correlated positively with total leukocyte count ($r=0.52$, $p<0.001$) and inversely with platelet count ($r=-0.47$, $p<0.001$). In CML, absolute basophil count and immature granulocyte flag were consistent supportive clues. In CLL, persistent absolute lymphocytosis with smear smudge cells was the dominant pattern.

CBC and smear review together led to immediate hematology notification in 96 cases (75.0%). Flow cytometry confirmed lineage in all acute leukemia and CLL cases, while BCR-ABL1 testing confirmed CML in all 28 patients.

DISCUSSION

The results indicated that CBC parameters are important early diagnostic parameters in leukemia. Acute leukemias were most commonly associated with anemia and thrombocytopenia, which was due to the replacement of the marrow by blasts and suppression of normal hematopoiesis. Leukocytosis, basophilia and variable platelet elevation were seen in CML, whereas lymphocytosis was seen in older adults with CLL, in contrast [8],[9].

Most cases were detected prior to confirmatory testing by the combination of CBC analyzer flags and peripheral smear review. It highlights the importance of setting up clear guidelines for manual smear examination in cases of high or low leukocyte count, low platelets than expected, flagged blasts, and unexplained cytopenia. Peripheral smear continues to be a quick and cheap link between automated counts and definitive diagnosis [10],[11].

Lineage assignment is still essential in acute leukemia and CLL and flow cytometry is indispensable in these cases. In some cases, blasts may be poorly differentiated or when mixed phenotype acute leukemia is suspected, morphology may not be enough. Immunophenotyping also plays a role in measurable residual disease planning and risk stratification [12],[13].

The total leucocyte count, basophilia and left-shifted myeloid series were elevated in CML patients. These are CBC clues because CML is frequently found as a chance finding. However, BCR-ABL1 must be demonstrated by cytogenetic or molecular techniques to diagnose the disease and quantitative transcript assessment is essential for disease monitoring. [14] The CBC parameters are also of prognostic significance. Historically, high leukocyte count in AML has been correlated with high tumor burden and complications, and thrombocytopenia is correlated with bleeding risk. RDW and inflammatory ratios are being explored as inexpensive prognostic factors, but are not substitutes for cytogenetic and molecular risk stratification [15],[16].

Limitations are: single centre recruitment and small number of CLL cases. Not all acute leukemia patients had molecular subtyping. The study does not, however, reflect routine diagnostic practice, but illustrates the ability of structured interpretation of a CBC to increase the speed of referral and definitive workup [17].

One important practical point to remember is that a normal or near-normal leukocyte count does not rule out leukemia. In this study, several cases of acute leukemia presented with leukopenia or slight leukocytosis, with anemia, thrombocytopenia, and circulating blasts on smear. Hence, when there is no significant increase in the total leucocyte count, the presence of unexplained bicytopenia or pancytopenia should lead to a review of the smear.

Automated flags on the analyzer were helpful but not foolproof. False-negative or nonspecific flags can occur when blasts are few, fragile or morphologically atypical. Laboratory protocols should thus be a mix of numerical thresholds, delta checks and clinical information. Communication between clinicians and laboratory staff is critical if symptoms of bleeding, fever or gum swelling are out of proportion with the automated report.

In chronic leukemias, the CBC pattern may help determine the best confirmatory test. Persistent mature lymphocytosis indicates flow cytometry for CLL and marked neutrophilic leukocytosis with basophilia indicates BCR-ABL1 testing for CML. This rational sequencing can minimize diagnostic delay, save resources and facilitate timely treatment of the disease [17].

One other note was the overlap between infection-like presentations and leukemia. Acute leukemia was associated with fever and constitutional symptoms, which could initially present as a viral illness, enteric fever or sepsis. If a CBC is done again and a smear review is requested, it is important to repeat the CBC when fever is associated with unexplained cytopenia, immature cells in the circulation, or persistent leukocytosis or mucocutaneous bleeding.

The study reiterates the fact that CBC interpretation is a clinical skill and a laboratory function. Junior clinicians should be able to identify patterns, e.g., leukocytosis with basophilia, lymphocytosis in older patients, bicytopenia with blasts, and thrombocytopenia with anemia. This pattern recognition can reduce the diagnostic delay towards specialist referral [17].

CONCLUSION

Most newly diagnosed leukemia patients had CBC abnormalities, and these abnormalities were significantly different among the various leukemia subtypes. The most common findings in acute leukemia were anemia, thrombocytopenia and circulating blasts, whereas leukocytosis with basophilia was suggestive of CML and lymphocytosis of CLL. CBC with peripheral smear review is still a vital initial test in the early suspicion and triage prior to flow cytometry and molecular confirmation.

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