Research Article

PATTERN OF LEUKEMIA IN PATIENTS PRESENTING TO A TERTIARY CARE HOSPITAL FROM WESTERN INDIA: A FOUR-YEAR STUDY IN THE DEPARTMENT OF CLINICAL HEMATOLOGY

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ABSTRACT

Background: Leukemia is a heterogeneous group of hematological malignancies originating from hematopoietic cells of the bone marrow and lymphatic system. As treatment and prognosis are different for each type of leukemia, identifying the distribution pattern is crucial for its prompt management.

Objective: This study was aimed to determine the distribution pattern of different types of leukemia among patients presenting to clinical hematology department at a tertiary care hospital of Western India.

Methods: This observational study was conducted over a period of 4 years on 684 patients of all ages presenting with leukemia. Participants were subjected to relevant investigations including bone marrow examination and special tests for hematological malignancies such as flow cytometry, immunohistochemistry, karyotyping, and molecular tests.

Results: The most common age group (23.8%) affected was 61-70 years with overall male preponderance(56.7%). The chronic leukemia (59.8%) was commoner than acute leukemia. Overall, chronic myeloid leukemia (CML) was the most common type (29.1%) followed by chronic lymphocytic leukemia, acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL). AML was dominant type among acute leukemia (50.9%), whereas CML was the commonest chronic leukemia (48.7%). In adults, the most common leukemia was CML (34.2%), whereas ALL was the commonest leukemia (66.7%) in children. Leukocytosis, anemia, and thrombocytopenia were among most common hematological abnormalities in various types of leukemia.

Conclusion: Pattern of various types of leukemia was different among adults and children as well as among both genders. Studies from various other regions of the country must be undertaken.

INTRODUCTION

Hematological malignancies are a group of neoplastic disorders that originate from hematopoietic cells of the bone marrow and lymphatic system [1,2]. They comprise a collection of heterogeneous conditions including leukemia, lymphoma, multiple myeloma, myelodysplastic syndrome and myeloproliferative neoplasms [2]. Leukemia is a heterogeneous group of hematological malignancies resulting from somatic mutations in pluripotent stem cells and progenitor cells. Based on hematopoietic stem cell involvement, leukemia is classified into myeloid and lymphoid type, whereas based on progression of the disease, leukemia can be grouped into acute and chronic leukemia [3].

Acute leukemia is fast-growing leukemia characterized by clonal expansion of immature myeloid or lymphoid precursors (blasts) in the bone marrow and infiltration of these blasts into peripheral blood circulation, solid organs, and lymphatic system. As per the WHO classification, the blasts should be 20% or more in the marrow or peripheral blood to diagnose acute leukemia [4,5]. Acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) are two major types of acute leukemia [6,7]. AML is the proliferation of myeloid blasts including myeloblasts, monoblasts, megakaryoblasts, erythroblasts, and their precursors in the bone marrow [8]. ALL is a malignant transformation and uncontrolled proliferation of abnormal, immature lymphocytes and precursors of B or T-lymphocytes. Around 75% of adult ALL cases affect the B-cell phenotype, whereas the remaining 25% cases affect the T-cell phenotype. ALL is predominant leukemia that affects children [9].

Chronic leukemia is a broad spectrum of slow-growing hematological malignancies characterized by uncontrolled proliferation and expansion of mature, differentiated cells of the hematopoietic system in the bone marrow as well as in peripheral circulation [2]. Chronic myeloid leukemia (CML) and chronic lymphocytic leukemia (CLL) are two common types of chronic leukemia [7]. CML is characterized by the

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presence of all stages of myeloid development in the peripheral blood and driven by the aberrant protein tyrosine kinase [10]. CLL is an indolent lymphoproliferative disorder manifested by the progressive accumulation of mainly mature B-lymphocyte in the blood, bone marrow, and lymphatic tissues [11].

Leukemia affects peoples of all nations and the world without discrimination based on their sociodemographic background. It constitutes a major proportion of hematopoietic neoplasms worldwide. It is the 8th to 12th most common malignancy across the globe [12]. It represents the eleventh most frequent cause of cancer-related mortality worldwide. There was an estimate of a total of 437 thousand new cases and 309 thousand cancer-related deaths from leukemia worldwide according to the global cancer statistics report 2018 [13]. Leukemia can affect all age groups but children and older adults are the most commonly affected populations. It is the most common form of cancer among all childhood malignancy and accounts for 30% of all cancers diagnosed in children under 15 years of age [14]. The incidence rates of all types of leukemia are slightly higher in males as compared to females and it might be affected by geographical and ethnic variations [15].

The causes for leukemia are not yet clearly known. However, epidemiological studies have suggested that several risk factors might be associated with the development and the increased risk for leukemia such as prolonged exposure to ionizing radiation, exposure to benzene, organic solvents, agricultural pesticides, and herbicides, cigarette smoking, previous cancer treatment with both chemotherapy and radiation therapy, immunological insults, hereditary inheritance, genetic mutations, and infection with some viral agents [1,15].

The impact of leukemia in developing countries including India is enormous due to premature death of children, loss of parents, loss of productivity due to a disability, and high medical cost that affects the socioeconomic and health welfare of the population. As prognosis and survival rate are different for each type of leukemia, classification of leukemia is essential for their effective treatment. There have been few studies conducted to investigate the distribution pattern of different types of leukemia in India. Even, no similar study was conducted in this region of country. Therefore, the main aim of this study was to determine the prevalence of different types of leukemia along with age and gender distribution among patients attending clinical hematology department at a tertiary center in Western India.

MATERIALS AND METHODS

Study design and study population

This prospective observational study was conducted in the Department of Clinical Hematology at Dr. SN Medical College and associated Mathura Das Mathur Hospital, Jodhpur, Rajasthan, India over a period of 4 years from April 2018 to March 2022. A total of 684 patients of either sex and all ages with newly diagnosed leukemia attending the inpatient or outpatient department were included in this study. Previously diagnosed cases of leukemia were excluded from the study.

Study procedure

Ethical approval for this study was obtained from the Institutional Ethics Committee. A written informed consent was taken from all patients prior to their enrolment in the study. A detailed medical history was obtained from each participant and relevant clinical examination was carried out. Routine blood investigations including complete blood count (CBC) were performed. All the hematological parameters were noted. Peripheral blood smear (PBS) examination was done in each case. Bone marrow (BM) examination including BM aspiration and trephine biopsy were performed in each case by standard methods. Furthermore, special stain like Myeloperoxidase (MPO), Periodic acid-Schiff (PAS) and Sudan black B (SBB) stains were applied for staining the smears whenever required, and the preparations were examined by experienced pathologist. The diagnosis of acute leukemia was made in cases where blasts were ≥20% according to WHO guidelines. Special tests for hematological malignancies including flow cytometry, immunohistochemistry, karyotyping, molecular tests and serum protein electrophoresis were also done wherever indicated.

Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) software version 21.0 for Windows (Version 21.0 for Windows; SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean ± standard deviation (±SD) or range as appropriate. Categorical variables were indicated as frequency (n) and percentage (%).

RESULTS

Age distribution of the study subjects

The age of patients ranged between 3 months and 95 years with a mean age of 34.7 years (standard deviation [SD] ±16.9 years). The most common (23.8%) age group affected was between 61 and 70 years followed by age group 51-60 years (12.6%) and 0-10 years (10.8%). Maximum number of cases of ALL (45%) were found below 10 years. Maximum number of cases of AML (22.1%) and CML (24.6%) were observed in the age groups of 31-40 years and 41-50 years respectively. CLL cases were found most frequently (52.5%) in the age group of 61-70 years (Table 1).

Table 1 Age distribution of all cases and four most common types of leukemia.

Age groups (years)	All cases (n=684) n (%)	Types of leukemia			
		AML (n=140) n (%)	ALL (n=131) n (%)	CML (n=199) n (%)	CLL (n=177) n (%)
0-10	74 (10.8)	10 (7.1)	59 (45)	2 (1)	0 (0)
11-20	83 (12.1)	26 (18.6)	41 (31.3)	10 (5)	0 (0)
21-30	41 (6)	16 (11.4)	10 (7.6)	13 (6.5)	0 (0)
31-40	71 (10.4)	31 (22.1)	8 (6.1)	32 (16.1)	4 (2.3)
41-50	89 (13)	19 (13.6)	5 (3.8)	49 (24.6)	14 (7.9)
51-60	86 (12.6)	17 (12.1)	2 (1.5)	36 (18.1)	22 (12.4)
61-70	163 (23.8)	10 (7.1)	3 (2.3)	42 (21.1)	93 (52.5)
71-80	60 (8.8)	7 (5)	2 (1.5)	11 (5.5)	36 (20.3)
81-90	15 (2.2)	3 (2.1)	1 (0.8)	4 (2)	7 (4)
91-100	2 (0.3)	1 (0.7)	0 (0)	0 (0)	1 (0.6)
Total	684 (100)	140 (100)	131 (100)	199 (100)	177 (100)

Abbreviations: AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; CML, chronic myeloid leukemia; CLL, chronic lymphocytic leukemia.

Distribution of different types of leukemia among study participants

Out of 684 study participants, 275 (40.2%) cases were of acute leukemia and 409 (59.8%) cases were of chronic leukemia. The myeloid type of leukemia was dominant and accounted for 51.9% of cases, whereas the lymphoid type of leukemia was accounted for 48.1% of cases. Overall, CML was the most common type of leukemia (29.1%) followed by CLL (25.8%), AML (20.5%), ALL (19.2%), chronic myelomonocytic leukemia (CMML) (1.4%) and hairy cell leukemia (HCL) (1.3%). Overall, a male preponderance was found with 388 (56.7%) cases were diagnosed in males and 296 (43.3%) in females. The male:femal eratio was 1.31:1. Moreover, prevalence of acute leukemia as well as chronic leukemia was also higher in males compared to females (25.4% vs 14.8% and 31.3% vs 28.5%, respectively). AML (overall and non-acute promyelocytic leukemia [APL] subtype), ALL, CLL and HCL cases were dominant among male patients, whereas APL and CML were more common in females (Table 2).

Table 2 Distribution of different types of leukemia among study participants according to age and gender category.

Types of leukemia	All cases (n = 684) n (%)	Age category		Gender category	
		<18 years (n = 132) n (%)	≥18 years (n = 552) n (%)	Male (n = 388) n (%)	Female (n = 296) n (%)
Acute leukemia	275 (40.2)	120 (17.5)	155 (22.7)	174 (25.4)	101 (14.8)
AML	140 (20.5)	26 (3.8)	114 (16.7)	84 (12.3)	56 (8.2)
-Non-APL	119 (17.4)	24 (3.5)	95 (13.9)	74 (10.8)	45 (6.6)
-APL	21 (3.0)	2 (0.3)	19 (2.7)	10 (1.4)	11 (1.6)
ALL	131 (19.2)	88 (12.9)	43 (6.3)	87 (12.7)	44 (6.5)
MPAL	3 (0.4)	1 (0.1)	2 (0.3)	2 (0.3)	1 (0.1)
UAL	1 (0.2)	0 (0)	1 (0.2)	1 (0.2)	0 (0)
Chronic leukemia	409 (59.8)	12 (1.8)	397 (58)	214 (31.3)	195 (28.5)
CML	199 (29.1)	10 (1.5)	189 (27.6)	93 (13.6)	106 (15.5)
CNL	4 (0.6)	0 (0)	4 (0.6)	2 (0.3)	2 (0.3)
CMML	10 (1.4)	0 (0)	10 (1.4)	6 (0.8)	4 (0.6)
JMML	2 (0.3)	2 (0.3)	0 (0)	2 (0.3)	0 (0)
CLL	177 (25.8)	0 (0)	177 (25.8)	98 (14.3)	79 (11.5)
PLL	2 (0.3)	0 (0)	2 (0.3)	2 (0.3)	0 (0)
HCL	9 (1.3)	0 (0)	9 (1.3)	7 (1.0)	2 (0.3)
PCL	4 (0.6)	0 (0)	4 (0.6)	3 (0.4)	1 (0.2)
LGL leukemia	2 (0.3)	0 (0)	2 (0.3)	1 (0.2)	1 (0.2)
Total	684 (100)	132 (19.3)	552 (80.7)	388 (56.7)	296 (43.3)

Abbreviations: AML, acute myeloid leukemia; APL, acute promyelocytic leukemia; ALL, acute lymphoblastic leukemia; MPAL, mixed phenotypic acute leukemia; UAL, undifferentiated acute leukemia; CML, chronic myeloid leukemia; CNL, chronic neutrophilic leukemia; CMML, chronic myelomonocytic leukemia; JMML, juvenile myelomonocytic leukemia; CLL, chronic lymphocytic leukemia; PLL, prolymphocytic leukemia; HCL, hairy cell leukemia; PCL, plasma cell leukemia; LGL, large granular lymphocytic

The majority of the study participants (80.7%) were adults (≥18 years). Adult group had 155 (56.4%) cases of acute leukemia compared to 120 (43.6%) cases within the pediatric age group. Almost all (97%) cases of chronic leukemia were present in adult age group compared to only 3% cases in children. Among adults, the commonest type of leukemia was CML (34.2%), whereas ALL (66.7%) was the most common leukemia in pediatric age group. Among acute leukemia cases, AML (non-APL as well as APL type) and mixed phenotypic acute leukemia (MPAL) were more common in adults, whereas ALL was commoner in children. Adult group had 114 (81.4%) cases of AML as compared to 26 (18.6%) cases among children. In contrast, 88 (67.2%) cases of ALL were present in children as compared to 43 (32.8%) cases in adults.

All types of chronic leukemia except juvenile myelomonocytic leukemia (JMML) were predominantly found in adults (Table 2).

Hematological parameters among patients with leukemia

Changes in the hematological parameters in cases of leukemia are shown in Table 3. Leukocytosis, anemia, and thrombocytopenia were common hematological abnormalities reported among various types of leukemia. Overall, 89 (63.6%) cases of AML, 98 (74.8%) of ALL, 193 (97%) of CML and 175 (98.9%) of CLL had leukocytosis, whereas 125 (89.3%) of AML, 98 (74.8%) of ALL, 111 (55.8%) of CML and 88 (49.7%) of CLL patients had anemia. In addition, 93 (66.4%) of AML, 65 (49.6%) of ALL, 19 (9.6%) of CML, and 63 (35.6%) of CLL patients had thrombocytopenia.

Table 3 Hematological parameters in patients with four most common subtypes of leukemia.

Hematological parameters	Value or Category	AML (n = 140) n (%)	ALL (n = 131) n (%)	CML (n = 199) n (%)	CLL (n = 177) n (%)
Hemoglobin (g/dL)	Range	1.9-13.2	4.1-13.8	6.7-16.8	5.1-12.4
	Mean ± SD	7.6±2.95	9.4±3.18	9.8±3.38	8.6±2.18
	Low	125 (89.3)	98 (74.8)	111 (55.8)	88 (49.7)
	Normal	15 (10.7)	33 (33.2)	86 (43.2)	89 (51.3)
	High	0 (0)	0 (0)	2 (1)	0 (0)
Total leucocyte count (10⁹/L)	Range	0.62-347	0.92-406	9.2-456	3.72-371
	Mean ± SD	72.64±46.3	36.5±16.8	114.5±45.2	34.6±16.4
	Low	37 (26.4)	15 (11.5)	0 (0)	2 (1.1)
	Normal	14 (10)	18 (13.7)	6 (3)	0 (0)
	High	89 (63.6)	98 (74.8)	193 (97)	175 (98.9)
Platelet count (10⁹/L)	Range	3-514	8-412	129-1736	11-558
	Mean ± SD	43±16	56.8±17.8	619±242	154±45
	Low	93 (66.4)	65 (49.6)	19 (9.6)	63 (35.6)
	Normal	43 (30.7)	66 (50.4)	131 (65.8)	109 (61.5)
	High	4 (2.9)	0 (0)	49 (24.6)	5 (2.9)

Abbreviations: AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; CML, chronic myeloid leukemia; CLL, chronic lymphocytic leukemia.

DISCUSSION

In this study, chronic leukemia (59.8%) was more common than acute leukemia (40.2%). This was consistent with the findings reported in other studies from India, Saudi Arabia, and Bangladesh [16-18]. On the contrary, acute leukemia was found to be more common than chronic leukemia in other studies from India as well as other countries [19-25]. In a recent study by Rathod et al from India, 69.18% of patients had acute leukemia while 29.72 % had chronic leukemia [25]. The possible reasons for this variation might be the variations in sample size, study population, geographical location, and socio-demographic pattern.

In the current study, CML was the most common type of leukemia accounted for 29.1% of cases followed by CLL (25.8%), AML (20.5%), ALL (19.2%), CMML (1.4%), and HCL (1.3%). These results were in line with the findings of previous studies from India and other countries where CML was also reported as dominant type of leukemia [19,21,22,26]. On the other hand, studies by Modak et al [23], Chen et al [24] and Rathod et al [25] reported AML as the most common type of leukemia. CLL was observed to be most common leukemia in some studies from other countries [19,27],while lower prevalence compared to the present finding was reported in other similar studies [21,22,24,25]. The possible reasons for this variation might also be the variations in sample size, study population, geographical location, and socio-demographic pattern.

Overall, a male preponderance was observed in our study with a prevalence of 56.7% in males and 43.3% in females (male:female ratio=1.31:1). This was in concurrent with findings reported in other previous studies from India and other countries [19-21,23,28-30]. The possible justification might be that male individuals are comparatively more exposed to the occupational and environmental carcinogenic agents which are at higher risk to the incidence of all kinds of leukemia. In our study, AML (overall and non-APL type), ALL, CLL and HCL cases were dominant among male patients, whereas APL and CML were more common in females. Similar to this, male predominance in ALL and AML, whereas female predominance in CML was also seen in studies by Rathod at al [25] and Singh *et al* [31].

In this study, majority of cases of acute leukemia (56.4%) were found within the adult age group (≥18 years), whereas 43.6% of cases were found within the pediatric age group (<18 years). This result was in contrast to the findings reported in some previous studies where the higher cases of acute leukemia were found in younger age [19,32,33]. Moreover, 97% cases of chronic leukemia in our study were found within the adult age group, whereas only 3% cases were found within the pediatric age group. This result was in line with the findings reported in other studies where the higher cases of chronic leukemia were found in the middle adult age [19,32,33]. In our study, majority of cases of AML (81.4%) were found within the adult age range, whereas 18.6% of cases were found within the younger age range. It is comparable with findings of other previous studies, where AML was also found to be more common in adult [30,31,34,35]. In children, ALL was the most prevalent type observed (66.7%) in current study. Similar results were also seen in other studies [29,31,34,35].

Our study results showed that leukocytosis, anemia, and thrombocytopenia were among the most common hematological abnormalities in various types of leukemia. Overall, 89 (63.6%) cases of AML, 98 (74.8%) of ALL, 193 (97%) of CML and 175 (98.9%) of CLL had leukocytosis, whereas 125 (89.3%) of AML, 98 (74.8%) of ALL, 111 (55.8%) of CML and 88 (49.7%) of CLL patients had anemia. In addition, 93 (66.4%) of AML, 65 (49.6%) of ALL, 19 (9.6%) of CML, and 63 (35.6%) of CLL patients had thrombocytopenia. This was in line with the findings reported in a study undertaken in Pakistan that showed that total leukocyte count was high in 52%, 66.6%, 87.5%, and 66.6% of ALL, AML, CML, and CLL cases, respectively, and low hemoglobin level was reported in 82%, 97.4%, 87.5%, and 100% of ALL, AML, CML and CLL cases, whereas low platelet count was found in 88%, 92.3%, and 58% ALL, AML and CLL cases, respectively [36]. Similarly, a study performed in Brazil showed that a high proportion of patients with AML had a high total leukocyte count and low platelet count [37]. Another study conducted in Pakistan showed that 80.1% and 96.3 % of AML patients had leukocytosis and thrombocytopenia respectively [38]. Consistent with our results, a study in Sudan reported comparable frequency of thrombocytopenia (39.1%) in CLL patients [39]. Contrary to our findings, a study from Kenya showed that patients with CML had higher prevalence of low platelet count and higher bleeding tendency [40]. The marked results in our study can be attributed to the late presentation as the degree of anemia, leukocytosis and thrombocytopenia are directly proportional to severity of bone marrow failure.

An important limitation of the present study is that it was conducted at a single center. Therefore, the exact pattern of leukemia prevalent in the whole region and other parts of India may not have been predicted in the study. Thus, further multicenter studies are required to understand the exact distribution pattern of leukemia among patients attending clinical hematology department.

CONCLUSION

The prevalence of chronic leukemia was more than acute leukemia in our study. Overall, male preponderance was seen. AML was found to be dominant type among acute leukemia, whereas CML was the commonest type among chronic leukemia. CML was also observed as the most common type of leukemia followed by CLL among all cases as well as in adults. In children, ALL was the most common leukemia followed by AML. Leukocytosis, anemia, and thrombocytopenia were among the most common hematological abnormalities noted in various types of leukemia.

This study helped us in understanding the distribution pattern of various types of leukemia among patients presenting to hematology department in this region. Studies from various other regions of the country must be undertaken. Such studies will provide great help in the understanding the prevalence and hematological abnormalities of different types of leukemia, and thereby managing patients with such critical diseases in better way.

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