CLINICAL AND HEMATOLOGICAL FEATURES OF ACUTE LEUKEMIA IN PEDIATRIC AND ADULT PATIENTS AT A TERTIARY CARE HOSPITAL LAHORE

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ABSTRACT

Background & Objectives: Acute leukemia is a rapidly progressing hematological malignancy characterized by the proliferation of abnormal leukocytes. Clinical and hematological features vary between pediatric and adult patients. Identifying the clinical and hematological feature is essential for accurate diagnosis and prompt initiation of treatment. To determine the clinical and hematological features of acute leukemia in pediatric and adult patients at a tertiary care hospital in Lahore.

Methods: A retrospective study was conducted at pathology department, AIMC.Bone marrow biopsy records of newly diagnosed cases of acute leukemia from 2020 to 2023 were reviewed for demographic data, clinical features, hematological parameters, and the category of acute leukemia. All cases were confirmed on bone marrow aspirate and trephine biopsy, and Sudan Black B cytochemical stain was used to confirm the myeloid origin of blasts. Frequencies and percentages were calculated for categorical variables, and chi-square test was applied to assess associations between age at presentation and leukemia.

Results: Of the 130 patients, 54.6% were male and 45.4% were female. The mean age at presentation was 32.18 ± 16.34. Fever was the most common clinical presentation (90.0%), followed by splenomegaly (44.6%), purpura (43.4%), bone and joint pain (41.9%), and weight loss (40.9%). Among AML subtypes, AML-M2 and AML-M3 were more prevalent in females, and Sudan Black Negative Leukemia showed a higher proportion of males (61.2%) compared to females (38.8%). Chi-square analysis revealed a statistically significant association between age and the acute leukemia category, with a p-value of 0.013.

Conclusion: Our study highlights that fever is the most prevalent symptom of acute leukemia, followed by splenomegaly and purpura. Significant association exists between age and acute leukemia subtypes, emphasizing the importance of prompt recognition of clinical symptoms by clinicians for timely evaluation and management.

Key Words: Acute Leukemia, Acute Lymphoblastic Leukemia, Acute Myeloid Leukemia, Hematological Malignancy, Sudan Black-B, FAB Classification

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Acute Leukemias are hematological malignancies characterized by clonal proliferation, leading to extensive infiltration of bone marrow and peripheral blood. Acute leukemia can be broadly classified into Acute Lymphocytic Leukemia (ALL) and Acute Myelogenous Leukemia (AML) based on the specific lineage of the affected cells.[1]

Acute Leukemias are among the most prevalent cancers, with approximately 20,000 new cases and over 10,000 annual deaths reported in the United States. In many developing countries, including Pakistan, there is a notable absence of population-based tumor registries. Consequently,

the annual incidence of cancer remains largely undocumented. Acute Lymphoblastic Leukemia (ALL) is the most prevalent childhood malignancy, constituting nearly a quarter of all cancers diagnosed in less than 18 years of age. The peak incidence of ALL is reported in children aged 2 to 5 years. In the United States, an estimated 2000-2500 new cases of childhood ALL are diagnosed each year. It is widely believed that the incidence rates are comparable internationally, including in Pakistan.[2] It is clinically and morphologically heterogeneous. Morphologically, it is classified according to FAB (French, American and British) criteria into L-1, L-2 and L-3 sub-types, which is clinically reproducible.[1]

Children diagnosed with Acute Lymphoblastic Leukemia (ALL) typically present with symptoms indicative of bone marrow failure (anemia, thrombocytopenia, and neutropenia) along with visceromegaly and lymphadenopathy. Effective risk stratification is crucial for determining prognosis and tailoring individualized therapy for ALL. According to the criteria established by the National Cancer Institute (NCI), the following factors contribute to high-risk disease: age <1 year or >10 years, initial white blood cell (WBC) count >50 × 10^9/L, T-cell ALL (T-ALL), initial central nervous system leukemia (CNSL), slow response to induction chemotherapy, positivity for breakpoint cluster region-Abelson murine leukemia (BCR-ABL)/mixed-lineage leukemia (MLL)-AF4, testicular infiltration, lymphadenopathy, splenomegaly, and hepatomegaly.[3]

Acute myeloid leukaemia (AML) is a group of heterogeneous malignant disorders. It primarily results from aberrant differentiation that leads to uncontrolled proliferation of immature myeloid cells. AML accounts for approximately 20% of acute leukaemias in children and 80% of acute leukaemia in adults.[4] The incidence of AML progressively increases with age. Adults over 65 years old have an approximately 30-fold higher incidence compared to children.[5]

AML is more commonly observed in adults and presents with symptoms associated with pancytopenia, including infections, fever, weakness, fatigue, and hemorrhagic manifestations such as petechiae, menorrhagia, and epistaxis. Leukemia cell infiltration may occur in the skin or gums and physical examination may reveal pallor, lymph node enlargement, hepatomegaly, and splenomegaly.[6] AML WHO and FAB Classification is based on genetic mutations, Cytogenetic analysis , clinical presentation and morphology . Thus, comprehensive studies are needed to document both common and rare AML presentations in clinical settings, facilitating prompt diagnosis and effective management.[7]

In many developing countries, including Pakistan, the absence of a population-based tumor registry means that the annual incidence of cancer remains unknown. This is particularly significant for Pakistan, situated in Asia where cancer is increasingly becoming a major health challenge and is the leading cause of death in Asia Pacific nations. Currently, there is limited data available in literature on the prevalence of different types of acute leukemias in Pakistan. Most national-level studies focus solely on the clinical presentation, hematological profile, and outcomes of pediatric ALL.[8,9,10] Given the diverse presentations of these malignancies, timely recognition of symptoms and physical findings is crucial for effective management, which can significantly improve remission and cure rates. The objectives of this study were to document the age and gender distribution of various types of acute leukemias and to identify their clinical findings. Additionally, it aimed to explore any possible association between these factors.

METHODS

A retrospective study was conducted in Department of Pathology at Allama Iqbal Medical College (AIMC), Lahore. After obtaining approval from the Institutional Review Board (IRB), we retrieved patient data from existing bone marrow biopsy records from January 2020 to December 2023. Only newly diagnosed cases of acute leukemia in both pediatric and adult patients, confirmed by bone marrow aspiration and trephine biopsy were included .Patient who had a previous diagnosis of acute leukemia or who underwent bone marrow examination for remission status were excluded..

Data was collected in Microsoft Excel sheets. Key variables included age, gender, presenting complaints, clinical findings on physical examination, CBC parameters (hemoglobin, total leukocyte count, and platelet count), and types of leukemia. Sudan Black B staining was used to verify the myeloid origin of blasts due to the unavailability of immunophenotyping by flow cytometry required to confirm the lineage and type of leukemia. AML

was categorized into various types from AML-M1 to AML-M7 subtypes according to the French-American-British (FAB) classification based on morphology and cytochemistry. Those cases that were Sudan Black Negative were reported as Sudan Black Negative Acute Leukemia and advised immunophenotyping by flow cytometry for confirmation of lineage and type of leukemia. However, SBB negativity alone does not confirm ALL, as certain AML subtypes, such as minimally differentiated AML, may also exhibit weak or negative SBB staining. While blast morphology and Sudan Black B cytochemistry provide initial diagnostic clues, definitive classification of ALL requires flow cytometry, cytogenetics, and molecular studies to confirm lymphoid lineage and exclude AML

Data analysis was carried out using SPSS version 26.0. Descriptive statistics were applied to summarize data, with results presented as frequencies and percentages. Chi-square tests were applied to assess associations between clinical features and leukemia category. P-value of < 0.05 (95% confidence level) is considered significant.

RESULTS

Of the 130 patients, 54.6% were male and 45.4% were female. The mean age at presentation was 32.18 ± 16.34. Among hematological parameters mean Hb level 7.73 g/dl±1.88, Total Leukocyte Count 53.2x10^3/µL± 70.7 and platelet count was 51.1 x10^3/µL ±53.6. Fever was the most common clinical presentation (90.0%), followed by splenomegaly (44.6%), purpura (43.4%), bone and joint pain (41.9%), and weight loss (40.9%) (Table No 1). Regarding distribution of clinical features among different age groups Lymphadenopathy (51.3) was the most common presentation in pediatric age group followed by Fever (Figure 3) Sudan Black Negative (SBN) Acute Leukemia accounts for the largest proportion (51.5%), comprising more than half of the cases. Among the Acute Myeloid Leukemia (AML) subtypes, the most frequently observed are AML-M3 (13.8%) and AML-M2 (13.1%), followed by AML-M1 (9.2%) and AML-M4 (8.5%). The least common AML subtypes are AML-M5 (2.3%) and AML-M6 (1.5%) (Figure No 1). Regarding gender distribution Among AML subtypes, AML-M2 and AML-M3 were more prevalent in females, and Sudan Black Negative Leukemia showed a higher proportion of males (61.2%) compared to females (38.8%) (Figure No 3). Chi-square analysis revealed a statistically significant association between age and the acute leukemia category, with a p-value of 0.013 which shows that the distribution of leukemia categories varies significantly across different age groups. No significant association was observed between gender and leukemia category, as the p-value is 0.33, which is greater than the standard significance threshold of 0.05 at a 95% confidence level. Statistical analysis revealed significant associations ($p < 0.05$) between weight loss, lymphadenopathy, purpura, and fever with the condition being studied. However, splenomegaly, hepatomegaly, and bone and joint pain did not show a statistically significant association ($p \geq 0.05$). These variations in clinical presentation may be attributed to differences in study populations, geographic regions, and disease subtypes.

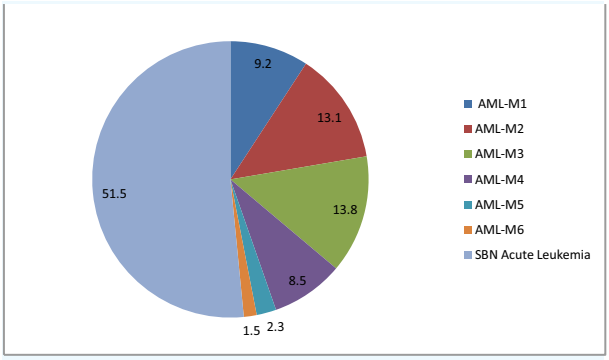

Figure-1: *Percentage Distribution of Various types of Acute Leukemia*

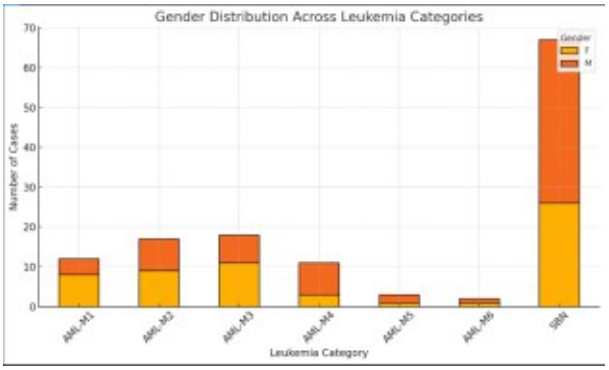

Figure-2: *Gender Distribution across Leukemia Categories*

Table 1: *Hematological Parameters and Clinical Manifestations in Acute Leukemia Patients*

Hematological Parameters and Clinical Features in Acute Leukemia patient		
Lab Parameter	**Mean value & SD**	**Range**
Hb (g/dl)	7.73±1.88	Minimum 3.40
		Maximum 12.50
WBC (10^3/µL)	53.2±70.7	Minimum 0.50
		Maximum 303.00
Platelet(10^3/µL)	51.1±53.6	Minimum 3.00
		Maximum 327.00
% of Blasts on Bone marrow aspirate	76.10±21.88	Minimum 22.00
		Maximum 98.00
Clinical Features	**Frequency(N)**	**Percentage**
Fever	117	90.00%
Bone and Joint Pain	54	41.50%
Wt. Loss	52	40.30%
Purpura	56	43.40%
Lymphadenopathy	41	31.50%
Hepatomegaly	42	32.60%
Splenomegaly	58	44.60%

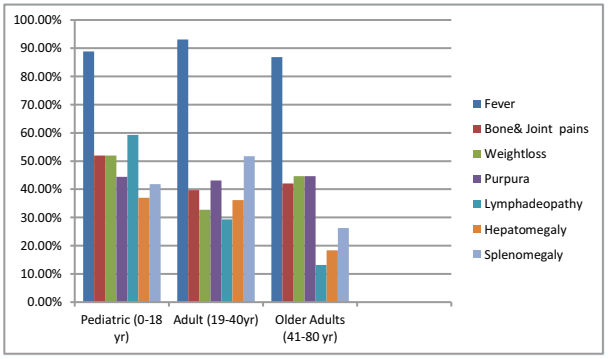

Figure-3: *Clinical Features across different age groups*

Discussion

Acute leukemia is a significant health concern in Pakistan. In northern Pakistan, it ranks as the second most common malignancy in males and the third most common in females. Given its prevalence, understanding the demographic distribution and clinical presentation of acute leukemia is crucial. This study analyzed the frequency of acute leukemia cases, their distribution by age and gender, and associated clinical features. Although some previous studies have explored the prevalence of acute leukemia in this region, the most recent one was conducted in 2014, highlighting the need for updated data.[1]

Among the 130 cases of acute leukemia in our study, 71 (54.6%) were males and 59 (45.4%) were females. The mean age at presentation was 32.18 ± 16.34 years, with an age range of 8 to 80 years. A national-level study by Shahab et al. also reported a higher prevalence in males (60% vs. 40%), consistent with our findings.[1] Similarly, Kulsum et al., in their study on the clinical presentation of AML, found that 60% of cases were male, with a mean age of 35.3 ± 17.1 years, which closely aligns with our results.[7]

International studies have also documented a male predominance in both AML and ALL cases. Mishra et al. reported a mean age of 47.1 years for AML patients, while Jamie et al. found that 58% of cases belonged to the 2–5 year age group.[11]

Chi-square analysis in our study revealed a statistically significant association between age and acute leukemia category ($p = 0.013$), indicating that the distribution of leukemia types varies significantly across different age groups. However, the Pearson Chi-Square test assessing the relationship between leukemia category and gender yielded p-values > 0.05, suggesting no statistically significant association between gender and leukemia category in our dataset.

The underlying reasons for the higher prevalence of leukemia and several other cancers in men remain unclear. Some research suggests that sex-specific hormones, such as estrogen, may have a protective role against certain cancers, including lymphoma. One study reported that males with childhood ALL experienced higher relapse rates and had a worse prognosis compared to females with the same diagnosis. Additionally, male pediatric leukemia survivors were found to be at a greater risk of developing secondary cancers.[12]

Among the leukemia cases in our study, Sudan Black B (SBB)-negative leukemia accounted for 67 (51.5%) cases, followed by AML with 63 (48.5%) cases. However, SBB negativity alone does not confirm ALL, as certain AML subtypes, such as minimally differentiated AML, may also exhibit weak or negative SBB staining. While blast morphology and Sudan Black B cytochemistry provide initial diagnostic clues, definitive classification of ALL requires flow cytometry, cytogenetics, and molecular studies to confirm lymphoid lineage and exclude AML.AML is

reported the most common form of leukemia in our study population, whereas ALL was most prevalent (46%), followed by AML(38%) reported by Shahab et al.[1] Variations exist across different studies, likely due to regional differences in leukemia prevalence. The incidence of leukemia varies by geographical location, influenced by environmental, genetic, and socio-economic factors. For instance, studies from Mosul have reported a higher cancer burden, potentially linked to prolonged exposure to environmental toxins, including nuclear waste from military conflicts.[13]

Among AML subtypes, the most common according to the FAB classification was AML-M3 (18 cases, 13.8%), followed by AML-M2 (17 cases, 13.2%). AML-M2 and AML-M3 were more prevalent in females, whereas Sudan Black B-negative leukemia had a higher proportion of males (61.2%) compared to females (38.8%).

In contrast, a study by Ranan et al reported AML-M2 as the most frequent FAB subtype (24.4%) among adult AML patients at Nanakaly Hospital for Blood Diseases.[4] Another study by Kulsoom B. et al. found that the most common subtype was AML with maturation, accounting for 183 cases (33.6%)[7]. These variations may be attributed to differences in study settings, geographic regions, and timeframe.

In our study, fever was the most common clinical presentation (90.0%), followed by splenomegaly (44.6%), purpura (43.4%), bone and joint pain (41.9%), and weight loss (40.9%). These findings are consistent with previous studies, though variations exist in reported frequencies. Kulsoom B. et al. identified fever as the most common symptom (71.9%), while Shahab F. et al. reported fever (77%), pallor (33%), and bleeding disorders (23%) as the primary presentations.[1,7] Similarly, Mishra K. et al. observed fever as the predominant symptom (60%) in AML patients with febrile neutropenia.[11]

Jaime-Pérez JC. et al. reported fatigue (62%), fever (60%), and bone and joint pain (39%) as the most frequent symptoms, with hepatomegaly (78%), splenomegaly (63%), and lymphadenopathy (57%) as the primary physical findings in childhood ALL cases.[14] Siddaiahgari SR. et al. found fever (92.3%), pallor (87.4%), hepatomegaly (85.4%), and splenomegaly (83.5%) to be the most prevalent clinical features.[15]

Khalid A. et al. also reported that the three most common symptoms in leukemic children were prolonged fever, followed by fatigue and body pain, and then frequent infections, which align with our findings.[16]

Statistical analysis revealed significant associations ($p < 0.05$) between weight loss, lymphadenopathy, purpura, and fever with the condition being studied. However, splenomegaly, hepatomegaly, and bone and joint pain did not show a statistically significant association ($p \geq 0.05$). These variations in clinical presentation may be attributed to differences in study populations, geographic regions, and disease subtypes."

The hematological parameters of our study population showed a mean hemoglobin (Hb) level of 7.73 ± 1.88 g/dL, mean white blood cell (WBC) count 53.2 ± 70.7 × 10^3/µL & mean platelet count was 51.1 ± 53.6 × 10^3/µL. Bone marrow aspirates revealed a mean blast percentage of 76.10 ± 21.88%, These findings are consistent with previous studies, though some variations exist. Ranan K. P. et al. reported a mean Hb level of 7.6 g/dL, WBC count of 34.5 × 10^6/L, platelet count of 39.6 × 10^9/L, and a blast percentage of 42.5% in peripheral blood and 65.9% in bone marrow[4]. Similarly, Kulsoom B. et al. found a mean hemoglobin level of 8.3 ± 2.4 g/dL and a red blood cell count of 2.9 ± 1.2 × 10^{12}/L. Jaime-Pérez J. C. et al. reported a median WBC count of 7.12 × 10^9/ a median Hb concentration of 7.5 g/ and a median platelet count of 47,400 × 10^9/L [7].The variations in hematological parameters observed across different studies may be attributed to differences in study populations, leukemia subtypes, geographic regions.

CONCLUSION

This study highlights the higher prevalence of acute leukemia in males and a significant association between age and leukemia subtype. Fever, weight loss, lymphadenopathy, and purpura were the most common clinical manifestations, underscoring their diagnostic importance. Further large-scale, multi-center research incorporating genetic and cytogenetic analysis is essential to improve disease characterization, risk stratification, and treatment outcomes.

AUTHORS CONTRIBUTION

Asma Akhtar: Design the methodology , Data collection ,analysis and interpretation, manuscript writing and revising the draft for intellectual content

Rabia Ahmad: Conceptualized the study, IRB approval, supervised the overall research activity, Data analysis and interpretation, and approved the final version.

Masuma Ghazanfar: Data analysis, Statistical analysis

Shizra Kaleemi: Sample Collection, Manuscript Writing and revision, Critical analysis.

Sabeen Fatima: Sample Collection, Manuscript Writing and revision, Critical analysis.

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