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Six Year Experience of 116 Leukaemic Children at Shaikh Zayed Hospital Lahore Pakistan.

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SUMMARY

To evaluate prevalence of childhood leukaemia according to FAB classification and its clinical manifestations at tertiary level referral teaching hospital. We retrospectively identified children with diagnosis of childhood leukaemia. They were classified according to FAB morphological classification. At the time of presentation symptomatology and physical findings of these patients were recorded and analysed. A total of 116 patients were diagnosed as childhood (age < 15 years) leukaemia, of these 110 (94.8%) had acute leukaemia (AL) and 6 children had chronic myeloid leukaemia (CML). Out of these 116 leukaemic children, 81 (70%) were males and 35 (30%) were females, with a male/female ratio of 2:3. Out of the 110 AL patients, 76 (69.1%) had acute lymphoblastic leukaemia (ALL) and 32 (29.1%) were suffering from acute myeloid leukaemia (AML) with ALL/AML ratio of 2.37, according to FAB-classification of AL. Two patient had bilineal morphology. Among ALLs L1 (63.2%) and L2 (34.2%) were the commonest sub-types, whereas M2 (50%) was commonest sub type of AML. The median ages for boys and girls were 6 years and 5 years for ALL, and these were 8 years and 10 years for AML respectively. In symptomatology, fever (65%) pallor (53%), gum bleeding (24%) swellings of body (20%) and discolouration of skin (20%) were the predominant complaints. On physical examination pallor (88%), hyperpyrexia (64%), hepatomegaly (60%), splenomegaly (56%) and cervical lymph-adenopathy (38%) were the commonst signs at the time of presentation. Among acute leukemias ALL is most prevalent. Fever, pallor and gum bleeding are most frequent complaints, whereas, anaemia, hyperpyrexia and hepatomegaly are the commonst signs in leukaemic children.

INTRODUCTION

Leukaemia is the most common malignancy of childhood, accounting for almost one-third of all cases malignancy in the United States, each year[1]. There appear to be geographic differences in the frequency and age distribution of childhood leukaemia throughout the world[3]. In Pakistan different aspects of leukaemia in children have been extensively described by Haneef et al[4]. Iftikhar and Kazi[5], Hassan et al.[6]). The frequency of leukaemia rapidly increases after birth, peaks at 4-5 years of age, and then declines. Acute lymphoblastic leukaemia (ALL) accounts for the early peak, whereas the incidence of acute myeloid leukaemia (AML) remains constant[7]. The most widely accepted classification of acute leukaemia (AL) is the FAB classification, proposed by the French Amarican-British (FAB) cooperative group in 1976. We report the results of a restrospective study, carried out to find the distribution of various types and subtypes of childhood leukaemia. Also we have tabulated symptomatology and signs of childhood leukaemia on the first day of presentation.

PATIENTS AND METHODS

This analysis was done as a part of the retrospective study on 116 leukaemic children of age < 15 years. All these children reported in the department of paediatrics or Haematology of Shaikh Zayed Hospital, Lahore. They were diagnosed and

classified according to the FAB morphological classification on bone marrow aspiration in the department of Haematology. Children with ambiguity in diagnosis, in age and diagnosed at other centres were excluded from this study. Children who were on treatment e.g steroids even, before reporting in our hospital were not enrolled. Only indiginous Pakistani resident children were entertained. Clinical record keeping and diagnostic procedures were done in the department of Paediatrics in collaboration with the department of Haematology. Clinical presentation (symptomatology and signs) were recorded by experienced paediatric registrar, verified by paediatric consultant (if needed) within 24 hours of the reporting In the hospital. Despite their educational handicap, the parents of the children devised various methods of remembering the year of birth, if not the exact birth day of their children in case of older children. Records of morphological classification and clinical features were recorded and analysed by correcting the percentages to the nearest whole number.

RESULTS

In our retrospective study we enrolled 116 newly diagnosed childhood leukaemic patients, over a period of 6 years (from Jan 1994 to Dec. 1999), at our hospital. Out of all these patients 110 (95%) cases were of acute leukaemia (AL) and 6 children had chronic myeloid leukaemia (CML). These 6 CML patients were excluded from the study. Of the 110 AL patients, 76 (69%) comprised of acute lymphoblastic leukaemia (ALL), 32 (29%) were of acute myeloid leukaemia (AML), according to the FAB morplogical classification of childhood AL. The overall ALL/AML ratio was 2.37. Two children had bilineal morphology (Table-1). Though the number of leukaemic patients varied each year yet a constant proportion was maintained between AL and other childhood malignancies (graph-I).

After infancy there was a peak increase in occurrence of ALL, with maximum incidence in >1-5 year age group, in boys and girls, boys outnumbering the girls. In the distribution of FAB-subtypes, L1 was the commonest (63%) among ALL patients, with maximum incidence in age group of >1-5 years. In contrast AML was observed in higher percentages In older age group with maximum incidence in > 10-15 year age group and the commonest sub-type was M2 (Tables 1, 2).

In clinical features, we observed male/female ratio of 2-3 and 2.2 for ALL and AML respectively. The median ages for ALL were 6 years and 5 years for males and females, whereas, these were 8 and 10 years for AML respectively. These features are compared with reports from other centres of Pakistan and different countries of world in Table 3.

In symptomatology the most common complaints in our study were fever 72 (65%) pallor 59 (53%), gum bleeding 26 (24%), skin discolouration 22 (20%) and swellings of the body 22 (20%), whereas pallor 97 (98%), hyperpyrexia 70 (64%), hepatomegaly 66 (64%), splenomegaly 62 (56%) and cervical lymphadenopathy 42 (34%) were the predominant physical findings in our patients. These clinical findings along with less frequently observed signs and symptoms are tabulated in Table 4.

Table 1: Age and sex distribution of childhood leukaemias (n=116).

Age (years)	ALL (n=76) 65%		AML (n=32) 28%		Bilineal (n=2) 2%		CML (n=6) 5%	
	M	F	M	F	M	F	M	F
< 1(5)	-	1	4	-	-	-	2	-
>1-5(39)	22	11	3	3	-	-	-	-
>5-10(38)	18	9	6	2	1	-	2	1
>10-15(31)	13	2	9	5	-	1	1	-
Total (n=116)	53	23	22	10	1	1	5	1

DISCUSSION

In childhood, acute lymphoblastic leukaemia (ALL) is the most common form (80%), acute myeloid leukaemia (AML) is the next commonest (17%) whereas chronic myeloid leukaemia (CML) and CML constitute about 3% in western world[2]. In contrast we found ALL and AML in 76 (65%) and 32 (28%) of our patients but the percentage of CML (5%) was similar to the reports from western world (Table 1). This is an indicator of presence of more

Table 2: Distribution of FAB types, in children with acute leukaemias (n=110)

Age (years)	*ALL (n=76) 69%*			*AML (n=32) 29%*							*Bilineal (n=2)*
	L1	*L2*	*L3*	*M0*	*M1*	*M2*	*M3*	*M4*	*M5*	*M6*	*M7*	
< 1	-	1	-	-	1	2	-	-	-	1	-	-
> 1-5	26	5	2	-	-	3	1	2	-	-	-	-
> 5-10	16	11	-	1	1	3	1	1	1	-	-	1
> 10-15	6	9	-	3	-	8	1	2	-	-	-	1
Total	48	26	2	4	2	16	3	5	1	1	-	2
Percentage	63	35	2	-	-	50	-	-	-	-	-	-

Table 3: Clinical manifestations of childhood leukaemias

No.	*Symptoms*	*Number*	*Percent*	*Signs*	*Number*	*Percent*
1	Fever	72	65	Pallor	97	88
2	Pallor	59	53	Hyperpyrexia	70	64
3	Gum bleeding	26	24	Hepatomegaly	66	60
4	Body swelling	22	20	Splenomegaly	62	56
5	Skin rash	22	20	Cervical lymphadenopathy	42	38
6	Mouth sore	20	18	Generalized lymphadenopathy	37	34
7	Lethargy	20	18	Gum bleeding	32	29
8	Resp. distress	9	8	Skin bleeding	18	16
9	Vomiting	7	6	Arthritis	7	6
10	Bone pains	5	4	Chloromas	3	3
11	Headache	3	3	Arthritis & chloroma	3	3
12	Weight Loss	1	1	Jaundice	2	2

resistant form of AL in Pakistani children. The most widely and commonly accepted classification of AL is FAB classification the same was adopted in our study. Our findings are in accord with reported by Williams et al from Africa, pointing toward the genetic and environmental factors in aetiology of childhood leukaemia. Peak incidence of ALL and especially of L1 sub-type is reported by many authors from Pakistan[3,4] and from Western developed world, in age group >1-5 years. The same was the the observation I in our study (Table-2).

Leukaemia are biologically diverse in terms of their hematopoitic cellular phenotype and presumed origins yet the symptomatology of AL varies little with cell type 1, we witnessed the same also.

A comparison of the clinical features of childhood AL, with other studies from Africa, Europe and America are shown in Table 3. The median ages for ALL were 6 years and 5 years for males and females whereas these were 8 years and 10 years for AML respectively. Similar figures are reported from Africa but median ages on the whole are less in reports from England. Similarly higher male/female ratio in our study indicates better care for male child but reason of highest ALL/AML ratio in Sweden is not understood (Table 3).

The onset of the symptomatology of leukaemia

Table 4: Comparison of age, sex in childhood leukaemias

Criteria	Pakistan			Africa	England	USA		Sweden
	Lahore Malik	Lahore Iftikhar	Rawalpindi Hussain	Ibadanb	MAN	White	Blacks	
Ac. Lymphoblastic Leukaemia								
M/F ratio	2.3	4	1	2.8	1.45	1.42	1.5	1.37
Mean age (years)								
Male	6	-	-	6	4.5	-	-	-
Female	5	-	-	4.75	4	-	-	-
Ac. Myeloid Leukaemia								
M/F ratio	2.2	1.6	3	4.5	0.75	1.09	0.83	1.08
Median age (years)								
Male	8	-	-	6.5	-	-	-	-
Female	10	-	-	7	-	-	-	-
ALL to AML ratio	2.37	3.2	4.5	1.9	3.9	3.36	2.7	5.87

may be insidious or abrupt and children may present with any combination of these complaints in varying degree of severity. The rapidity with which these symptoms progress varies greatly[10,11]. In our experience the child is usually seen with relatively few symptoms and physical findings but this will depend upon the type of referral and type of institution. Occasionally these children may have no peripheral blood or clinical abnormality.

In this study we have demonstrated fever (65%), pallor (53%), gum bleeding (24%) swellings of the body (20%) and skin discolouration (20%) as most common complaints, (Table 4), whereas these were reported in (61%), (65%), (52%) (15%) and (52%) of the children from USA by George et al[11].

Hassan et al[6], reported fever and pallor in 100% of their patients reflecting different cultural social attitude of parents towards the health of their kids. In our observation on physical examination at the time of presentation, the five most common signs were pallor (88%), hyperpyrexia (64%) hepatomegaly (60%), splenomegaly (56%) and cervical lymphadenopathy, Table 4. The very high percentage of pallor in our patients points towards the pre existing nutritional and other anaemias in our children. Other large differences between physical findings reported by us are not explainable. Hepatomegaly, splenomegaly and cervical lymphadenopathy were found in 79%, 69% and 62% of the leukaemic patients reported by the south west oncology group from USA.[10]. Chloromas were found in 3% of our patients, and all of these were having swollen joints also. Skin bleeding (purpura/pedtichiae) was present in 16% of our patients, whereas only 2 children had jaundice at the time of presentation. Signs and symptoms of central nervous system involvement and skin infiltration are rarely present at the time of initial diagnosis[3,1]. and this was affirmative in our study.

We conclude the affirmation of diversity of leukaemia in terms of types, sub-types and clinical presentation throughout the world and even in the same country. It is recommended that thorough evaluation should be done of patients with ordinary diagnosis, but behaving abnormally in terms of response to the standard treatment.

CONCLUSION

Amongst acute leukaemic cases, ALL is the most common type. Morphological subtype L1 is the most common form of ALL in children. ALL-

L2 subtype is relatively more frequent in Pakistani children when compared with the Western population. Relative frequency of AML is also found to be considerably higher in our children.

A distinct male predominance is observed practically in all age groups and in both the major types of acute leukaemia. Fever, progressive pallor and gum bleeding are the most frequent complaints, whereas, anaemia, hyperpyrexia and hepatomegaly are the commonst signs in leukaemic children. It is recommended that thorough evaluation should be done of patients with ordinary diagnosis but behaving abnormally in terms of response to the standard treatment.

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