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RESEARCH ARTICLE

EPIDEMIOLOGICAL AND CLINICAL CORRELATES OF ACUTE LEUKAEMIAS.

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Abstract

Background: The prevalence of leukemia is known to vary throughout the India. The observed geographic variation in incidence remains unexplained as yet. Due to the lack of any nationwide leukaemia screening program, the majority of the people are not aware of the disease. Epidemiological study can play a vital role in understanding the occurrence and outcome of the disease. Methods: Study of 100 cases of leukaemia, diagnosed in Department of Pathology, Government medical college was done. We analysed the pattern by morphological subtype, gender, age at diagnosis, distribution according to prevalence, seasonal variation and associated clinical features of leukaemia. Results: In present study, the minimal incidence of acute leukaemia as per data collected was found out to be 0.91 per 100,000 population in Jammu region. 52% patients were suffering from acute lymphoblastic leukemia(ALL) while 48% suffered from acute myeloid leukaemia(AML). Amongst ALLand AML, L1(67.3%) and M2 (50%) were the commonest subtype respectively. Leukemia was more frequently observed in adults more common in the winter season with majority of cases seen in the months of October to March. Male to female ratio was 2:1. Conclusion: Generalized weakness and fever were the most common modes of presentation. Pallor due to anaemia was the most frequently observed physical sign.

Keywords: Acute lymphoblastic leukemia(ALL), Acute myeloid leukaemia(AML),Clinical features, Hematology, Incidence &leukemia.

INTRODUCTION

Acute Leukaemias are a heterogenous group of neoplasms arising from the transformation of uncommitted or partially committed haematopoietic stem cells followed by proliferation and accumulation of abnormal clones. It typically results from the malignant transformation of white blood cells or their precursors. Subtypes are identified on the basis of the cell of origin as lymphocytic (B-cell or T-cell) or myeloid (granulocytic, erythroid or megakaryocytic) and clinical course as acute or chronic leukaemia (Stewart BW and Kleihues P, 2003)[1]. In India in

2014,52,380 new cases were detected (3.1% of all new cancer cases)and estimated deaths were 24,090(4.1% of all cancer deaths)[2]. Males have been accounted for more than 57 percent of the new cases of leukaemia[3.]It is the most common cancer in children and majority of cases are ALL.AML and CLL are most common in adults[4].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 haematological malignancies due to population growth,aging and urbanization, changing dietary habits, better control of infections, and increasing tobacco consumption [5].

Epidemiologically, screening is very crucial to prevent the disease. In developing country like India, there is paucity of clinicoepidemiological data of leukemias in northern regions. An attempt has been made to estimate the minimal incidence of leukaemia in population and correlation of various demographic and clinical features with leukemia.

MATERIALS AND METHODS

This study was performed on 100 patients diagnosed with leukemia in the Department of Pathology, Government Medical College, Jammu over a period of 2.5 years. These patients were evaluated especially regarding sex, age at diagnosis, seasonal variation and chief complaints. Slides were prepared with PBF (Peripheral Blood Film) by using 'Leishman stain' in all patients of leukaemia .All patients were then subsequently subjected to bone marrow examination to confirm leukaemia .Trephine biopsy was performed in cases where bone marrow findings were inconclusive.

RESULTS:

Incidence of acute leukemia came out to be (Number of new cases diagnosed as leukemia divided by total number of hospital admissions which were 1,63,006(100/163006).Reflecting the above figures on general population, the minimum incidence of acute leukemia comes out to be 0.91 per 100,000 population per annum taking the population of Jammu as 43, 95,712 as per 2001 census.

Minimal incidence was calculated by the formula given by **(WHO, IARC-Lyon, 1978)**

$$= \frac{\text{Number of cases in n years}}{\text{Population}} \times \frac{1}{n} \times 10^5$$

(n= number of years)

$$= \frac{100}{4395712} \times \frac{1}{2.5} \times 10^5$$

= 0.91 per 100,000 population per annum.

The mean age of 100 patients of acute leukaemia was 23.9 years with the range from 1 month to 72 years and majority (35%) of cases were in the age group of 0-10 years. The mean age of ALL patients was 12.3 years with the range from 10 months to 60 years and majority (32%) of cases lying in the age group of 0-10 years. The mean age of AML patients was 31.4 years with the range from 46 days to 72 years and majority (14%) of cases lying in the age group of 20-30 years. 1 case was diagnosed as congenital leukaemia of ALL type at 1 month of age. There was

significant correlation between age and type of leukaemia with ALL more in younger age groups as compared to AML.

Acute leukemia was more common in males (66%) as compared to females (34%), male to female ratio being 1.94:1. In ALL, male to female ratio was 2.05:1 and in AML, male to female was 1.82:1.

Majority of the cases of ALL-L1 were in the age group of 0-10 years. Most of the cases of ALL-L2 were in the age group of 0-10 years and 10-20 years .The youngest patient was of 10 months of age and oldest patient was of 60 years of age.

As seen from table no.3 AML M1, M2, M5 were most commonly seen in the age group of 20-30 years. AML-M4 was most commonly seen in the age group of 10-20 years .The youngest patient was of 46 days of age and oldest patient was of 72 years of age .However no patient belonged to M6 and M7 category.

In our study, it was found that acute leukaemias were more common in winter season (59%) especially during the months of October to December (37%) and January to March (22%). Out of 59%, 33% patients were of ALL and 26% patients were of AML.

As seen from table no.5, lymphadenopathy was more commonly seen in cases of ALL as compared to AML.

Table no.6 depicts that bleeding manifestations were seen almost equally in both ALL and AML. In ALL, most of the patients presented with small petechiae all over the body, Amongst AML, ecchymotic spots were the most common manifestation .DIC was seen in 2 cases of AML-M3 prior to chemotherapy.

TABLE NO:1AGE WISE DISTRIBUTION OF LEUKAEMIA PATIENTS

Age (years)	ALL n(%)	AML n(%)	Total n(%)
0-10	32(32)	3(3)	35(35)
10-20	11(11)	10(10)	21(21)
20-30	5(5)	14(14)	19(19)
30-40	2(2)	5(5)	7(7)
40-50	1(1)	5(5)	6(6)
50-60	0(0)	6(6)	6(6)
60-70	1(1)	3(3)	4(4)
70-80	0(0)	2(2)	2(2)
Total	52(52)	48(48)	100(100)

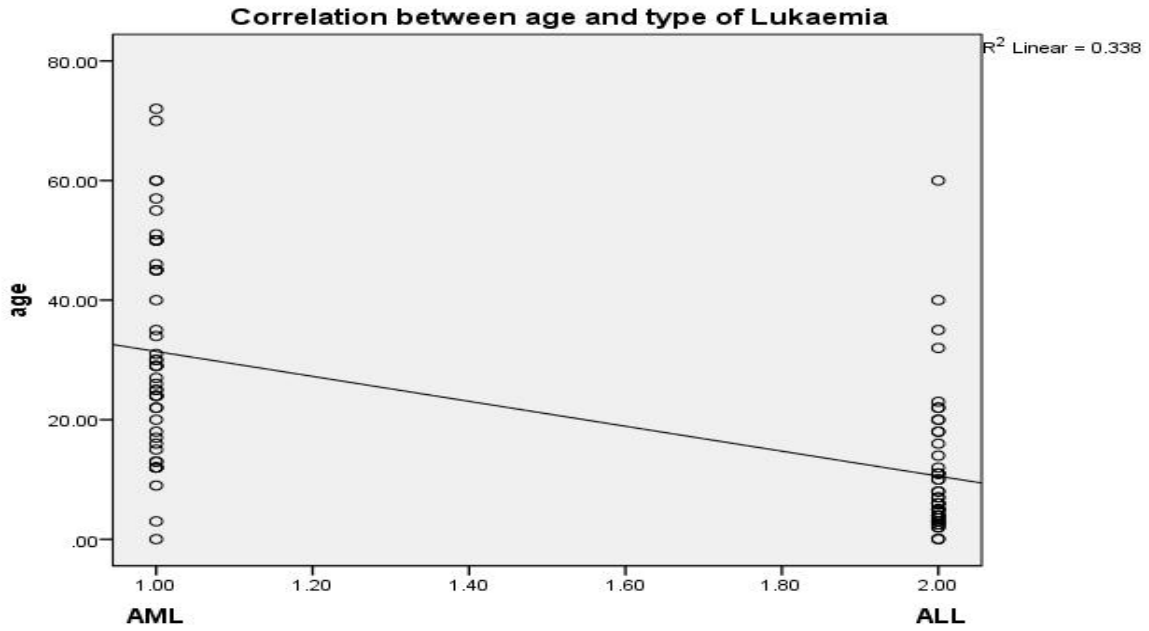

FIGURE 1: SEX WISE DISTRIBUTION

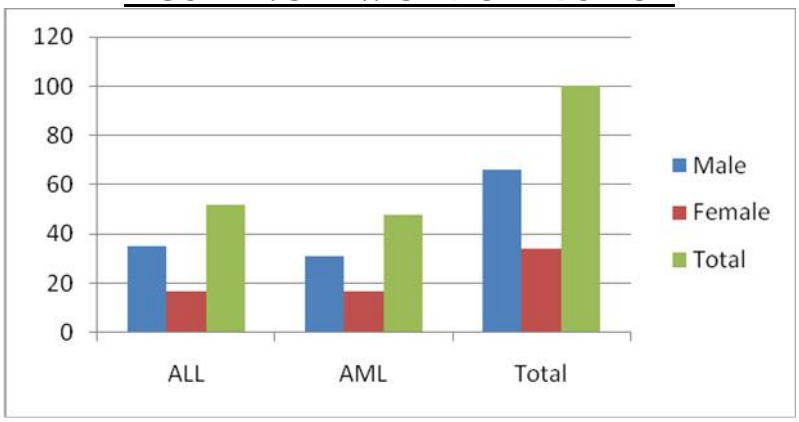

TABLE-NO:2 AGE WISE DISTRIBUTION IN ACUTE LYMPHOBLASTIC LEUKAEMIA (ALL)

Age (years)	ALL-L1	ALL-L2	ALL-L3	Total
0-10	27	5	-	32
10-20	5	5	1	11
20-30	1	3	1	5
30-40	1	1	-	2
40-50	-	-	1	1
50-60	-	-	-	-
60-70	1	-	-	1
70-80	-	-	-	-
Total	35	14	3	52

TABLE-N0:3 AGE WISE DISTRIBUTION IN ACUTE MYELOID LEUKAEMIA (AML)

Age (years)	AML-M1	AML-M2	AML-M3	AML-M4	AML-M5	TOTAL
0-10	1	2	-	-	-	3
10-20	3	4	-	3	-	10
20-30	4	8	1	-	1	14
30-40	1	3	-	1	-	5
40-50	2	1	2	-	-	5
50-60	1	4	-	1	-	6
60-70	2	1	-	-	-	3
70-80	1	1	-	-	-	2
Total	15	24	3	5	1	48

Table No. 4: SEASONAL VARIATION

Season	No. of patients	Percentage
January-March	22	22
April-June	22	22
July-September	19	18
October-December	7	37
Total	100	100

Table No. 5: LYMPHADENOPATHY IN ACUTE LEUKAEMIA

Lymphadenopathy	ALL(n=40)	AML(n=18)
<1 cm	18	8
1-1.5 cm	12	5
1.5-2 cm	6	3
>2 cm	4	2

Chisquare-0.05 p value-0.9 ,not significant

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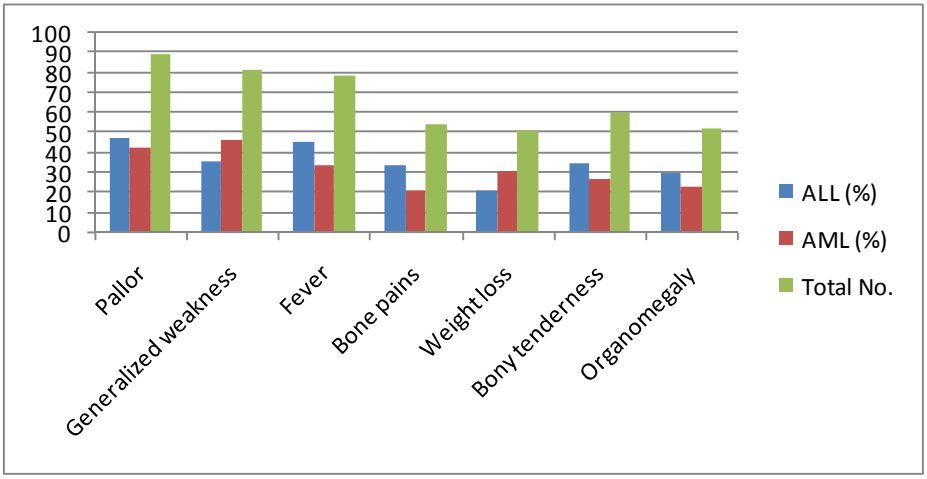
TABLE No.6:BLEEDING MANIFESTATIONS IN ACUTE LEUKAEMIA

Bleeding manifestation	ALL(n=24)	AML(n=22)
Petechiae	12	7
Ecchymotic spots	7	8
Bleeding gums	5	5
D.I.C	-	2

Chi square- 3.3, p value 0.3, not significant.

FIGURE-2 CLINICAL PRESENTATION OF LEUKAEMIA PATIENTS



DISCUSSION:

In the present study, 100 cases of acute leukaemia were diagnosed out of a total of 1,63,006 hospital admissions and the incidence was 0.06 per 100 hospital admissions. Reflecting on the general population, the minimum incidence of acute leukaemia came out to be 0.91 per 100,000 population per annum. However, this incidence cannot be taken as the final conclusion because it is likely that some patients did not report to this institution, some may have died while a few possibly migrated outside the region.

This incidence coincided with the study conducted by Paul B et al (1992), [6]Ghalaut PS et al (2000)[7] who reported an incidence of 1.0 per 100,000 per year and Capra M et al (2007)[8] who reported an annual incidence of 1.11 per 100,000 per year. However, these do not match with study of Kemp IW and George JS[9] (1980) who reported an incidence of 6.1 per 100,000 population per year. In the western countries, the overall incidence of ALL is 1.4 per 100,000 population per year and AML is 3.4 per 100,000 population per year (Wintrobes 2004)[10]. The higher incidence in western countries may be due to more health consciousness and better medical facilities, besides by and large higher socio-economic status in the west.

In our study, ALL was more common of the two acute leukaemias. This observation was comparable to that of Boggs DR et al (1962),[11]Rao VSK et al (1971)[12], Magotra M et al (1978),[13] Khalil SH et al (1995)[14] and Rego MF et al (2003)[15] who reported ALL in more

cases as compared to AML. However, AML was found more common in studies conducted by Shome DK et al (1985)[16], Hassan K et al (1994)[17], Idris M et al (2004)[18], Jmili NB et al (2004)[19] and Sachdeva MU et al (2006)[20] who found AML to be more frequent than ALL.

This study reveals that both ALL and AML, were more common in males as compared to females. There were 66% males and 34% females with male to female ratio being 1.94:1. This observation is comparable to the studies conducted by[11],[12],[16],[18],[19], Harani MS et al (2005)[21] and Hasanbegovic E (2006)[22]. But they do not confirm to the observations of Pratap V et al (1975) (3.1:1)[23],[13] and [6]

In our study, it was found that acute leukaemias were more common in winter season (59%) as compared to summer (41%). Most cases were seen in the months of October to December (37%) and January to March (22%). This may be explained due to migration of people from hilly areas to plains during winter season or possibly due to aggravation of leukaemic process by some infectious etiology in winters esp. frequent respiratory tract infections, coryza, etc. However, it is not possible for us to substantiate this point in the absence of any similar study documented in the past.

In our study, bone marrow aspiration was done in all the 100 patients of acute leukaemia and all the cases were further classified into morphological subtypes according to the FAB classification. Out of 52 cases of ALL, L1 was the commonest subtype seen in 67.3% of cases followed by L2 (26.9%) and L3 (5.8%) respectively. These findings were comparable to the studies conducted by [16],[17] ,Lilleyman et al (1986)[24], and Van EJ et al (1986)[25] . However these findings did not match with those of Dick FR et al (1982)[26] who reported L2 as the most commonest subtype seen in 60% cases followed by L1 (31%) and L3 (9%) respectively. Paul B et al (1992)[6] reported L2 morphology in 69% of cases of ALL.

AML was seen in 48 cases, out of which M2 was the commonest subtype seen in 50% of cases followed by M1 (31.2%), M4 (10.4%), M3 (6.3%) and M5 in 2.1% cases. M6 and M7 were not identified. These findings were in accordance with the studies conducted by Dick FR et al (1982)[26] [16],[14]Horibe K et al (2001)[27], Rego MF et al (2003)[15] and Rodrigues CA et al (2003)[28]. However these findings do not confirm to the observations of [6]. Hassan K et al (1994)[17] in their study reported M4 as the commonest subtype of AML followed by M2, M1, M3 and M5 and M6 and M7 respectively. Harani MS et al (2005)[21] also reported M4 as the predominant FAB subtype seen in 36.2% of cases followed by M2 (30.25%), M3 (10.4%), M1 (8.7%), M0 (7.7%), M5a (3.5%), M5b (2.5%) and M6 (0.8%). Capra M et al (2007)[8] reported increased incidence of cases of AML-M3 in patients of de novo AML.

The symptomatology of patients suffering from acute leukaemia is variable but, by analyzing the cases a common spectrum of presentation was noted. Generalized weakness and fever were the most common presenting symptoms followed by bone pains, weight loss and bleeding manifestations respectively. Bleeding manifestations were seen in the form of petechiae, ecchymotic spots and bleeding from gums with cases of AML-M3 showing features of DIC. This was comparable with the studies of [11],[23],[16],[18][,29]Hasanbegovic E (2006)[22] found high temperature, fatigue and paleness as the most dominant clinical signs. Pallor was the most frequently observed sign along with bony tenderness, lymphadenopathy and hepatospleenomegaly. Lymphadenopathy was more common in ALL as compared to AML.

CONCLUSION

The incidence of Acute Leukaemia in this region is close to 1.0 per 100,000 population per annum with male preponderance and majority of the cases occur during winter. ALL is slightly more frequent than AML.ALL-L1 FAB is common under the age of 10 years whereas ALL-L2 FAB and ALL-L3 FAB are more frequent in older children. AML is more frequently seen in older children and adults. AML-M2 FAB is the commonest subtype followed by AML-M1 FAB and involves the patients in age group of 20-30 years. Combined PBF and Buffy coat smear examination is most important, especially in cases with a history of pallor, fever, bone pains of short duration with or without purpuric spots and showing in the PBF, normal or low TLC with a few atypical or no abnormal cells along with the presence of nRBCs. Population screening is very crucial to recognise early signs and symptoms of leukaemia to ensure early diagnosis of disease so as timely referral could be done from primary to secondary and tertiary health care centres for detailed haematological analysis and management.

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