Acute Leukaemia in Adults: Morphological Profile of 101 Patients

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A total of 101 consecutive patients of acute leukaemia were diagnosed in adults (age range 16-74), during a period of 6½ years. These patients included 74 males (73.3%), and 27 females (26.7%) with male/female ratio of 2.74:1. AML was the most frequent type accounting for 73 patients (72.3%), followed by ALL, 25 patients (24.8%) and 3 patients (2.9%) were diagnosed as bilineal leukaemia on morphological and cytochemical grounds. Overall AML/ALL ratio was 2.9:1. Amongst AML, M2 was the most frequent subtype accounting for 67.1%, followed by M4, M1, M3, M5, M0 and M6. Amongst ALL, L2 was the most frequent subtype accounting for 64% followed by L1 and L3. Total cases of acute leukaemia and AML showed a bimodal age related distribution. ALL showed highest incidence in younger adults (age 16-25 years), and a sharp progressive decline in incidence thereafter.
Key words: AML, ALL, Bilineal leukaemia, FAB group

Acute leukaemia accounts for approximately 10% of all human cancers and is the leading cause of cancer deaths in adults less than 35 years of age[1]. Acute leukaemias represent a heterogeneous group of malignant disorders of the pleuripotent stem cells resulting in clonal expansion of blast cells arrested at a specific stage of haematopoiesis (acute myeloid leukaemia [AML]), or lymphopoiesis (acute lymphoblastic leukaemia [ALL])[1,2].

AML occurs primarily in adults and infants younger than 1 year[3]. In contrast, ALL which is the most frequent childhood cancer, accounts for approximately 20% of adult acute leukaemias[4]. Acute leukaemia is generally more common in males than in females[5].

The French American British (FAB) classification recognizes three morphological subtypes of ALL: L1, L2 and L3. The L1 subtype consists of small uniform lymphoblasts. The L2 subtype is characterized by large pleomorphic lymphoblasts. Leukaemic cells in L3 subtype resemble Burkitt lymphoma[4,6].

AML is subdivided into 8 FAB subtypes i.e. M0 and M1 to M7. These subtypes are named as under[6-9].

M0 Minimally differentiated AML,
M1 AML without maturation,
M2 AML with maturation,
M3 Acute promyelocytic leukaemia,
M4 Acute myelomonocytic leukaemia,
M5 Acute monocytic leukaemia,
M6 Acute Erythro-leukaemia, and
M7 Acute megakaryocytic leukaemia

Although leukaemic cells generally exhibit characteristics of a single lineage; they sometimes co-express both lymphoid and myeloid features. Numerous terms have been used to designate these cases, but standard nomenclature is still lacking. Various terms like hybrid acute leukaemias, biphenotypic leukaemias, bilineal leukaemias and acute mixed lineage leukaemias (AMLL) are suggested to describe this lineage heterogencity[10]. They however are not as yet included in FAB classification.

In this study we present the analysis of 101 adult patients of acute leukaemia, diagnosed in the Department of Haematology, Shaikh Zayed Hospital, Lahore over a period of 6½ years (January 1994 to June 2000). The morphological pattern of acute leukaemia in adults (age > 15 years) was observed. The comparative trends in age and sex related incidence of AML and ALL were also analysed.

Patients and Methods

This study was conducted at the Department of Haematology, Shaikh Zayed Hospital, Lahore in collaboration with Department of Medicine which was also the main source of patients included in this study. During the period of this study which extended from January 1, 1994 to June 30, 2000 (6½ years), a total of 101 consecutive patients of acute leukaemia were diagnosed in adults. These patients of adult acute leukaemia were diagnosed among the 1621 consecutive patients from various inpatient and out patient departments of Shaikh Zayed Hospital, Lahore, who underwent bone marrow examination for different indications during the same period. Patients of both sexes over 15 years of age were included in this study.

The examination of both peripheral blood and bone marrow films is necessary for the diagnosis and classification of acute leukaemia[11]. The diagnosis of acute leukaemia was therefore made by examining giemsa stained, pretreatment blood films and bone marrow aspirates. To avoid discrepancies and to obtain a complete agreement on the diagnosis of acute leukaemias, several cytochemical techniques are recommended to supplement the morphological evaluation of the leukaemic blast cells[11,12]. Cytochemical stains including Sudan black B (SBB), meyloperoxidase (MPO), chloracetate esterase (CAE), alpha naphthyl acetate esterase (ANAE), acid phosphatase and periodic acid schiff (PAS) were used in

various combinations to diagnose and subtype the acute leukaemias in this study.

All the 101 patients diagnosed as acute leukaemia were subtyped according to the criteria proposed by FAB cooperative group[6-9]. In case of ALL, the scoring system proposed by Bennett et al[13] was used. The score ranged from a minimum score of –4 to a maximum +2. Score 0 to +2 was assigned L1 subtype, whereas -1 to -4 was labelled as L2 subtype[13,14]. Scoring system is elaborated in Table 1.

Table 1: Scoring system for L1 and L2.

Criteria*	Score~
High N/C ratio ≥ 75% of cells	+
Low N/C ratio ≥ 25% of cells	-
Nucleoli: 0 to 1 (small) ≥ 75% of cells	+
Nucleoli: 1 or more (prominent) ≥ 25% of cells	-
Irregular nuclear membrane ≥ 25% of cells	-
Large cells ≥ 50% of cells	-

*The following are not scored: (1) intermediate or indeterminate criteria; (2) regular nuclear membrane in > 75% of cells, and (3) <50% large cells, regardless of cell size heterogeneity
~Positive (+) or negative (-)
Possible score: -4 to +2
Bennett et al. (1981)

Diagnosis of AML - M0 was suggested on morphological and cytochemical features only. Diagnosis of bilineal leukaemia was suggested when morphologically and cytochemically two distinct populations of leukaemic blasts were distinguishable.

All the adult patients diagnosed as acute leukaemia were analyzed to observe the morphological pattern of the disease and its age and sex related incidence. Trends in adult AML and ALL were also compared.

Results

During the period of this study a total of 101 consecutive patients of acute leukaemia were diagnosed in adults with a median age of 30 years (range 16-74 years). The cases of adult acute leukaemia constituted 6.23% of the 1621 patients entered in bone marrow registry from January 1, 1994 to June 30, 2000.

Of 101 patients, 74 (73.3%) were male with a median age of 30 years (range 16-74 years), and 27 (26.7%) were female, also with a median age of 30 years (range 16-68 years). Overall male/female ratio was 2.74:1 (Tables 3, 4). Table 4 and 5 show M/F ratio in various types of acute leukaemia with reference to different age groups.

Table 2. Acute leukaemia in adults: General distribution (n=101).

Type	No	%age
Acute myeloid leukaemia (AML)	73	72.3
Acute lymphoblastic leukaemia (ALL)	25	24.8
Bilineal leukaemia	3	2.9
Total	101	100.00

Total patients of adult acute leukaemia included AML, 73 patients (72.3%) with a median age of 36 years (range 16-70 years), ALL, 25 patients (24.8%) with a median age of 22 years (range 16-60 years) and acute bilineal leukaemia, 3 patients (2.9%) with a median age of 25 years (range 22-74 years) (Tables 2, 6). Presenting age for both the sexes in different types of acute leukaemia is depicted in Table 6.

Table 3: Acute leukaemia in adults: Sex distribution (n=101).

Sex	No. of cases	%age
Male	74	73.3
Female	27	26.7
Total	101	100.00
Male : Female ratio	2.74:1	

Table 4:Acute leukaemia in adults: Sex distribution in different age groups

Age groups	No. of cases	Male	Female	M/F Ratio
16-25	39	28	11	2.54:1
26-35	21	17	4	4.25:1
36-45	13	7	6	1.16:1
46-55	18	14	4	3.5:1
56-65	7	6	1	6:1
66-75	3	2	1	2:1
Total	101	74	27	2.74:1

AML / ALL ratio in adults was 2.9:1. AML:ALL ratio in different age groups showed a progressive increase from 1.5:1 in age group 16-25 years to 17:1 in age group 46-55 years. Subsequently this ratio was observed to be 6:1 in patients aged 56-65 years and 2:0 in patients over 65 years of age (Table 7).

Distribution of acute leukaemia showed a maximum number of 39 patients (38.6%) in the age group 16-25 years, followed by a progressive decline till 45 years of age. A second smaller peak with 18 patients (17.9%) occurred in age group of 46-55 years which was again followed by a sharp decline in number of patients occurring in older age groups. AML distribution also showed a similar pattern with a maximum number of 22 patients (30.1%) from 16-25 years of age, and a second comparatively smaller peak with 17 patients (23.3%) occurring in age group of 46-55 years. ALL showed 15 patients (60%) in age group 16-25 years and subsequently a sharp progressive decline in number of ALL patients was observed in older age group. Of 3 patients, diagnosed as bilineal leukaemia 2 were in age group 16-25 years while one was 74 years of age (Table 7).

FAB subtype distribution of adult AML showed M2 to be the most common subtype representing 49 cases (67.1%) with a median age of 33 years (range 16-70 years), followed by 8 cases of M4 (11%) with a median age of 47 years (range 19-58 years), 7 cases of M1 (9.6%) with a median age of 35 years (range 18-68 years) and 5 cases of M3 (6.8%) with a median age of 30 years (range 22-48 years). M5 accounted for 2 patients (2.7%) and 1 patient (1.4%) each was diagnosed as M0 and M6. No patient with M7 was identified (Table 8). Amongst adult ALL, L2 accounted for 16 patients (64%) with a median age of 23.5 years (range 16-60 years) and L1 for 8 patients

(32%) with a median age of 19 years (range 16-45 years). One patient (4%), diagnosed as L3 was 35 years of age (Table 9). Table 10 shows a complete breakdown of FAB subtypes in different age groups.

Special consideration was given to the 4 cases in which we encountered diagnostic difficulty due to non-availability of immunophenotypic markers and electron microscopy (EM) analysis. In one of the cases AML-M0 was suggested as the most likely diagnosis. By definition diagnosis of AML-M0 requires less than 3% MPO positive and/or SBB positive blasts, expression of myeloid associated markers, and lack of B/T (lymphocytic) lineage associated antigens[9,15]. Thus, for the recognition of AML-M0, immunophenotypic evaluation is integrated in the FAB scheme as a part of diagnostic procedure[15]. In the above mentioned patient blast cells were minimally differentiated and the cytochemical analysis showed upto 25 blasts positive for SBB and/or MPO, per 1000 consecutive leukaemic blasts counted on the different bone marrow smears of the same patient. Although the diagnosis of AML-M0 was suggested, no further confirmation of this diagnosis was possible. In the three other patients the diagnosis of acute bilineal leukaemia was suggested as morphologically and cytochemically two distinct populations of leukaemic blasts were clearly distinguishable on the bone marrow examination. A definite diagnosis of bilineal leukaemia or mixed lineage leukaemia can only be pursued through morphological, cytogenetic, immunophenotypic, molecular and EM analysis of the bone marrow in newly diagnosed cases[16]. We therefore could only highly suspect and not confirm the diagnosis of bilineal leukaemia due to non-availability of the required facility.

Table 5:Acute leukaemia in adults: Sex distribution of main types in different age groups

Age group	AML (n=73)			ALL (n=25)			Bilineal (n=3)		
(Years)	Male	Female	M:F	Male	Female	M:F	Male	Female	M:F
16-25	17	5	3.4:1	10	5	2:1	1	1	1:1
26-35	11	3	3.7:1	6	1	6:1	-	-	-
36-45	7	5	1.4:1	-	1	0:1	-	-	-
46-55	14	3	4.7:1	-	1	0:1	-	-	-
56-65	5	1	5:1	1	-	1:0	-	-	-
66-75	1	1	1:1	-	-	-	1	-	1:0
Total	55	18	3.1:1	17	8	2.1:1	2	1	2:1

Table 6: Acute leukaemia in adults: Presenting age and sex distribution.

Type	Sex	No. of cases	Age (Years)	
			Range	Median
AML	**M+F**	**73**	**16-70**	**36**
	M	55	16-70	35
	F	18	18-68	38
ALL	**M+F**	**25**	**16-60**	**22**
	M	17	16-60	22
	F	8	16-49	25
Bilineal	**M+F**	**3**	**22-74**	**25**
	M	2	25-74	-
	F	1	22	-
Acute leukaemia	**M+F**	**101**	**16-74**	**30**
(AML+ALL+Bilineal)	M	74	16-74	30
	F	27	16-68	30

Table 7: Distribution of acute leukaemia in different age groups.

Age Group	AML(n=73)		ALL(n=25)		Bilineal (n=3)		Acute leukaemia (n=101)		AML/ALL Ratio
(Years)	No.	%	No.	%	No.	%	No.	%	
16-25	22	30.1	15	60	2	66.7	39	38.6	1.5:1
26-35	14	19.2	7	28	-	-	21	20.8	2:1
36-45	12	16.4	1	4	-	-	13	12.9	12:1
46-55	17	23.3	1	4	-	-	18	17.9	17:1
56-65	6	8.2	1	4	-	-	7	6.9	6:1
66-75	2	2.8	-	-	1	33.3	3	2.9	2:0
Total	73	100	25	100	3	100	101	100	2.9:1

Table 8: AML in adults: Presenting age in different subtypes.

Subtypes	AML(n=73)		Age (Years)	
	No	%age	Range	Median
M0	1	1.4	60	-
M1	7	9.6	18-68	35
M2	49	67.1	16-70	33
M3	5	6.8	22-48	30
M4	8	11.0	19-58	47
M5	2	2.7	30-48	-
M6	1	1.4	18	-
M7	Nil	-	-	-
Total	73	100	16-70	36

Table 9: ALL in adults: Presenting age in different subtypes.

Subtypes	ALL (n=25)		Age (years)	
	No	%age	Range	Median
L1	8	32	16-45	19
L2	16	64	16-60	23.5
L3	1	4	35	-
ALL (L1+L2+L3)	25	100	16-60	22

Table 10: Age related distribution of FAB subtypes.

Age (Years)	AML (n=73)							ALL (n=25)			Bilineal* (n=3)
	M0	M1	M2	M3	M4	M5	M6	L1	L2	L3	
16-25	-	2	17	1	1	-	1	6	9	-	2
26-35	-	2	8	2	1	1	-	1	5	1	-
36-45	-	2	8	1	1	-	-	1	-	-	-
46-55	-	-	11	1	4	1	-	-	1	-	-
56-65	1	-	4	-	1	-	-	-	1	-	-
66-75	-	1	1	-	-	-	-	-	-	-	1
Total	1	7	49	5	8	2	1	8	16	1	3

*Not a FAB subtype.

Discussion

Reports on morphological aspects of acute leukaemias in general and particularly in adults are limited in recent literature specially originating from the developed world. It can partly be attributed to the fact that presently more emphasis is being laid on immunophenotypic, cytogenetic, molecular and electron microscopic (EM) analysis of acute leukaemias. The other factor is that childhood acute leukaemia has invoked more interest among researchers because of the fact that it is now being considered a potentially curable disease in majority of the patients who receive appropriate therapy and support[17].

In the present study we have classified the 101 consecutive adult acute leukaemia patients mainly according to the FAB system which is invaluable in providing common ground for comparing patients in different studies and for providing useful prognostic information[18].

Acute leukaemias are reported to be the leading cause of cancer death in adults, younger than 35 years of age[1]. This fact is indirectly supported by the results generated from our analysis which showed acute leukaemias to be much more frequent in adults upto 35 years of age than afterwards (Table 7, Fig. 1).

Although AML is reportedly more common than ALL in adults, their relative frequency varies considerably in different studies from Pakistan[19,20] and abroad[21-23]. Generally higher AML rates are noted in developed countries[24]. About 80% of the acute leukaemias in adults are reported to be AML[18]. In the present study AML constituted 72.3% of the total acute leukaemias in adults with an AML:ALL ratio of 2.9:1. In other studies from Pakistan Hassan et al[19] and Khalid et al.[20] have reported the AML/ALL ratio of 2.57:1 and 1.02:1 respectively. In comparison, relative frequency of AML and ALL expressed as AML/ALL ratio in studies from Australia[21], Denmark[22] and Norway[23] was 3.4:1, 5.17:1 and 10.33:1, respectively. The relative frequency of AML in adults therefore appeared to be lower in our patients when compared with developed countries.

Acute leukaemias are more common in males than in females[18,25-27]. Male to female rate ratio is usually 1.1 to 1.2:1[25]. The M/F ratio of 2.74:1 observed in our study therefore reflected much larger male predominance in adult acute leukaemia. A similar distinct male preponderance was observed virtually in all the age groups and in the different types of acute leukaemia (Tables 4, 5).

Incidence of AML reportedly increases with the age[25]. Relatively low incidence of AML is noted in young adults[24]. A continuous increase in rate is described to begin at age of 50 years[24]. In the present study we, however observed a different bimodal pattern of AML distribution in adults. Highest rate was observed in ages 16-25 years and a second but smaller peak in ages 46-55 years followed by a significant decline in incidence in older age groups. Relative frequency of AML in comparison to ALL however increased with advancing age (Table 7). AML therefore, appeared to affect significantly younger adults in the present study.

ALL is primarily a disease of first two decades of life. It is uncommon between ages 25 and 60 years, but increases in incidence with age particularly after 60[25]. Taylor et al[28]. from UK have reported that the patients aged 60 years and over accounted for 31% of all the adult ALL patients. In contrast, present study showed that the rate of ALL was highest among adults upto 25 years, accounting for 60% of the total ALL patients in adults, and

a sharp progressive decline afterwards with only 4% aged 60 years and over.

Median age at the time of diagnosis for AML and ALL was 36 and 22 years respectively. Presenting age of our adult patients was significantly lower than 58-66 years[15,23] reported for AML and 31 years[29] for ALL in adults. Similarly median age for total adult acute leukaemia was observed to be 30 years in comparison to 63 years reported in an Australian study[21].

Considering presenting age at the time of diagnosis and their age related distribution, acute leukaemias appeared to affect much younger adults in our population when compared with developed countries. The factors partly responsible for this observation could include low overall life expectancy and the fact that very old patients have even poorer access to the medical care which results in diagnostic omission.

AML-M2 is reported to be the commonest subtype of AML[15,20,27,30]. In the present study although M2 was found to be the most frequent subtype of AML, its relative frequency of 67.1% was significantly higher than 22-32.3% described in different studies[15,20,30]. M4 was the second most frequent subtype of AML and showed a median age of 47 years in contrast to 33 years for M2, 35 years for M1 and 30 years for M3 (Table 8). AML-M4 therefore appeared to affect relatively older adults.

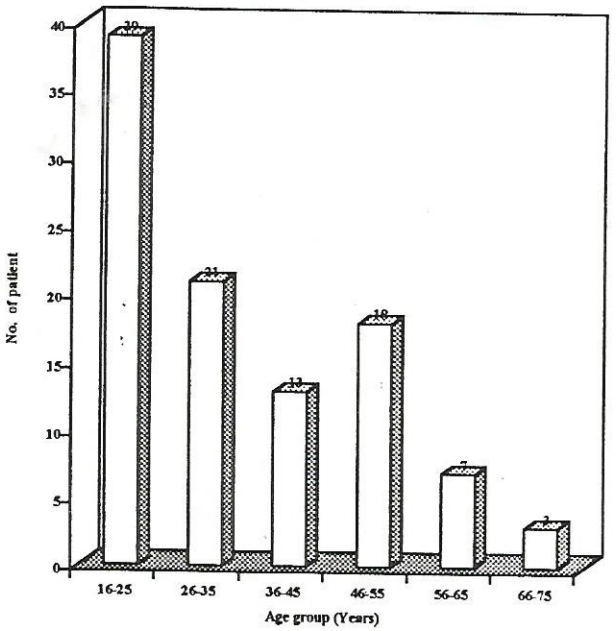
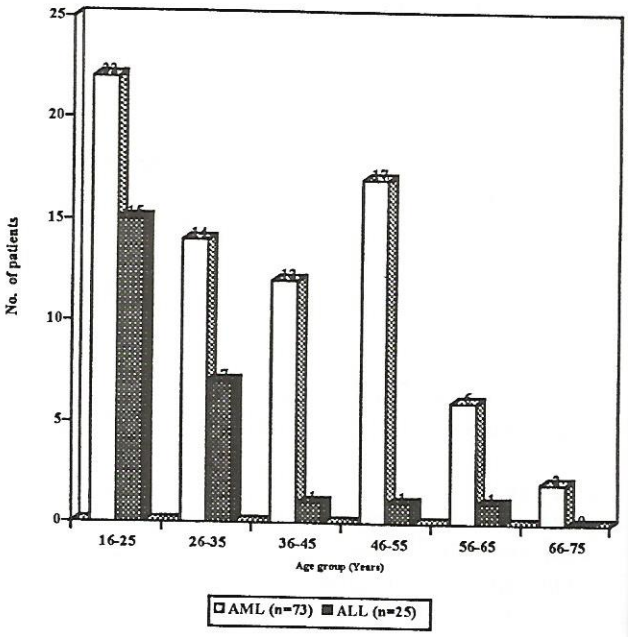


Fig.1. Age related distribution of acute leukaemia in adults (n=101)

Distribution of ALL subtypes showed L2 to be the main subtype affecting 64% of the total adult ALL patients. The relative frequency of L2 observed in our study was significantly higher than 48.7% and 55.6% reported by Bennett et al.[13] and GIMEMA group[29], in adult ALL. Only one case of ALL-L3 (4%) was diagnosed in the present study. ALL-L3 is generally reported to account for about 1-3% of all cases of ALL[31,32]

Fig.2. Age related comparative distribution of AML and ALL in adults.



Conclusions

Acute myeloid leukaemia (AML) was found to be the most frequent type of acute leukaemia diagnosed in adults. The relative frequency of AML was however noted to be lower, when compared with developed countries.

- In comparison to the studies from West, much larger male excess was observed. Male preponderance in our study may partly be reflective of relatively better health care for males in our society, or it could be due to genetic and different environmental factors.
- Age related distribution of acute leukaemia in adults showed a different pattern when compared with data from developed countries. Acute leukaemia appeared to affect much younger adults in our population.

Among the different morphological subtypes of acute leukaemias, M2 was the commonest form of AML whereas L2 was the commonest form of ALL. The frequency of M2 and L2 was however higher in our patients when compared with international data.

References

1. Acute leukemias in adults. In: Manual of clinical Hematology (ed. Mazza JJ), 2nd edition, pp. 222-235, Bostan: Little, Brown and Company, 1995.
2. Lanzkowsky P. Leukemias. In: Manual of Pediatric Hematology and Oncology (ed. Lanzkowsky P.), pp. 217-249. New York: Churchill Livingstone: 1989.

3. McKenzie SB. Acute leukemia. In: Text book of Hematology (ed. McKenzie SB), 2nd edition, pp. 375-400. Baltimore: Williams and Wilkins. 1996.
4. Champlin R, Gale RP. Acute lymphoblastic leukemia: Recent advances in biology and therapy. Blood 1989; 73: 2051-66.
5. Heath CW, Jr. Epidemiology and hereditary aspects of acute leukemia. In: Neoplastic diseases of the blood (eds. Wiernik PH, Canellos GP, Kyle RA, Schiffer CA), 2nd edition, pp. 157-168. New York: Churchill Livingstone. 1991.
6. Bennett JM, Catovsky D, Daniel MT, et al. Proposals for the classification of the acute leukaemias. Br J Haematol 1976; 33: 451-458.
7. Bennett JM, Catovsky D, Daniel MT, et al. Proposed revised criteria for the classification of acute myeloid leukaemia. Annals of Internal Medicine 1985; 103: 626-629.
8. Bennett JM, Catovsky D, Daniel MT, et al. Criteria for the diagnosis of acute leukaemia of megakaryocyte lineage (M7). Annals of Internal Medicine 1985; 103: 460-462.
9. Bennett JM, Catovsky D, Daniel MT, et al. Proposal for the recognition of minimally differentiated acute myeloid leukaemia (AML-M0). Br J Haematol 1991; 78: 325-329.
10. Pui C, Raimondi SC, Head Dr, et al. Characterization of childhood acute leukemia with multiple myeloid and lymphoid markers at diagnosis and at relapse. Blood 1991; 78: 1327-37.
11. Bain B, Catovsky D. Current concerns in haematology 2: classification of acute leukaemia. J Clin Pathol 1990; 43: 882-887.
12. Reiffers J, Dachary D, Bernard P, et al. Morphological classification of acute myeloid leukemias using the FAB system. Reterospective analysis of 106 cases. Nouv Rev Fr Hematol 1982; 24: 237-40.
13. Bennett JM, Catovsky D, Daniel MT, et al. The morphological classification of acute lymphoblastic leukaemia: concordance among observers and clinical correlations. Br J Haematol 1981; 47: 553-61.
14. Lilleyman JS, Hann IM, Stevens RF, et al. Cytomorphology of childhood lymphoblastic leukaemia: a prospective study of 2000 patients. Br J Haematol 1992; 81: 52-57.
15. Venditti A, Del Poeta G, Buccisano F, et al. Minimally differentiated acute myeloid leukemia (AML-M0): comparison of 25 cases with other French-American-British subtypes. Blood 1997; 89: 621-629.
16. Kantarjian HM, Hirsch-Ginsberg C, Yee G, et al. Mixed-lineage leukemia revisited: acute lymphocytic leukemia with myeloperoxidase - positive blasts by electron microscopy. Blood 1990; 76: 808-13.
17. Greaves M. A natural history of pediatric acute leukemia. Blood 1993; 82: 1043-51.
18. Weinstein HJ, Griffin JD. Acute myelogenous leukemia. In: Blood: Principles and practice of Hematology (eds. Handin RI, Lux SE, Stossel TP), pp. 543-574. Philadelphia: JB Lippincott Company, 1995.
19. Hassan K, Ikram N, Shah SH. A morphological pattern of 234 cases of leukaemias. JPMA 1994; 44: 145-148.
20. Khalid A, Zahid M, Rehman A, et al. Clinicoepidemiological features of adult leukemias in Pakistan. JPMA 1997; 47: 119-122.
21. Shapiro J, Brown S, Briggs P, et al. Adult acute leukaemia - a reterospective study of 66 consecutive patients. Aust N Z J Med 1997; 27: 301-306.
22. Johnson HE, Bergmann OJ, Ellegaard J, Bastrup-Madsen P. Acute myeloid and lymphoblastic leukemia in adults: The course of the disease in 315 patients from one region, during a ten-year period. Dan Med Bull 1989; 36: 189-93.
23. Lanvik J, Dybedal I, Hammerstrom J, Waage A. Acute leukemia in middle Norway 1984-88. Leuk Lymphoma 1994; 16: 65-71.
24. Linet MS. Mortality and morbidity. In: The Leukemias: Epidemiologic aspects (Monographs in epidemiology and biostatistics; vol. 6), pp. 20-65. New York: Oxford University Press, 1985.
25. Linet MS. Heterogeneity of the leukemias. In: The Leukemias: Epidemiologic Aspects (Monographs in epidemiology and biostatistics; vol. 6), pp. 3-13. New York: Oxford University Press, 1985.
26. Yang C, Zhang X. Incidence survey of leukemia in China. Chin Med Sci J 1991; 6: 65-70.
27. Khan MQ, Shivarudrappa AS, el-Bialy S, et al. Leukaemia cases in Central Hospital, Riyadh. J Indian Med Assoc 1991; 89: 38-42.
28. Taylor PR, Reid MM, Bown N, et al. Acute lymphoblastic leukemia in patients aged 60 years and over: a population - based study of incidence and outcome. Blood 1992; 80: 1813-7.
29. GIMEMA Cooperative Group. GIMEMA ALL 0183: a multicentric study on adult acute lymphoblastic leukaemia in Italy. Br J Haematol 1989; 71: 377-386.
30. Bennett JM. The classification of acute leukemias: cytochemical and morphologic consideration. In: Neoplastic Diseases of the Blood (eds. Wiernik PH, Canellos GP, Kyle RA, Schiffer CA), pp. 201-217. New York: Churchill Livingstone: 1985.
31. Flandrin G, Brouet JC, Daniel MT, Preud' homme JL. Acute leukemia with Burkitt's tumour cells: A study of six cases with special reference to lymphocyte surface markers. Blood 1975; 45: 183-188.
32. Fenaux P, Lai JL, Miaux O, et al. Burkitt cell acute leukaemia (L3 ALL) in adults: a report of 18 cases. Br J Haematol 1989; 71: 371-376.

Erratum

Previous article titled "Morphological Pattern Of Childhood Lymphoblastic Leukaemia at Shaikh Zayed Hospital, Lahore (1994-1999)
Authors: M J Asif Z Iqbal A Malik M F Alam A Hayee
Vol. 6, No.3, Jul-Sep 2000: page 254: Abstract, line 2 – **lymphoblastic** instead of **lymboblastic**
Page 257 - Add key to Fig.2

L1 L2 L3