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## Spectrum & Clinicopathological Profile of Leukemia in a Tertiary Care Center in Northern India

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### HIGHLIGHTS

- Chronic Myeloid Leukemia predominated
- Chronic leukemias common
- Male predominance observed
- Significant age association
- Acute Lymphoblastic Leukemia in children

### Key Words:

Leukemia  
Chronic Myeloid Leukemia  
Acute Leukemia  
Epidemiology  
Northern India  
Hematological Malignancies

### ABSTRACT

**Introduction:** Leukemia comprises a heterogeneous group of hematological malignancies with varying clinical and epidemiological patterns across different regions. Understanding the local distribution of leukemia subtypes is important for improving early diagnosis, treatment strategies, and patient management. **Aim & Objectives:** This study aimed to evaluate the spectrum of leukemia and analyze its distribution according to age and gender in a tertiary care center in Northern India. **Material & Methods:** A retrospective observational study was conducted on 108 diagnosed cases of leukemia. Diagnosis was established using hematological, morphological, and cytochemical evaluation. Demographic and clinical details, including age, gender, and leukemia subtype, were collected from hospital records and analyzed statistically using the Chi-square test, with  $p < 0.05$  considered statistically significant. **Results:** Chronic leukemias accounted for most cases (86.11%), with Chronic Myeloid Leukemia being the predominant subtype (75.92%), followed by Chronic Lymphocytic Leukemia (10.18%). Among acute leukemias, Acute Lymphoblastic Leukemia (9.25%) was slightly more common than Acute Myeloid Leukemia (4.62%). A mild male predominance was observed (M:F = 1.28:1), although no significant association was found between gender and leukemia subtype ( $p = 0.900$ ). Age-wise distribution showed a significant association with leukemia subtype ( $p < 0.001$ ), with ALL predominating in children, CML in middle-aged adults, and CLL in elderly individuals. **Conclusion:** Chronic leukemias, particularly CML, were the most common leukemias observed in this region, with distinct age-related patterns across different subtypes.



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**INTRODUCTION**

Leukemia represents a diverse group of hematological malignancies characterized by clonal proliferation of abnormal hematopoietic cells, leading to bone marrow failure and systemic complications. Despite advances in diagnostic and therapeutic modalities, leukemia continues to impose a substantial global health burden. According to the Global Burden of Disease (GBD) 2019 analysis, leukemia accounted for approximately 474,000 new cases and over 300,000 deaths annually, with a steady increase in incidence in low- and middle-income countries (LMICs) [1,2]. Recent GLOBOCAN 2022 estimates further indicate that leukemia contributes to nearly 2.5-3% of all cancers worldwide, with significant geographic variability in incidence and survival outcomes [3].

The epidemiological distribution of leukemia demonstrates a characteristic bimodal age pattern, with peaks observed in early childhood and late adulthood. Acute lymphoblastic leukemia (ALL) remains the most common malignancy in children, whereas acute myeloid leukemia (AML) predominates in adults, particularly in older age groups [4]. Chronic leukemias, including chronic myeloid leukemia (CML) and chronic lymphocytic leukemia (CLL), are largely diseases of adulthood, with increasing prevalence in aging populations [5]. However, disparities in survival persist, with high-income countries reporting significantly improved outcomes due to access to targeted therapies, immunotherapy, and advanced diagnostics, while LMICs continue to face challenges related to delayed diagnosis and limited treatment infrastructure [2,6].

Leukemia encompasses a biologically heterogeneous spectrum of disorders broadly classified into acute and chronic types based on the rate of disease progression and the maturity of malignant cells. Acute leukemias are characterized by the rapid proliferation of immature precursor cells (blasts), resulting in bone marrow suppression and acute clinical presentation. In contrast, chronic leukemias exhibit a relatively indolent course with accumulation of more differentiated but functionally abnormal cells [7].

The major subtypes include ALL and AML among acute leukemias, and CML and CLL among chronic leukemias. These entities differ not only in their clinical behavior but also in their underlying genetic and molecular profiles. For instance, recurrent chromosomal abnormalities such as t(12;21) in ALL and mutations in FLT3 or NPM1 in AML significantly influence prognosis and therapeutic response [8]. Similarly, the presence of the Philadelphia chromosome (BCR-ABL1 fusion gene) is pathognomonic for CML and forms the basis for targeted therapy with tyrosine kinase inhibitors [9].

The World Health Organization (WHO) classification integrates morphology, immunophenotyping, cytogenetics, and molecular genetics to provide a comprehensive framework for leukemia diagnosis and classification [10]. This multidimensional approach has improved diagnostic accuracy and enabled personalized therapeutic strategies, particularly with the advent of precision medicine.

The clinical presentation of leukemia varies widely depending on subtype and disease burden. Acute leukemias typically

## Spectrum & Clinicopathological Profile of Leukemia

### A Comprehensive Overview of Hematological Malignancies

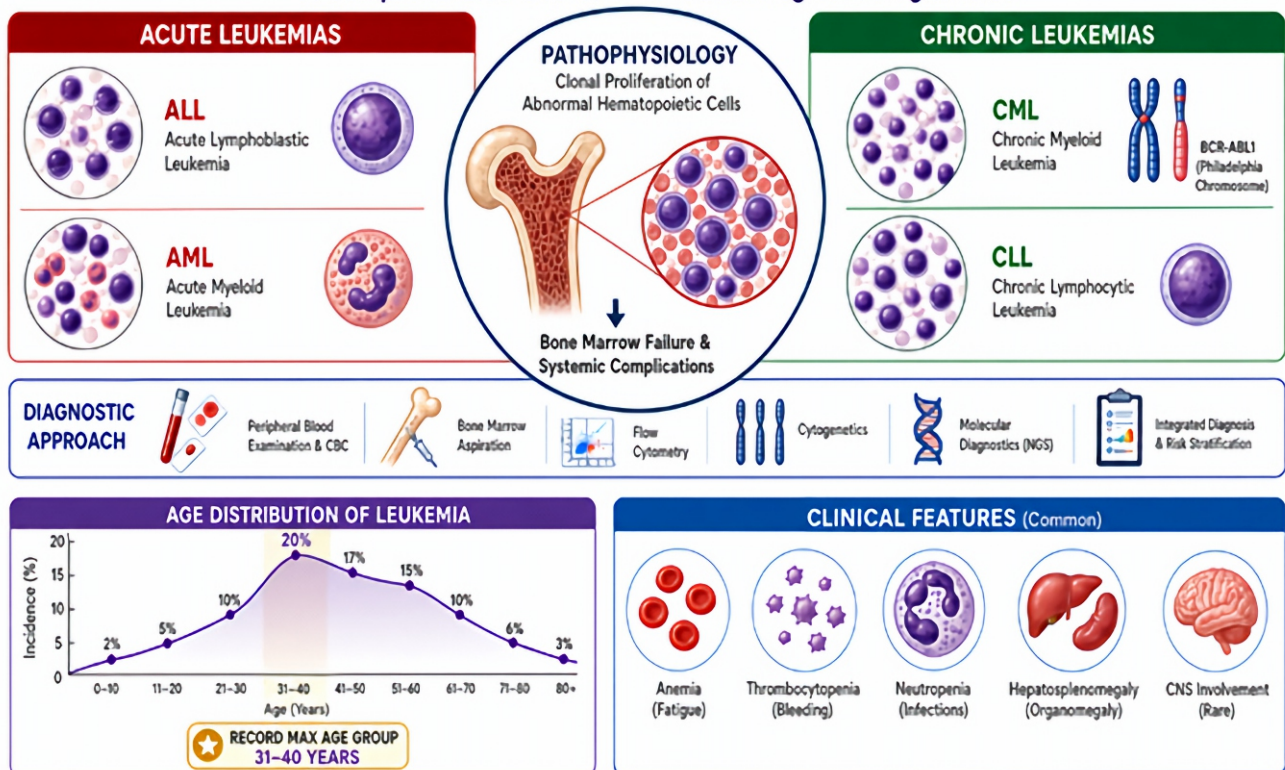


Figure 1: Spectrum, clinicopathological profile, diagnostic approach, and clinical features of Leukemia.

present with symptoms related to bone marrow failure, including anemia, thrombocytopenia, and neutropenia, manifesting as fatigue, bleeding tendencies, and recurrent infections [11]. Organ infiltration may lead to hepatosplenomegaly, lymphadenopathy, or central nervous system involvement. Chronic leukemias, on the other hand, may remain asymptomatic for prolonged periods and are often detected incidentally during routine hematological evaluation [12].

Diagnosis relies on a combination of clinical assessment and laboratory investigations. Peripheral blood examination and complete blood count (CBC) provide initial clues, while bone marrow aspiration remains the gold standard for confirming diagnosis and determining blast percentage. Advanced modalities, including flow cytometry, cytogenetics, and molecular diagnostics, further refine classification and prognostication [10,14].

Recent advances in next-generation sequencing (NGS) have uncovered a wide array of genetic mutations and epigenetic alterations in leukemia, facilitating risk stratification and guiding targeted therapy. These developments underscore the evolving landscape of leukemia diagnosis and management, emphasizing the importance of integrating traditional and modern diagnostic approaches [15].

Leukemia exhibits significant geographic and demographic variability, influenced by genetic predisposition, environmental exposures, and healthcare accessibility. In high-income countries, chronic leukemias-particularly CLL-constitute a larger proportion of cases, whereas acute leukemias are more prevalent in LMICs [16]. Such differences may reflect variations in population age structure, diagnostic capabilities, and environmental risk factors.

India presents a unique epidemiological profile, with a higher burden of acute leukemias and relatively lower reported incidence of CLL compared to Western populations [17]. Furthermore, the median age of presentation for CML in India is nearly a decade younger than that observed in Western countries, suggesting potential genetic and environmental influences [19].

Environmental factors, including exposure to benzene, pesticides, radiation, and industrial pollutants, have been implicated in leukemia pathogenesis. Regions with intensive agricultural activity, such as parts of North India, have reported higher incidence rates, possibly linked to chronic pesticide exposure [20]. Additionally, socioeconomic determinants, including access to healthcare and diagnostic facilities, significantly influence disease detection and outcomes, contributing to regional disparities in leukemia burden [6].

Within India, leukemia epidemiology demonstrates marked heterogeneity across regions. Hospital-based studies from North and Eastern India consistently report a predominance of acute leukemias, accounting for approximately 60–70% of cases, with a male predominance across all subtypes [18,21]. Pediatric ALL remains a major contributor to childhood cancer

burden, while adult AML and CML constitute significant proportions of cases in middle-aged populations.

The variability in subtype distribution and clinical presentation highlights the need for region-specific data to inform healthcare planning. Tertiary care hospitals, serving as referral centers for diverse populations, provide a valuable opportunity to study these patterns comprehensively. Such data are crucial for optimizing diagnostic strategies, resource allocation, and treatment protocols, particularly in resource constrained settings.

Despite substantial global literature on leukemia, there remains a paucity of region-specific data from many parts of India, particularly from semi-urban and rural populations. Existing studies often focus on selected subtypes or specific age groups, limiting the understanding of the overall disease spectrum. Additionally, variations in environmental exposures, socioeconomic factors, and healthcare access necessitate localized studies to capture the true burden and characteristics of leukemia in different settings. Spectrum, clinicopathological profile, diagnostic approach, and clinical features of Leukemia (**Figure 1**).

The present study is therefore designed to address these gaps by analyzing the spectrum of acute and chronic leukemias in a tertiary care hospital setting. By integrating clinical, hematological, and cytochemical data, the study aims to provide a comprehensive overview of leukemia patterns in the study population. Such insights are expected to contribute to improved diagnostic accuracy, early detection, and effective management strategies.

The primary objective of this study is to evaluate the spectrum of leukemia based on clinical presentation, hematological parameters, and morphological characteristics. Secondary objectives include assessing the distribution of leukemia subtypes across age groups and genders and identifying the most prevalent leukemia subtypes in the study population. These objectives align with the broader goal of enhancing understanding of leukemia epidemiology and improving patient care in tertiary healthcare settings.

## MATERIALS & METHODS

This retrospective observational study was conducted in the Department of Pathology, G.S.V.M. Medical College, Kanpur, India, to evaluate the spectrum and distribution of leukemia cases. A total of 108 cases of leukemia diagnosed over the study period were included after applying predefined inclusion and exclusion criteria. Patients of all age groups and both genders with a confirmed diagnosis of leukemia based on hematological parameters, peripheral smear examination, bone marrow findings (where available), and cytochemical staining were included in the study. Only cases with complete clinical and laboratory records were considered. Cases with incomplete or missing data, inconclusive diagnosis, patients already on treatment elsewhere with insufficient baseline diagnostic details, &

duplicate or repeat samples were excluded from the analysis.

All cases were evaluated using a standardized diagnostic approach. Complete blood counts were performed using automated hematology analyzers, followed by peripheral blood smear examination for morphological assessment. Bone marrow aspiration findings, where available, were reviewed to determine cellularity and blast percentage. Diagnosis of acute leukemia was established based on standard criteria, including the presence of  $\geq 20\%$  blasts in bone marrow or peripheral blood, and further classification into subtypes was done according to established WHO/FAB guidelines.

Relevant demographic and laboratory data, including age, gender, leukemia subtype, and cytochemical findings, were extracted from hospital records and entered a structured dataset using Microsoft Excel. Statistical analysis was performed using SPSS software. Categorical variables were expressed as frequencies and percentages. Associations between variables such as gender and leukemia subtype, as well as age group and subtype distribution, were assessed using the Chi-square test. A p-value of less than 0.05 was considered statistically significant.

## RESULT

A total of 108 cases of leukemia were analyzed during the study period. The distribution of cases revealed a predominance of chronic leukemias, accounting for 93 cases (86.11%), while acute leukemias comprised 15 cases (13.88%) (**Figure 2 & Table 1**). Chronic leukemias formed the majority of cases, with chronic myeloid leukemia (CML) being the most common subtype, observed in 82 cases (75.92%), followed by chronic lymphocytic leukemia (CLL) in 11 cases (10.18%). Among acute leukemias, acute myeloid leukemia (AML) was identified in 5 cases (4.62%), while acute lymphoblastic leukemia (ALL) was seen in 10 cases (9.25%) (**Figure 3 & Table 2**). Thus, CML emerged as the most prevalent subtype, whereas AML was the least common in the study population.

### Gender Distribution

Out of the 108 cases, 61 were males (56.48%), and 47 were females (43.52%), yielding a male-to-female ratio of 1.28:1 (**Table 3**), indicating a mild overall male predominance. Subtype wise distribution revealed that CML was more common in males, while AML & ALL showed relatively balanced gender

distribution, and CLL demonstrated a slight male preponderance (**Figure 4 & Table 4**). However, statistical analysis using the Chi-square test showed no significant association between gender and leukemia subtype ( $\chi^2 = 0.58$ ,  $p = 0.900$ ). These findings suggest that although a numerical male predominance exists, gender does not significantly influence the distribution of leukemia subtypes in this study population.

### Age-wise Distribution

The association between age group and leukemia subtype was analyzed using the Chi-square test, which demonstrated a highly statistically significant association ( $\chi^2 = 82.91$ ,  $p < 0.001$ ). The age-wise distribution showed that the 31–40-year age group was the most affected (26.85%), followed closely by the 41–50-year age group (14.81%). Subtype-specific trends revealed that ALL was predominantly observed in the adolescent age group (11–20 years), while AML was more frequent in young adults, particularly in the 21–30 years group. CML showed a marked predominance in middle-aged individuals, especially between 31 and 50 years, accounting for most cases in these age groups. In contrast, CLL was primarily observed in older age groups, with increasing frequency beyond 50 years and peak occurrence in the 61–70 years group (**Figure 5 & Table 5**). These findings indicate a clear and statistically significant age-related variation in leukemia subtype distribution, with acute leukemias predominating in younger individuals and chronic leukemias, particularly CML and CLL, occurring more frequently in middle-aged and elderly populations. Overall, the findings demonstrate a clear predominance of chronic leukemias, particularly CML, in the study population, with a mild male preponderance. The peak incidence was observed in the 31–40 years age group, while subtype-specific patterns showed ALL predominating in children and CLL in the elderly (**Table 6**). These results indicate an age-related shift from acute leukemias in younger individuals to chronic leukemias in older age groups. Peripheral blood smear findings in Chronic Myeloid Leukemia (**Figure 6**). Bone marrow aspirate findings in Chronic Myeloid Leukemia (**Figure 7**). Peripheral blood smear findings in Chronic Lymphocytic Leukemia (**Figure 8**). Peripheral blood smear findings in Acute Myeloid Leukemia (**Figure 9**). Peripheral blood smear findings in Acute Lymphoblastic Leukemia (**Figure 10**). Bone marrow aspirate findings in Acute Lymphoblastic Leukemia (**Figure 11**).

**Table 1: Distribution of Acute vs Chronic Leukemia**

Type of Leukemia	Number of Cases	Percentage (%)
Acute Leukemia	15	13.88%
Chronic Leukemia	93	86.11%
<b>Total</b>	<b>108</b>	<b>100%</b>

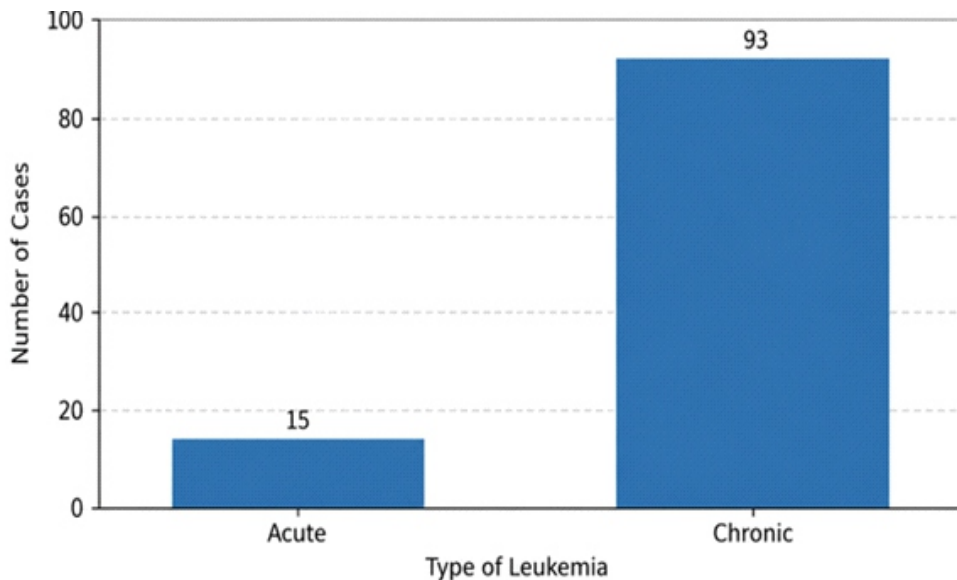


Figure 2: Distribution of leukemia types showing predominance of chronic leukemia over acute leukemia.

Table 2: Subtype Distribution of Leukemia

Leukemia Subtype	Number of Cases	Percentage (%)
CML	82	75.92%
CLL	11	10.18%
AML	5	4.62%
ALL	10	9.25%
<b>Total</b>	<b>108</b>	<b>100%</b>

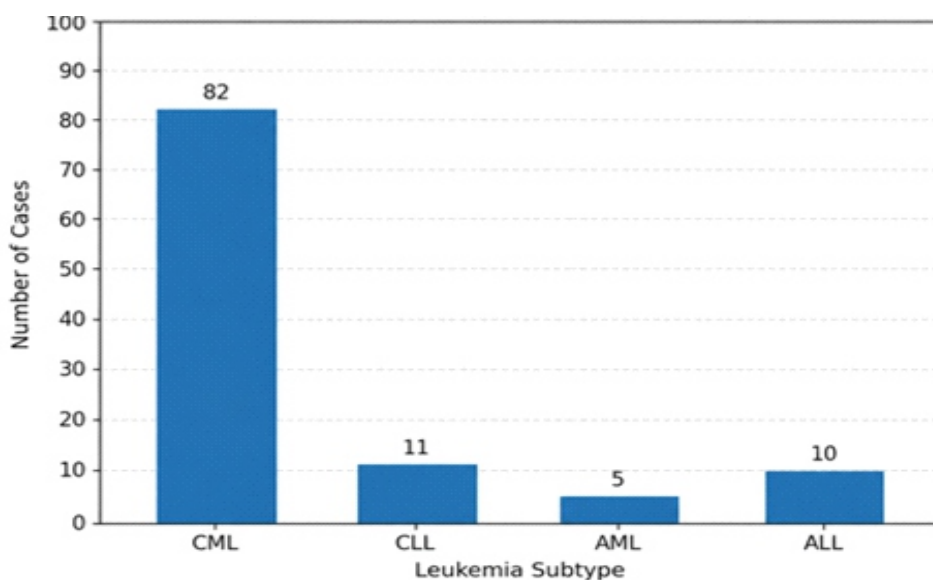


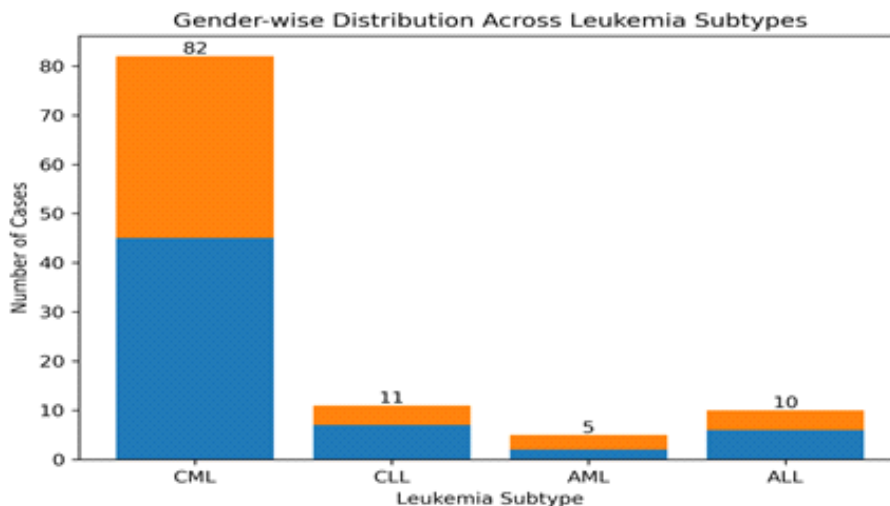
Figure 3: Distribution of leukemia subtypes with chronic myeloid leukemia (CML) being the most prevalent subtype.

Table 3: Overall Gender Distribution

Gender	Number of Cases	Percentage (%)
Male	61	56.48%
Female	47	43.52%
<b>Total</b>	<b>108</b>	<b>100%</b>

**Table 4: Gender-wise Distribution Across Leukemia Subtypes**

Leukemia Type	Male (n, %)	Female (n, %)	Total (n, %)
CML	45 (41.66%)	37 (34.25%)	82 (75.92%)
CLL	8 (7.40%)	3 (2.77%)	11 (10.18%)
AML	2 (1.85%)	3 (2.77%)	5 (4.62%)
ALL	6 (5.55%)	4 (3.70%)	10 (9.25%)
<b>Total</b>	<b>61 (56.48%)</b>	<b>47 (43.52%)</b>	<b>108 (100%)</b>

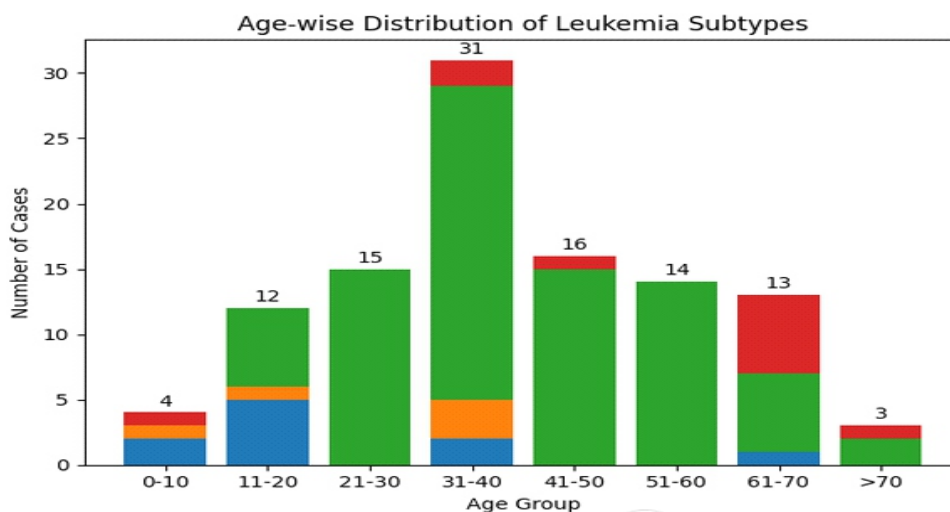


*Note- Blue colour is male and orange is for female*

**Figure 4: Gender-wise distribution of leukemia subtypes showing male predominance across most subtypes, particularly in CML.**

**Table 5: Age-wise Distribution of Leukemia Cases**

Age Group	ALL	AML	CML	CLL	Total (n, %)
0–10	2	1	0	1	4 (3.70%)
11–20	5	1	6	0	12 (11.11%)
21–30	0	0	15	0	15 (13.89%)
31–40	2	3	24	2	31 (28.70%)
41–50	0	0	15	1	16 (14.81%)
51–60	0	0	14	0	14 (12.96%)
61–70	1	0	6	6	13 (12.04%)
>70	0	0	2	1	3 (2.78%)
<b>Total</b>	<b>10</b>	<b>5</b>	<b>82</b>	<b>11</b>	<b>108 (100%)</b>

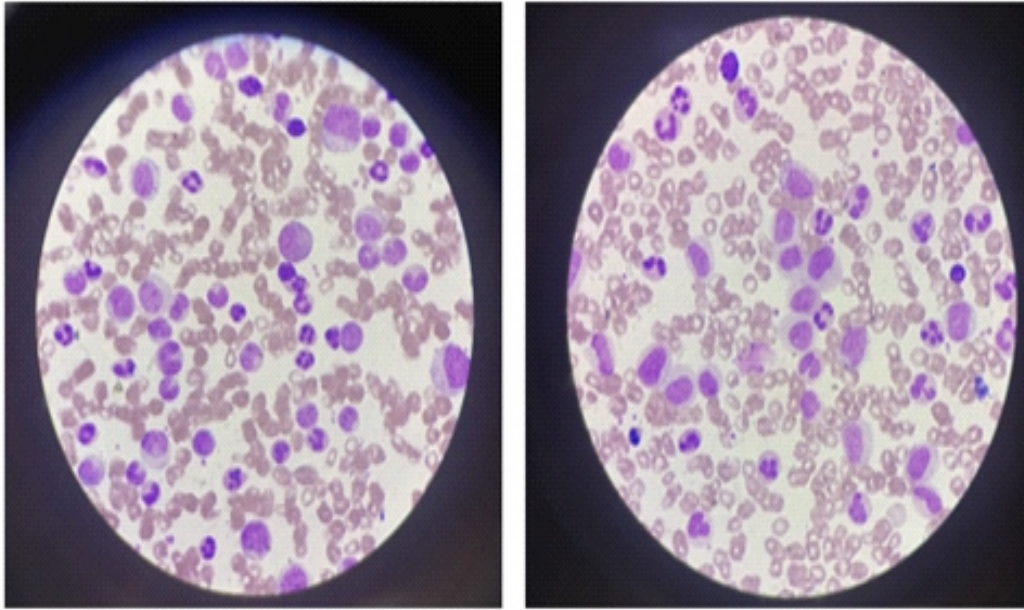


*Note- Green is for CML, Red is for CLL, Blue is for ALL, Orange is for AML*

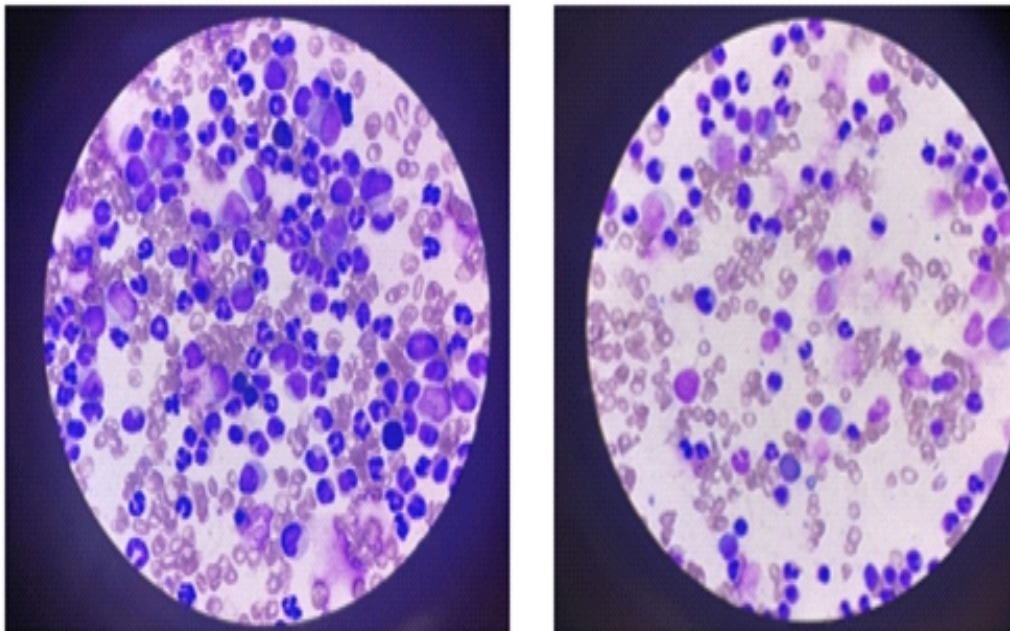
**Figure 5: Age-wise distribution of leukemia subtypes showing predominance of acute leukemias in younger age groups and chronic leukemias, particularly CML, in middle-aged and older individuals.**

**Table 6: Summary of Key Findings**

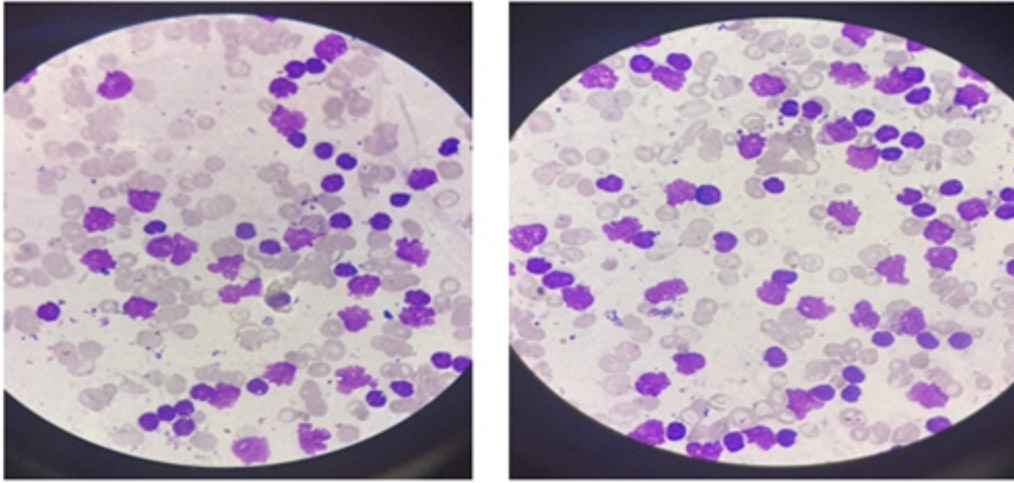
Variable	Key Finding
Predominant Type	Chronic leukemia (8 6.11%)
Most Common Subtype	CML (75.92%)
Least Common Subtype	AML (4.62%)
Gender Predominance	Male (M:F = 1.28:1)
Peak Age Group	31–40 years
Pediatric Predominance	ALL
Elderly Predominance	CLL



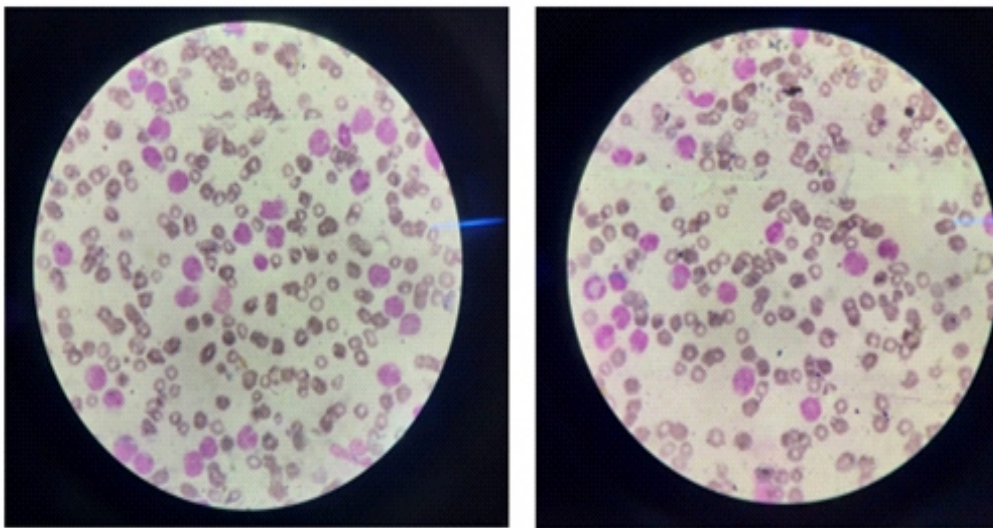
**Figure 6: Peripheral blood smear in Chronic Myeloid Leukemia (CML).** Photomicrographs showing marked leukocytosis with a spectrum of myeloid cells at various stages of maturation (left shift), including myelocytes, metamyelocytes, and occasional blasts. Features such as basophilia and eosinophilia may also be appreciated, consistent with CML. (*Leishman stain, oil immersion 1000×*).



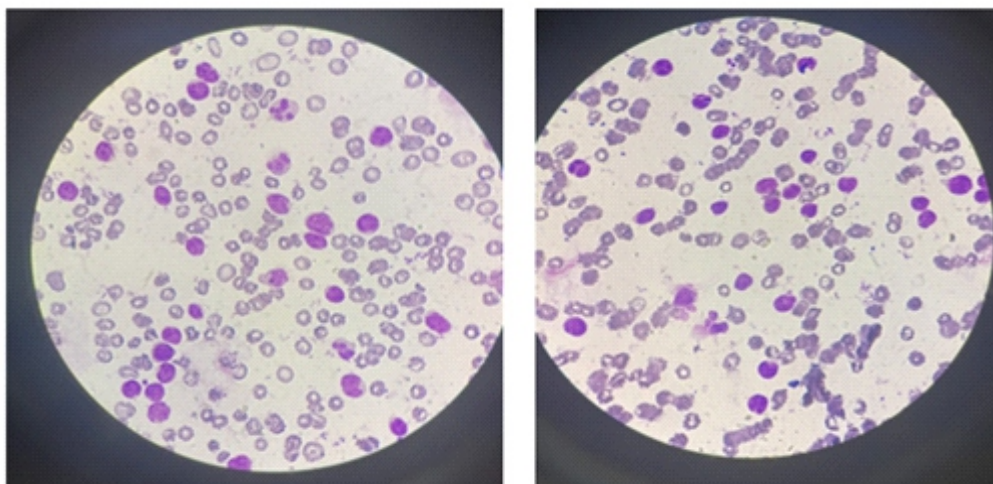
**Figure 7: Bone marrow aspirate in Chronic Myeloid Leukemia (CML).** Photomicrographs demonstrating a markedly hypercellular marrow with predominant myeloid hyperplasia and a full spectrum of granulocytic precursors at various stages of maturation. The myeloid-to-erythroid ratio is significantly increased, consistent with CML. (*Leishman stain, oil immersion 1000×*).



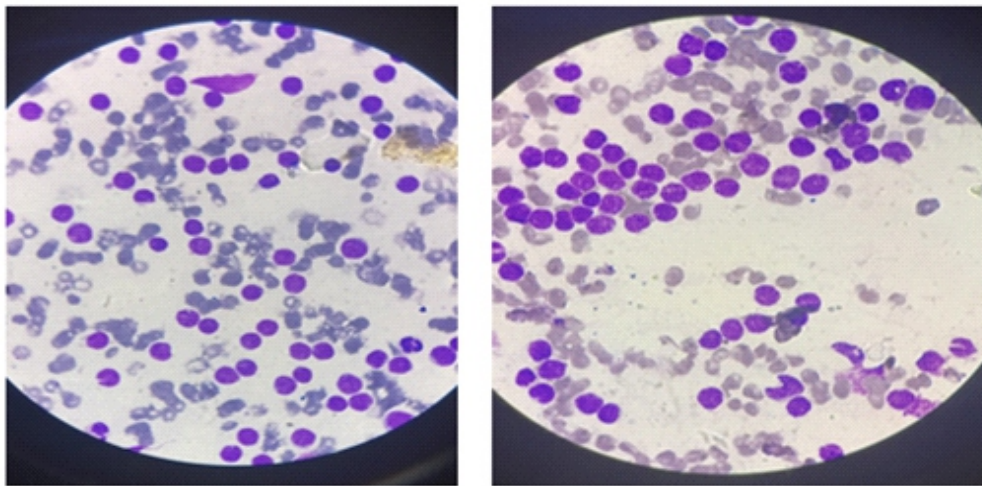
**Figure 8: Peripheral blood smear in Chronic Lymphocytic Leukemia (CLL).** Photomicrographs showing marked lymphocytosis with predominance of small, mature-appearing lymphocytes characterized by condensed (clumped) chromatin and scant cytoplasm. Numerous smudge cells (basket cells) are also evident, which are characteristic of CLL. (*Leishman stain, oil immersion 1000×*).



**Figure 9: Peripheral blood smear in Acute Myeloid Leukemia (AML).** Photomicrographs showing circulating myeloblasts characterized by large cells with high nuclear-to-cytoplasmic ratio, fine chromatin, and prominent nucleoli. Occasional Auer rods may be identified within the cytoplasm, supporting myeloid lineage. Background shows reduced mature elements. (*Leishman stain, oil immersion 1000×*).



**Figure 10: Peripheral blood smear in Acute Lymphoblastic Leukemia (ALL).** Photomicrographs showing circulating lymphoblasts characterized by small to medium-sized cells with high nuclear-to-cytoplasmic ratio, scant cytoplasm, fine chromatin, and inconspicuous nucleoli. Background shows relative paucity of mature leukocytes. (*Leishman stain, oil immersion 1000×*).



**Figure 11: Bone marrow aspirate in Acute Lymphoblastic Leukemia (ALL).** Photomicrographs showing a hypercellular marrow extensively infiltrated by lymphoblasts. The blasts are small to medium-sized with high nuclear-to-cytoplasmic ratio, scant cytoplasm, fine chromatin, and inconspicuous nucleoli, resulting in near replacement of normal hematopoietic elements. (*Leishman stain, oil immersion 1000×*).

## DISCUSSION

The present study provides a comprehensive evaluation of the spectrum of leukemia in a tertiary care setting, highlighting important epidemiological and clinicopathological trends. Chronic leukemias constituted the majority of cases (86.11%), with chronic myeloid leukemia (CML) emerging as the most prevalent subtype (75.92%), followed by CLL, ALL, and AML. This predominance of chronic leukemia contrasts with several Indian studies, where acute leukemias have been reported to be more common. For instance, **Das et al. [18]** and **Singh et al. [13]** reported a higher proportion of acute leukemias (approximately 60–70%) in tertiary care centers. Such variation may be attributed to differences in referral patterns, demographic characteristics, and increased detection of chronic leukemias through routine hematological screening.

The predominance of CML is consistent with findings from other Indian studies. **Thakur et al. [17]** and **Ning et al. [19]** have reported a high burden of CML in India, often presenting at a younger age compared to Western populations. The increasing availability of automated hematological investigations and improved awareness may contribute to early detection, thereby increasing the observed prevalence of CML in hospital-based studies.

Acute leukemias constituted a smaller proportion (13.88%), with ALL being slightly more common than AML. This observation aligns with global epidemiological patterns, where **AML predominates in adults and ALL is more common in children**, as described by **Pui et al. [4]**. However, several Indian studies report a higher burden of ALL in pediatric populations, indicating regional variability in subtype distribution.

A mild male predominance (M:F = 1.28:1) was observed, which is consistent with previous studies. **Kumar et al. [21]** and **Das et al. [18]** have also reported male preponderance across leukemia subtypes. However, the association between gender & leukemia

subtype was not statistically significant ( $p = 0.900$ ), indicating that gender does not significantly influence subtype distribution. The observed male predominance may be influenced by biological susceptibility as well as sociocultural factors such as differential healthcare access and utilization.

Age-wise analysis demonstrated a highly significant association between age group and leukemia subtype ( $p < 0.001$ ), indicating distinct age-related patterns. The peak incidence in the 41–50 years age group corresponds with the predominance of chronic leukemias, particularly CML. Similar findings have been reported by **Thakur et al. [17]**, who observed a higher incidence of CML in middle-aged individuals. Furthermore, **Ning et al. [19]** highlighted that the median age of CML presentation in India is lower than in Western populations, suggesting the influence of genetic and environmental factors.

Subtype specific age distribution revealed that ALL predominantly affected the pediatric population, consistent with global observations. **Pui et al. [4]** identified ALL as the most common childhood malignancy. AML was more frequently observed in young adults, reflecting its known epidemiological pattern. In contrast, CLL was predominantly seen in older individuals, consistent with its established association with aging, as described by **Campo et al. [12]**.

Cytochemical findings further supported accurate subtype classification. AML cases demonstrated positivity for myeloperoxidase (MPO), while ALL cases showed positivity for periodic acid-Schiff (PAS), confirming their respective lineages. These findings are consistent with earlier studies, including **Singh et al. [13]**, which emphasize the continued relevance of cytochemical staining in differentiating leukemia subtypes, particularly in resource limited settings where advanced molecular diagnostics may not be readily available.

Environmental and socioeconomic factors may also contribute to the observed patterns. Exposure to carcinogens such as benzene,

pesticides, and industrial pollutants has been implicated in leukemia pathogenesis. Aggarwal et al. [20] reported higher incidence rates of hematological malignancies in regions with significant agricultural activity, suggesting a role of environmental exposure. Additionally, disparities in healthcare access and diagnostic infrastructure, as highlighted by Du et al. [6], may influence disease detection and reporting.

Overall, these findings underscore the importance of region specific epidemiological data in understanding leukemia patterns. The predominance of chronic leukemias, particularly CML, along with distinct age related trends, highlights the need for strengthening diagnostic infrastructure and implementing targeted healthcare strategies for effective leukemia management.

## CONCLUSION

The present study highlights the epidemiological and clinicopathological spectrum of leukemia in a tertiary care setting, demonstrating a clear predominance of chronic leukemias, particularly chronic myeloid leukemia (CML). Acute leukemias constituted a smaller proportion, with acute lymphoblastic leukemia (ALL) slightly more common than acute myeloid leukemia (AML). A mild male predominance was observed; however, gender did not significantly influence subtype distribution. Age showed a strong association with leukemia subtype, with ALL predominantly affecting the adolescence population, CML occurring mainly in middle-aged individuals, and CLL being more common in the elderly. These findings emphasize the importance of region-specific data in understanding leukemia patterns and underscore the need for early diagnosis, improved diagnostic infrastructure, and targeted management strategies to enhance patient outcomes.

## LIMITATIONS & FUTURE PERSPECTIVES

The study's limitations include a single-centre setting, a relatively small sample size, and a short study duration, which may limit the broader applicability of the results. Future studies should incorporate multicentre designs with larger populations to enhance validity, assess long-term outcomes, and investigate advanced diagnostic and management approaches. Such efforts will improve overall patient care and help minimize complications.

## CLINICAL SIGNIFICANCE

The clinical significance of this study lies in its potential to bridge the gap between research findings and practical healthcare applications. It emphasizes the importance of translating scientific observations into meaningful improvements in patient care, diagnosis, and treatment outcomes. By highlighting real-world relevance, the study contributes to evidence based medical practice and supports informed clinical decision making. Ultimately, the findings aim to enhance patient quality of life, optimize therapeutic strategies, and promote better disease management in clinical settings.

## ABBREVIATIONS

**CLL:** Chronic Myeloid Leukemia

**AML:** Acute Myeloid Leukemia

**ALL:** Acute Lymphoblastic Leukemia

**MPO:** Myeloperoxidase

**M:F ratio:** Male-To-Female Ratio

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## AUTHOR CONTRIBUTIONS

All authors significantly contributed to the study conception and design, data acquisition, or data analysis and interpretation. They participated in drafting the manuscript or critically revising it for important intellectual content, consented to its submission to the current journal, provided final approval for the version to be published, and accepted responsibility for all aspects of the work. Additionally, all authors meet the authorship criteria outlined by the International Committee of Medical Journal Editors (ICMJE) guidelines.

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## CONFLICT OF INTEREST

Authors declared that there is no conflict of interest.

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All necessary consent & approval was obtained by authors.

## CONSENT FOR PUBLICATION

All necessary consent for publication was obtained by authors.

## DATA AVAILABILITY

All data generated and analyzed are included within this research article. The datasets utilized and/or analyzed in this study can be obtained from the corresponding author upon a reasonable request.

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