

## INCIDENCE OF ACUTE AND CHRONIC FORMS OF LEUKEMIA IN HARYANA

RADHA RATHEE<sup>1</sup>, MINAKSHI VASHIST<sup>2\*</sup>, ASHOK KUMAR<sup>3</sup>, SUNITA SINGH<sup>4</sup><sup>1,2</sup>Dept. of Genetics, M. D. University, Rohtak, Haryana, India, <sup>3</sup>Dept. of Zoology, CRA College, Sonapat, Haryana, India, <sup>4</sup>Dept. of Pathology, Pt. B. D. Sharma University of Health Sciences, Rohtak, Haryana, India. Email: mvashist@rediffmail.com

Received: 20 Jan 2014, Revised and Accepted: 02 Mar 2014

## ABSTRACT

**Objective:** The prevalence of leukemia is known to vary throughout the India. The observed geographic variation in incidence remains unexplained as yet. Previous studies have shown important differences in geographic, racial/ ethnic, age and trend patterns for different leukemia subtypes. Thus, suggesting that subtypes may have different etiologic factors. So, an attempt was made to find out geographic pattern of leukemia and its distribution throughout the Haryana.

**Methods:** Study of 650 cases of leukemia, with cooperation from the Department of Pathology, during 2008-12 was done. We analyzed the pattern by morphological subtype, gender, age at diagnosis, distribution according to prevalence, risk factors, laboratory parameters and clinical features of leukemia.

**Results:** In present study, 51% patients were suffering from acute forms of leukemia while 49% suffered from chronic type. Leukemia was more frequently observed in adults. Male to female ratio was 2:1 and majority of the patients (88.92%) belonged to six districts (i.e. Rohtak, Jind, Bhiwani, Sonapat, Jhajjar, Hissar).

**Conclusion:** Low grade fever, progressive pallor, weakness and body aches were the commonest symptoms (70% cases) while pallor was the frequently observed sign.

**Keywords:** Clinical features, Hematology, Incidence & leukemia.

## INTRODUCTION

A hematological malignancy arises when something goes wrong in the regulation of the division or the life span of a blood cell or its precursor [1]. It is characterized by widespread, rapid and disorderly proliferation of leukocytes and their precursor and by the presence of immature leukocytes in blood often in very large numbers. Leukemia is one of the most frequently occurring cancers in all races or ethnicities with relative proportion vary between 25-40% [2]. In 2013, males have been accounted for more than 57 percent of the new cases of leukaemia [3]. High incidence of subtypes of leukemia in males was due to more exposed to occupational and environmental carcinogens [4,5]. Epidemiology has played a vital role in learning about the causes of leukemia in the past few decades. The developing countries have greater burden of cancer including hematological malignancies due to population growth, aging and urbanization, changing dietary habits, better control of infections, and increasing tobacco consumption [6]. This is further challenging to take these findings in detecting different types of leukemia earlier and ideally to prevent the disease. This is a fundamental step to estimate the burden of blood cancer in Haryana and to understand how the occurrence of this disease varies according to prevalence, risk factors, laboratory parameters and clinical features of this hematological malignancy.

## MATERIALS AND METHODS

**Patients:** This study was performed on 650 patients diagnosed with leukemia from the Department of Pathology, during 2008-12. These patients were evaluated especially regarding sex, age at diagnosis, risk factors, occupation, and chief complaints.

**Hematological analysis:** The whole blood samples of patients were taken with informed consent for hematological analysis. This study was approved by Institutional ethical committee of MD University, Rohtak. Percentage of blast cell, red blood cell indices, white blood cell indices, number of platelets and the amount of hemoglobin was determined according to standard laboratory procedures. Slides were prepared with PBF (Peripheral Blood Film) by using 'Leishman stain' to find out the blast cells morphology in peripheral blood sample of all patients of blood cancer. Diagnosis of leukemia was done by 20% blast criteria and then 'Sudan Black B' was used to distinguish between AML & ALL.

**Statistical analysis:** Analysis of variance (ANOVA) was used for interactions of factors affecting leukemia patients. Data on leukemia patients was analyzed and then subjected to ANOVA. In order to find out whether there was any interaction of factor like age/gender/subtype affecting leukemia or not.

## RESULTS

In present research, 650 cases were analyzed with leukemia during the period 2008-2012. Thirty three point eight percent of patients were affected with AML, 39% patients with CML, 17.2% patients with ALL and 10% with CLL. There were 71.4% male patients with chronic leukemia and 62.6% male patients with acute leukemia. Acute and chronic leukemia had 28.6% and 37.4% female patients respectively. Among four major type of leukemia, ALL was observed in 58% male patients and in 42% female patients, AML in 65% male and 35% female patients, CML in 69% male and 31% female patients and CLL in 80% male patients and in 20% female patients (Table-1). Acute lymphocytic leukemia (ALL) was more commonly noted in children (<15 years) whereas AML was more commonly noted in adults (>15 years). Both CML and CLL were observed only in adults.

**Table 1: Percentage frequency of various types of leukemia patients diagnosed during the period of study.**

Gender	CML n (%)	AML n (%)	CLL n (%)	ALL n (%)
Male	176 (69.3)	143 (65)	51 (79.6)	65 (58)
Female	78 (30.7)	77 (35)	13 (20.4)	47 (42)
Z-test	8.6961	6.2929	6.7175	2.4054
p-value	0*	0*	0*	0.01596**

Significant by z-test at \*p< 0.01, \*\*p< 0.05

Incidence of leukemia has increased from last decade. In present study, majority of the cases belonged to six districts i.e. Rohtak, Jind, Bhiwani, Sonapat, Jhajjar, Hissar. Highest incidence of leukemia were noted from Rohtak district followed by Jind and Bhiwani. The prevalence in these areas was high due to the vicinity of regional cancer center to these districts. Cases from other states were excluded from the study. The frequency of leukemia was highest in 012, with sex ratio (SR) 2.23 and lowest in 2010, with an SR of 1.9. In 2011, none case of CLL was reported in females. There were geographical variations in frequency distribution of leukemia (Fig.1).

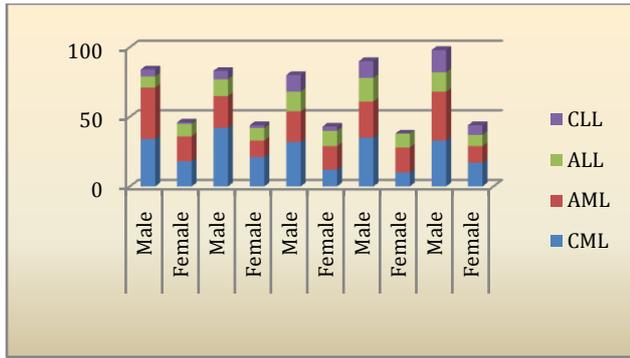


Fig. 1: Year-wise and gender-wise distribution of percentage frequency of leukemia subtypes.

**Clinical Features**

The majority of our patients were presented with low grade fever, progressive pallor, generalized weakness, anemia and bodyaches with a mean value of 89.15%, 77.57%, 72.45%, and 72.08% respectively. Lymphadenopathy, jaundice, purpura and retinal hemorrhages were not seen in patients of chronic lymphocytic leukemia. Hepatosplenomegaly was commonly seen in patients of ALL and AML. Bleeding was also present in some patients of ALL and AML. It was most commonly from the mucosa, skin and gums but retinal hemorrhages were present only in the AML cases (Fig.2).

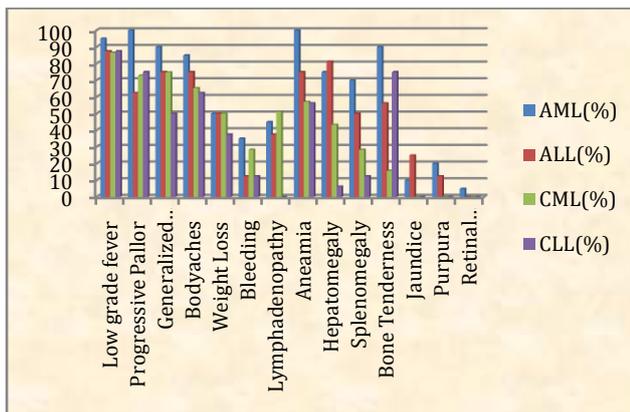


Fig. 2: Clinical features of leukemia subtypes

**Laboratory parameters**

All patients were studied for laboratory parameters like hemoglobin conc., leukocyte count and platelet count (Table-2). Mean hemoglobin was found 7.5g/dl in ALL, 8.5g/dl in AML, 6.8g/dl in CML and 6.3g/dl in CLL. Mean total leukocyte count was 44X10<sup>9</sup>/L in AML, 140X10<sup>9</sup>/L in CML, 70X10<sup>9</sup>/L in ALL and 52X10<sup>9</sup>/L in CLL. Mean platelets count was in 67X10<sup>9</sup>/L AML, 137X10<sup>9</sup>/L in CML, 65X10<sup>9</sup>/L in ALL and 250X10<sup>9</sup>/L in CLL. The leukemic blasts in the peripheral blood was highest in the AML with a median blast cell count 45% followed by CML (42%), ALL (38%) and CLL (35%).

Table 2: Different hematological parameters in leukemia

Parameters	AML	ALL	CML	CLL
Median age in years	28	22	26	58
Age range in years	5-70	1-50	15-65	50-75
Mean Hb in gm/dl	8.5	7.5	6.8	6.3
Mean WBC X10 <sup>9</sup> /L	44	70	140	52
Mean platelets count X10 <sup>9</sup> /L	67	65	137	250
Median Blast cell (%)	45	38	42	35

**Interactions of various factors affecting leukemia**

Various factors play significant role in diagnosis of leukemia. Age of diagnosis helps in determining the type of leukemia. In the present study, it was found that ALL affects children primarily and AML affects adults while CML also affects in elder age and CLL is the disease of older people. Age was having significant effect on type of leukemia. The interaction of age with any other factor like gender or subtype of leukemia plays very significant role (Table-3). Various factors said to be significant mean statistically significant either at the 0.001, 0.01, or 0.05 probability levels (p values) which were indicated. All other differences having p value greater than 0.05 were said to be nonsignificant (NS).

**DISCUSSION**

Hematological malignancies are common in our country. Different studies have been conducted on various aspects of individual hematological malignancies in the past. Many workers have compiled information on hematological malignancies in India [1]. They have reported that in India all hematological malignancies were commonest in Delhi followed by Mumbai. Rural areas have least incidence of these malignancies. It was observed that all cancers occur two decade earlier in Haryana. In present study acute leukemia (51%) was more prevalent as compare to chronic type (49%) and similar findings have been reported in a previous study [7]. However two other studies have reported more cases of chronic leukemia in their study (60%) as compared to acute leukaemia [8,9]. In our study, commonest type of leukemia was CML followed by AML, ALL and CLL (Table -4). Previous studies have reported more cases of myeloid leukaemia [7,9,10,18]. These studies have reported more cases of CML than AML. A higher incidence of CML has also been reported by two earlier studies from India [5,11]. This difference could be attributed to geographical variation. Among lymphoid leukemia, all was far more common 112/650 (17.2%) than CLL 64/650 (10%) in our research. Similar findings have been reported in several previous studies [9,10,12,13,14,15]. However, a markedly high incidence of CLL has been reported by some another studies [8,16,17]. They have reported CLL as being more common than CML in Denmark, Poland and Scandinavia. Compared to another series from Mumbai, by some workers, we have fewer cases of ALL and more cases of AML [5]. ALL is reported to be the intermediate in the West, central and most frequent in the South [5,10,19]. Interestingly, the incidence of ALL is lesser in East India as well as Northern areas and also observed by us in the present research (Table-4) [9,11,21]. The incidence was intermediate in the East, Centre and West and in one series from South (Table-4) [5,10,11,20]. This compilation reveals geographic variation in frequency of leukemia.

Table 3: Interactions of factors affecting leukemia patients using ANOVA

Source	Df	MS	F - value	%Variance
Age	3	11101.85	1556401.	15.864**
Type of leukemia	3	268.408	37628.91	0.384
Sex	1	270.036	37857.16	0.129
Age X Type of leukemia	9	16537.11	2318387.	70.890***
Age X Sex	3	4448.889	623702.8	6.357**
Type of leukemia X Sex	3	272.472	38198.69	0.389
Age X Type of leukemia X Sex	9	1396.385	195763.3	5.986**
Error	608	0.007		.002

Df =Degree of freedom, MS=Mean square, \*\* =p<0.01,\*\*\*=p<0.001

Table 4: Percentage frequency of various Leukemia's in India.

Reference	Region	ALL	AML	CML	CLL	Others	Total (n)
Chatterjee et al (11)	Calcutta (1949-1961)	22.5	32.5	35.9	5.9	3.2	544
Advani et al (6)	Mumbai (1960-1975)	30	13	40	9	8	1126
Prakash et al (20)	Pondicherry (1970-1979)	35	29.5	30.8	3.2	6.5	278
Rani et al (9)	Delhi (1970-1979)	15.5	30.8	45.3	5.7	2.7	490
Verghese et al (19)	Kerala (1980-1983)	39.2	19.6	16.4	1.9	22.9	1016
Kushawaha et al (14)	Lucknow (1971-1984)	9.3	38.7	48	2.6	1.4	970
Shome et al (7)	Chandigarh (1975-1983)	24	29.3	36.7	8.8	1.2	820
Dicosta et al (15)	Mumbai (1975-1984)	36	22	38	2	2.0	242
Rathee et al (Our study)	Haryana (2008-2012)	17.2	33.8	39	10	-	650

We found a male preponderance in our study. This has also been reported by earlier studies [1,4,5,9,10,14,18,24]. Increased incidence of all leukemia in males seems to arise as males are comparatively more exposed to occupational and environmental carcinogens as has been suggested by some workers [1,4,24].

The leukemic blasts in the peripheral blood was highest in the AML with a median blast cell count 45% followed by CML (42%), ALL (38%) and CLL (35%) as in table-2. These findings were also comparable with earlier studies [4,25]. It was observed that low grade fever, progressive pallor, generalized weakness and bodyaches were the most frequent symptoms, while pallor was the most frequently found sign in AML and ALL and splenomegaly alone was noted most frequently in CML (Fig.2). Bone tenderness was most common in ALL and AML being the next. Lymphadenopathy was observed in CLL, ALL it was seen in 78%, 74% patients respectively. Interestingly, retinal hemorrhages were seen in 15% cases of AML. Bleeding was also observed in acute leukemia. Our findings are not much different from the earlier studies [26, 27, 28].

The incidence of hematological malignancies were greater in urban as compared to rural areas. The possible explanation is that the rural and urban populations are different with regard to environmental and socioeconomic factors. Urban cities in Haryana are industrialized and fairly populated. Socioeconomic status of people is higher and dietary habits and lifestyle tends to tilt toward Western styles. In rural areas, on the other hand, people stick to traditional eating habits and lifestyle. These factors may be responsible for the relative differences in the incidence of hematological malignancies in urban versus rural population.

#### CONCLUSION

Present study revealed that acute leukemia was more prevalent than chronic leukemia. The most common type of leukemia was CML followed by AML, ALL and CLL. Overall leukemia was more commonly seen in male patients. Age has significant effect on type of leukemia. ALL was more commonly observed in children whereas both CML and CLL were only observed in adults. The incidence of AML was higher in adults as compare to children and decrease towards older age. The majority of patients had lower hemoglobin, high leukocyte count and lower platelet count. Low grade fever, progressive pallor, generalized weakness, anemia and bodyaches, lymphadenopathy, jaundice, purpura and retinal hemorrhages were most common characteristics in patients.

#### ACKNOWLEDGMENT

The authors are grateful to University Grant Commission (UGC) New Delhi, India, for financial assistance.

#### REFERENCES

- Chaudhari S, Desai JS, Adam A, Mishra P. Jak/stat as a novel target for treatment of leukemia. *Int J Pharm Pharm Sci*, 2014; 6(1): 1-7.
- Arora RS, Eden TOB, Kapoor G. Epidemiology of childhood cancer in India. *Indian J of Cancer*, 2009; 46(4): 264-73.
- Cancer Facts & Figures. Atlanta, GA: American Cancer Society; 2013.
- Kumar A, Rathee R, Vashist M, Kamal N, Singh S, Gupta S. Acute Lymphocytic Leukemia: An epidemiological and hematological study from Haryana. *Biosci Biotech Res Asia*, 2012; 9(2): 813-7.
- Advani SH, Jussawala DJ, Nagaraj RD, Gangadharan P, Shetty PA. A study of 1226 leukemia cases-Epidemiologic and end result analysis. *The Indian J of Cancer*, 1979; 16: 8-17.
- Magrath I, Litvak J. Cancer in developing countries: opportunity and challenge. *J Natl Cancer Inst*, 1993; 85(11): 862-74.
- Shome DK, Ghosh K, Mohanty D, Das K. Leukaemia in North West India. *Acta Haematol*, 1985; 73: 244.
- Hansen NE, Karle H, Jensen OM. Trends in the incidence of leukemia in Denmark, 1943-1977: An epidemiologic study of 14,000 patients. *J Natl Cancer Inst*, 1983; 71(4):697-701.
- Rani S, Beohar PC, Mohanty TK, Mathur MD. Leukemic Pattern in Delhi - A Ten year study of 490 cases. *Indian J of Cancer*, 1982; 19:81-6.
- Pradhan PK, Tiwari SK, Dabke AT, Agarwal S. Pattern of leukemia in Raipur (Madhya Pradesh) - An Analysis of 162 cases. *Indian J of Cancer*, 1982; 19:20-23.
- Chatterjee JB, Ghose S, Ray RN. Incidence of Leukemia. An analysis of 544 cases studied in Calcutta. *J Assoc Phy Ind*, 1962; 10: 673-76.
- Kasthuri AS, Jaiprakash MP, Panicker NK, Gupta MM, Rajoor GS, Basu SK, Sambandam S, Bhalla IP. A clinical study of adult leukemias. *J Assoc Physicians India*, 1991; 39(3): 291-92.
- Roda L, Vathaire F, Rio B, Tourneau A, Petididier P, Laudon F et al. Incidence of hematological malignancies in French Polynesia between 1990 and 1995. *Leukemia Research*, 1999; 23(4):349-55.
- Kushwaha MRS, Bagchi M, Mehrotra RML. Leukemia at Lucknow- a study of 200 cases. *Ind J Cancer*, 1978; 15:28-34.
- Dicosta GG, Siddique HM, Pradhan RM, Gupte SS. Pattern of leukemias: a ten year incidence study of 242 cases. *J Postgraduate Med*, 1989; 35:191.
- Kwiatkowski A. Trends in the incidence of leukemia in Poland, 1963-1990: an epidemiologic study. *Eur J Cancer Prev*, 1994; 3(3):277-83.
- Brincker H. Population based age and sex specific incidence rates in the 4 main types of leukemia. *Scand J Haematol*, 1982; 29(3):241-49.
- Yeolle BB, Jussawala DJ, Advani SH. Descriptive epidemiology of leukemias in Greater Mumbai. *Natl Med J India* 1998; 11(3):116-19.
- Varghese PR, Elayidom NB, Joseph CD, Kumar S. Epidemiological observations on leukaemia in Kerala (A study of 1016 cases over three years). *Ind J Haematol*, 1984;2:15-17.
- Prakash S, Ramamurthi GR, Aurora AL. Leukemias at Pondicherry. *Ind J Cancer*, 1981 18:1-6.
- Sakhuja SA, Agrawal A, Kumud GS. Paper presented at Ind. Assoc. Pathol. & Microbiol. Conference, Kanpur, Dec. 1984.
- Khodaskar MB, Lele VR, Landge MM, Deshmukh V. Leukemia in children. (A retrospective study of ten years). *Ind J Haematol*, 1984;11:260-62.
- Rajarajeswari G, Viswanathan J. Leukaemia in children. A review of 100 cases with typical clinical manifestations. *Ind. Pediatr*, 1980;17:37-44.
- Kusum A, Negi G, Gaur DS, Kishore S, Meena H, Sharma A et al. Hematological malignancies diagnosed by bone marrow examination in a tertiary hospital at Uttarakhand, India. *Indian J Hematol Blood Transfus*, 2008; 24(1): 7-11.
- Sazawal S, Kumar B, Hasan SK, Dutta P, Kumar R, Chaubey R, et al. Haematological & molecular profile of acute myelogenous leukaemia in India. *Indian J Med Res*, 2009; 129: 256-61.
- Das K, Aboobacker CM, Mathew O. Clinical presentation of leukemias in children in South Kerala. *Ind Pediatr*, 1974; 11: 431-8.
- Meighan SS. Leukemia in children. Incidence, clinical manifestation, and survival in an unselected series. *J Amer Med Assoc*, 1964; 190:578-82.
- Savage DG, Szydlo RM, Goldman JM. Clinical features at diagnosis in 430 patients with chronic myeloid leukemia seen at a referral centre over a 16 year period. *Br J Haematol*, 1997; 96:111-1.