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ASSESSMENT OF LEUKEMIA SUBTYPES IN BONE MARROW AND PERIPHERAL BLOOD SMEAR: A CROSS-SECTIONAL STUDY FROM TERTIARY CARE HOSPITALS IN LAHORE, PAKISTAN

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Acute Myeloid Leukemia; Acute Lymphoblastic Leukemia; Chronic Myeloid Leukemia; Chronic Lymphocytic Leukemia; Peripheral Blood Smear; Bone Marrow Examination; Pakistan; Diagnostic Concordance

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Abstract

Background: *Leukemia accounts for 3–4% of the global cancer burden and represents a significant cause of haematological morbidity in Pakistan. Accurate subtype identification is essential for appropriate treatment yet comprehensive diagnostic data from Lahore's tertiary hospitals remain scarce.*

Methods: *A descriptive cross-sectional study was conducted in selected tertiary care teaching hospitals in Lahore over six months. One hundred and thirty-nine confirmed leukemia patients (all ages, both sexes) were enrolled by non-probability purposive sampling. Peripheral blood smears (PBS) and bone marrow aspiration (BMA) were performed for each patient.*

Results: *AML was the most frequent subtype (34.5%), followed by ALL (31.7%), CML (22.3%), and CLL (11.5%). A male predominance was observed (M:F = 1.57:1). Age-subtype association was highly significant ($\chi^2 = 84.604$, $p < 0.001$): ALL predominated in children/adolescents; AML and CML in working-age adults; CLL exclusively in adults ≥ 46 years. Peripheral smear sensitivity was 89.6% for AML, 88.6% for ALL, 90.3% for CML, and 62.5% for CLL. Overall diagnostic concordance between PBS and BMA was 86.3% (Cohen's $\kappa = 0.816$).*

Conclusion: *Peripheral blood smear is a rapid, low-cost, and highly informative first-line test that, when read by trained morphologists, achieves near-excellent agreement with bone marrow diagnosis for AML, ALL, and CML.*

INTRODUCTION

Leukemia is a heterogeneous group of hematopoietic malignancies arising from bone marrow stem and progenitor cells. It remains a major global health burden, with approximately 487,000 new cases and more than 305,000 deaths reported worldwide in 2022 (Bray et al., 2024). Leukemia ranks among the leading causes of cancer-related morbidity and mortality in both pediatric and adult populations, particularly in low- and middle-income countries where access to advanced diagnostic facilities is often limited (Liang et al., 2024; Hirsch et al., 2023).

In Pakistan, leukemia represents a significant hematological malignancy, with acute leukemias occurring at a younger age compared to Western populations (Ashfaq et al., 2023; Raza et al., 2023). Due to the absence of a comprehensive national cancer registry, epidemiological information remains fragmented and is largely derived from hospital-based studies. Previous investigations from major Pakistani cities have consistently identified acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) as the predominant subtypes, followed by chronic myeloid leukemia (CML) and chronic lymphocytic

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leukemia (CLL) (Raza et al., 2023; Saeed et al., 2024).

Problem Statement

Limited data are available on leukemia subtype distribution and the diagnostic agreement between peripheral blood smear and bone marrow examination in Lahore, Pakistan. As peripheral smear assessment is often the first-line diagnostic tool in resource-limited settings, evaluating its accuracy against bone marrow findings is essential. Therefore, this study aimed to assess leukemia patterns and determine the diagnostic value of peripheral blood smear for improving early and accurate leukemia diagnosis.

Objectives & Research Questions

1. To determine the distribution of leukemia subtypes (AML, ALL, CML, and CLL).
2. To assess age and gender patterns among leukemia patients.
3. To evaluate peripheral blood smear and bone marrow findings.
4. What is the distribution of leukemia subtypes?
5. How do leukemia subtypes vary by age and gender?
6. What are the characteristic smear and bone marrow findings?

Therefore, the present study was conducted in tertiary care hospitals of Lahore, Pakistan, to determine the distribution of leukemia subtypes, evaluate their demographic and morphological characteristics, and assess the diagnostic performance of peripheral blood smear relative to bone marrow examination.

2. Materials and Methods

2.1 Study Design and Setting

A hospital-based, descriptive cross-sectional study was conducted at selected tertiary care teaching hospitals in Lahore, Pakistan over six months following Institutional Review Board approval.

2.2 Participants

All patients presenting with clinically suspected leukemia who underwent both PBS and BMA during the study period were eligible. Patients already on cytotoxic therapy at the time of BMA, those with HIV or major immunosuppressive disease, and those with rare leukemia subtypes (e.g., hairy cell leukemia, JMML) were excluded to preserve diagnostic clarity. The minimum sample size of 139 was calculated using the single-proportion formula ($Z = 1.96$, $p = 0.10$, $E = 0.05$).

3. Results

3.1 Subtype Distribution and Demographics

Leukemia Subtype	n (%)	Male, n (%)	Female, n (%)	M:F Ratio	Predominant Age Group
AML	48 (34.5)	29 (60.4)	19 (39.6)	1.53:1	31–45 years
ALL	44 (31.7)	26 (59.1)	18 (40.9)	1.44:1	<30 years
CML	31 (22.3)	20 (64.5)	11 (35.5)	1.82:1	31–45 years
CLL	16 (11.5)	10 (62.5)	6 (37.5)	1.67:1	≥46 years
Total	**139 (100)**	**85 (61.2)**	**54 (38.8)**	**1.57:1**	—

Note. AML = Acute Myeloid Leukemia; ALL = Acute Lymphoblastic Leukemia; CML = Chronic Myeloid Leukemia; CLL = Chronic Lymphocytic Leukemia.

Interpretation

A significant association was observed between leukemia subtype and age group, $\chi^2(12) = 84.60$, $p < .001$, indicating distinct age-related patterns of disease occurrence. However, gender distribution did not differ significantly among leukemia subtypes, $\chi^2(3) = 0.25$, $p = .969$.

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Table 3.2

Distribution of Leukemia Subtypes and Gender Characteristics (N = 139)

Leukemia Subtype	n (%)	Male, n (%)	Female, n (%)	M:F Ratio	Predominant Age Group
AML	48 (34.5)	29 (60.4)	19 (39.6)	1.53:1	31–45 years
ALL	44 (31.7)	26 (59.1)	18 (40.9)	1.44:1	<30 years
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Peripheral Smear Findings

Table 3.3

Peripheral Blood Smear Parameters According to Leukemia Subtype

Variable	AML (n = 48)	ALL (n = 44)	CML (n = 31)	CLL (n = 16)
Total Leukocyte Count ($\times 10^9$/L)	60.6 ± 38.9	46.8 ± 27.6	159.5 ± 69.6	75.7 ± 26.8
Hemoglobin (g/dL)	7.5 ± 1.7	7.7 ± 1.7	9.9 ± 1.7	11.2 ± 1.6
Platelet Count ($\times 10^9$/L)	52.9 ± 30.1	62.0 ± 35.9	187.1 ± 97.2	150.1 ± 54.1
Peripheral Blood Blasts (%)	60.1 ± 17.7	62.8 ± 19.1	6.0 ± 4.6	0.7 ± 0.6
Auer Rods, n (%)	33 (68.8)	0	0	0
Smudge Cells, n (%)	0	0	1 (3.2)	16 (100)
Basophilia, n (%)	5 (10.4)	0	26 (83.9)	0

Table 4.8: Peripheral Smear Findings by Leukemia Subtype. Auer rods were essentially exclusive to AML; smudge cells defined CLL; basophilia and eosinophilia marked CML. Values are mean ± SD or n (%).

AML was characterized by frequent Auer rod positivity (68.8%), while ALL demonstrated the highest peripheral blast burden. CML exhibited the highest leukocyte count and marked basophilia, whereas all CLL patients demonstrated smudge cells, confirming their diagnostic relevance.

Bone Marrow Findings by Leukemia Subtype

Table 3.4

Leukemia Subtype	Mean BM Blasts (%)	SD
AML	69.80	17.34
ALL	71.04	12.27
CML	8.10	4.09
CLL	1.86	0.92

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One-way ANOVA demonstrated significant differences in bone marrow blast percentages among leukemia subtypes, $F(3, 135) = 276.07$, $p < .001$. Post hoc analysis revealed significant differences between acute and chronic leukemias ($p < .001$), whereas AML and ALL showed comparable blast percentages ($p = .954$).

Table 3.5

Diagnostic Performance of Peripheral Blood Smear Relative to Bone Marrow Examination

Leukemia Subtype	True Positive	False Negative	Sensitivity (%)	95% CI
AML	43	5	89.6	77.8–95.5
ALL	39	5	88.6	76.0–95.0
CML	28	3	90.3	75.1–96.7
CLL	10	6	62.5	38.6–81.5
Overall	**120**	**19**	**86.3**	**79.6–91.1**

Note: Diagnostic Performance of Peripheral Smear against Bone Marrow Examination (Reference Standard). Sensitivity is high in AML, ALL and CML but lower in CLL, where early disease can present with only modest lymphocytosis and few smudge cells. 95 % CI by Wilson

Peripheral blood smear demonstrated excellent sensitivity for AML, ALL, and CML (88–90%), supporting its utility as an effective first-line diagnostic tool. Sensitivity was lower for CLL (62.5%), likely due to the subtle hematological manifestations of early-stage disease.

Multiple Linear Regression: Predictors of BM Blast Percentage

Table 3.6

Predictor	B	SE B	β	*t*	*p*
Constant	-25.42	31.06	—	-0.82	.414
Age (years)	-0.21	0.10	-0.14	-2.16	.033*
TLC ($\times 10^9$/L)	-0.05	0.03	-0.09	-1.62	.108
Hb (g/dL)	-1.81	1.30	-0.12	-1.39	.166
Platelets ($\times 10^9$/L)	-0.17	0.04	-0.41	-4.74	< .001***
BM Cellularity (%)	1.31	0.32	0.30	4.09	< .001***

Note. *B = unstandardized regression coefficient; SE B = standard error of B; β = standardized regression coefficient; TLC = total leukocyte count; Hb = hemoglobin; BM = bone marrow. $p < .05$. *** $p < .001$.*

Presenting Clinical Features by Subtype

Table 3.7

Presenting Feature	AML (n = 48), n (%)	ALL (n = 44), n (%)	CML (n = 31), n (%)	CLL (n = 16), n (%)
Fatigue/Pallor	43 (89.6)	41 (93.2)	26 (83.9)	10 (62.5)
Fever	33 (68.8)	33 (75.0)	9 (29.0)	3 (18.8)
Bleeding/Bruising	28 (58.3)	21 (47.7)	4 (12.9)	1 (6.3)
Bone/Joint Pain	16 (33.3)	23 (52.3)	5 (16.1)	1 (6.3)

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Presenting Feature	AML (n = 48), n (%)	ALL (n = 44), n (%)	CML (n = 31), n (%)	CLL (n = 16), n (%)
Splenomegaly	21 (43.8)	19 (43.2)	30 (96.8)	9 (56.3)
Hepatomegaly	16 (33.3)	18 (40.9)	21 (67.7)	6 (37.5)
Lymphadenopathy	9 (18.8)	22 (50.0)	3 (9.7)	13 (81.3)
Weight Loss	19 (39.6)	20 (45.5)	17 (54.8)	5 (31.3)

Discussion

This study provides contemporary evidence regarding the demographic distribution, morphological characteristics, and diagnostic performance of peripheral blood smear in leukemia patients from tertiary care hospitals in Lahore, Pakistan. AML emerged as the most common subtype, followed by ALL, CML, and CLL. These findings are consistent with previous Pakistani studies reporting a predominance of acute leukemias within the regional population (Ashfaq et al., 2023; Raza et al., 2023; Saeed et al., 2024). A clear male predominance was observed across all leukemia subtypes. Similar sex-related patterns have been reported in both local and international studies, suggesting the influence of biological susceptibility, environmental exposures, and healthcare-seeking behaviors (Liang et al., 2024; Saeed et al., 2024). Furthermore, a highly significant association between age and leukemia subtype was identified. ALL was more prevalent among younger individuals, AML and CML were common among middle-aged adults, and CLL occurred predominantly in older patients. These findings closely mirror established global epidemiological trends (Liang et al., 2024; Ashfaq et al., 2023).

Bone marrow examination confirmed all leukemia diagnoses and demonstrated significantly different blast percentages among leukemia subtypes. These findings reinforce the role of bone marrow assessment as the definitive diagnostic standard and highlight its importance in disease classification and prognostic evaluation (Arif et al., 2024; Khoury et al., 2022). A major finding of this study was the high overall concordance (86.3%) between peripheral blood smear and bone marrow examination, with a Cohen's κ value of 0.816, indicating near-perfect agreement. This result is comparable to previous studies that reported diagnostic accuracies ranging from 81% to 84% for peripheral smear-based leukemia diagnosis (Murray et al., 2024; Sharma et al., 2023).

Conclusion

AML is the most prevalent leukemia subtype in tertiary hospitals in Lahore, followed by ALL, CML, and CLL. A consistent male predominance and a highly significant age-stratified subtype distribution are documented. Peripheral blood smear examination achieves 86.3% overall concordance (κ = 0.816) with bone marrow-confirmed diagnosis, with high sensitivity for AML, ALL, and CML, but limited sensitivity for CLL.

Limitations

- Cross-sectional design prevented assessment of treatment outcomes and survival.
- Small sample size, particularly for CLL, may limit statistical power.
- Purposive sampling may reduce generalizability..

Recommendations

Conduct larger multicenter studies with follow-up data.

- Incorporate immunophenotypic and molecular testing into routine diagnosis.
- Strengthen hematology diagnostic facilities and training.
- Establish a national leukemia registry for improved surveillance and research.

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