

Acute Lymphoblastic Leukaemia: Clinicohaematological Features, Laboratory Characteristics and Prognostic Factors: A Single Center Experience

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ABSTRACT

Objective: To study clinico-haematological features, Laboratory results and prognostic factors in patients of acute lymphoblastic leukaemia.

Study Design: Descriptive study.

Place and Duration of Study: This study included all newly diagnosed cases of acute lymphoblastic Leukaemia coming to Armed Forces Institute of Pathology Rawalpindi from Jun 2008-Feb2010.

Materials and Methods: The detailed clinical history with physical findings were charted on the proforma. About 3ml blood from each patient was taken in EDTA container. The blood was analyzed on Haematology analyzer Sysmex KX 21. Quality control was maintained by running normal and abnormal controls. Bone marrow aspiration was done at the time of diagnosis. Five push smears were made from each case; 2 for leishman stain, one for Sudan black B, one for periodic acid schiff, and one for acid phosphatase.

Results: The common clinical features in children were pallor (100%), fever (93%), hepatomegaly (70%), splenomegaly(64%), lymphadenopathy (58%), bleeding manifestations (27%) and bone pain(9%). Pallor(100%)and fever(89%) were also common manifestations in adults.

Initial high white cell count (> 50x10⁹/l) was observed in 9 (12%) patients. Three patients showed hyperleucocytosis (> 100x10⁹/l). Haemoglobin < 8gm/dl was seen in 30(11%)patients and platelet count less than 20x10⁹/l was observed in 8(10.8%) cases. About 9 (12%)patients showed pancytopenia.

According to French-American-British (FAB) criteria ALL-L1 was the commonest FAB type (81%), followed by L2 (16%) and L3 (3%) in children while ALLL2 was high among adult age group .

Conclusion: We found that ALL is a frequent childhood hematological malignancy in our setting and is more prevalent in males both in children and adults. ALL- L I type being more common than other types of ALL. Considering the prognostic factors of age, WBC count, lymphadenopathy, T immunophenotyping an FAB classification; most of our patients constitute a better prognostic group.

Key words: ALL, clinicohaematological features, lab findings, prognostic factors.

Introduction

Acute lymphoblastic leukaemia is a malignant disorder of lymphoid progenitor cells.¹ It results from neoplastic transformation of lymphoid stem cell due to altered genome of stem cells. There is lack of differentiation beyond blast stage and progressive accumulation of leukaemic blasts in the bone marrow² with resultant suppression of normal haematopoiesis leading to anemia, thrombocytopenia and neutropenia.³ The lymphoblasts also accumulate in various extramedullary sites, especially the liver, spleen , lymph nodes,

meninges, gonads and thymus.¹

Acute lymphoblastic leukaemia is mainly a childhood malignancy.⁴ It affects both children and adults with peak incidence between 2-5 year⁵ and a rise again after 50 years of age.⁶ Younger patients especially those younger than age 50years have a better prognosis than older patients.⁷ ALL in elders is a rare disease.¹ Acute lymphoblastic leukaemia is still the most common cause of death in children suffering from cancer".⁸

Materials and Methods

It was a descriptive study conducted on seventy four patients of ALL selected on the basis of non probability purposive sampling. All newly diagnosed patients of ALL were included in the study.

The subjects of study were 74 cases of ALL. All of the cases came to Armed Forces

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Institute of Pathology Rawalpindi for bone marrow aspiration and were diagnosed by standard morphology i.e blast cells having high N/C ratio, moderately open nuclear chromatin, 0-2 inconspicuous nucleoli and scanty or absence of cytoplasmic granules) & cytochemical methods i.e blast cells showing SBB negativity, acid phosphatase and periodic acid Schiff positivity).

Demographic data including name, age, sex, telephone no. was recorded. Clinical examination for liver, spleen, lymph nodes enlargement, bleeding manifestations and bone pains was recorded. Hematological parameters including Total leucocyte count, Haemoglobin and Platelets count were also recorded. Blood counts were performed on Sysmax KX 21. Percentage of blasts in peripheral blood and bone marrow at the time of diagnosis was charted on the proforma.

Results

A total of 74 patients of acute lymphoblastic leukaemia were studied

The age of patients with ALL ranged between 1 and 80 years. The total no. of children were 45(60%) and adult were 29(40%). The percentage of patients between 1-14 years is 43%. The mean age for children (<15 yrs) was 5.68±3.32 and the mean age for adults was 36.12±17.9. (Table I)

There were 45(61%) males and the females were 29(39%) cases.

Regarding Children, males were 28(62%) cases and females were 17(38%). (Fig 1.1) In adults males constituted 17(59%) and females were 12(41%). (Table II)

In children Pallor and fever were the two most common presenting features (100% and 93%) respectively, the next common were hepatomegaly (70%), splenomegaly (64%), lymphadenopathy (58%), bleeding manifestations (27%). Other less common symptom was bone pain which was seen in

9% of cases. (Fig 1)

Pallor(100%) and fever(89%) were also common manifestations in adults followed by hepatomegaly (59%), splenomegaly (36%), lymphadenopathy (25%), bleeding manifestations (25%). Bone pain was seen in 9% of adult cases and mediastinal Mass in 2 (3%) cases. (Fig 2)

Using FAB criteria, 60(90%) children showed L1 morphology, 12(16%) children showed L2 morphology and 2 (3%) patient had L3 morphology. (Fig 3) While in adults 29(39%) patients showed L1 morphology, 42(56%) patients showed L2 morphology and 4(5%) patient had L3 morphology. (Fig 4)

Table I: Age distribution, no. of patients and mean age of patients with ALL (n=74)

Age in years	No. of patients	Age Mean \pm SD
1-14	32(43%)	4.60 \pm 2.11
15-30	18(24%)	17.3 \pm 2.70
31-50	9(12%)	35.7 \pm 1.88
>50	15 (20%)	56.8 \pm 3.11

Table II: Gender distribution of patients with ALL (n=74)

Total	Male	Female
Children	28(62%)	17(38%)
Adults	17(59%)	12(41%)
Grand Total	45(61%)	29(39%)

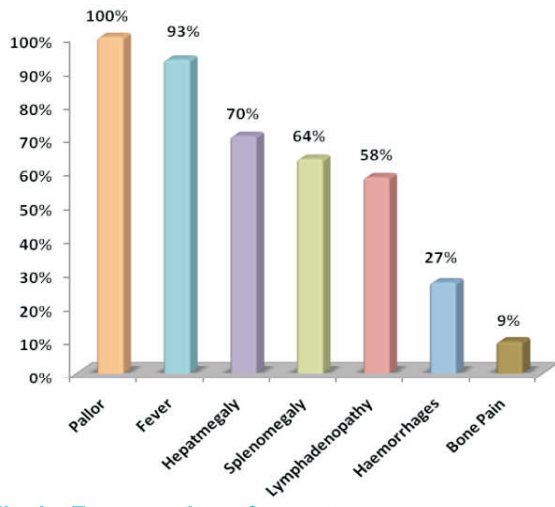


Fig 1: Frequencies of symptoms among children of ALL(n=74)

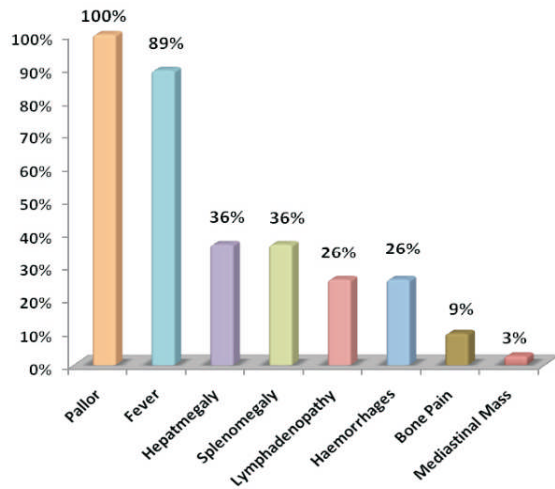


Fig 2: Frequencies of symptoms among adults of ALL(n=74)

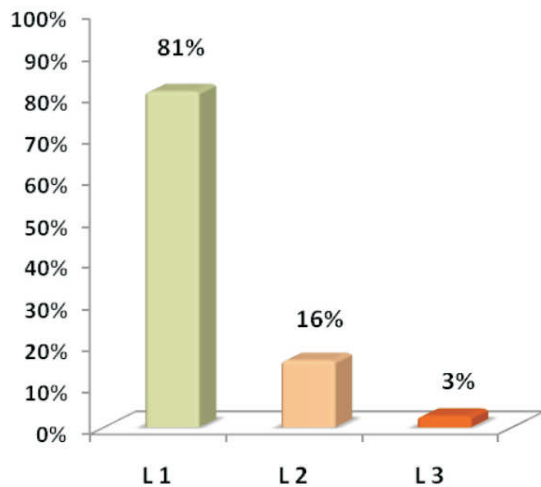


Fig 3: FAB types of ALL in Children.(n=74)

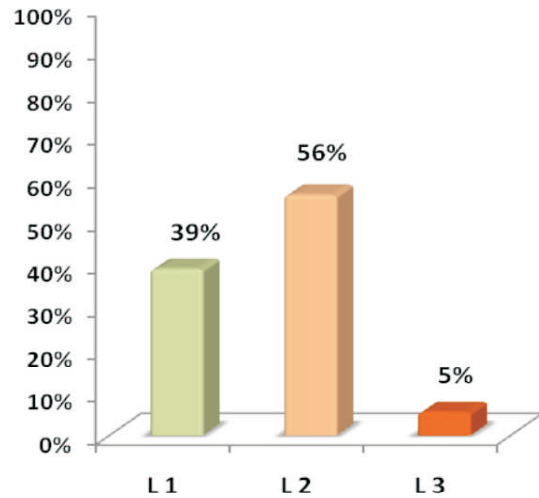


Fig 4: FAB types of ALL in adults.(n=74)

Discussion

Acute lymphoblastic leukaemia constitutes 12% of all leukaemias.⁹ It affects both adults and children and can occur at any age.¹⁰ There has been a gradual increase in the incidence of ALL in the past 25 years.¹¹ However with improvement in diagnosis and treatment, overall cure rate for children with acute lymphoblastic leukemia has reached 90%.¹²

ALL is more common than other acute leukaemias especially in children. Few researchers have made the high percentage of ALL among different types of leukaemias in their study groups.¹³

The highest incidence of ALL is found in Italy, United States (US), Switzerland, and Costa Rica.¹⁴ In the United States there are approximately 2,900 children and adolescents younger than 20 years diagnosed with ALL each year.¹⁵

The peak age in our study was seen between 2-7 years, a later peak between 10-17 years and a slight rise between 21-28 years. Hence as far as age is concerned all of these patients fall in good prognostic group. The age distribution in children and adolescent in our study has been in agreement with other observations.¹⁶ The male preponderance 2:1 has also been well observed by other

researchers.¹⁷ The mean age for children was also in agreement with other studies.¹⁸ Regarding FAB ALL type; approximately 81% of children with L1 morphology fall in good prognostic group while 56% of adults with ALL L2 morphology fall in moderate prognostic group.

Clinical features of ALL varies. Generally patients with ALL presents with fever, easy fatigability, shortness of breath, infections, haemorrhagic manifestations especially oozing from gums and epistaxis.¹¹ Pallor, petechiae, echymoses, weight loss, hepatosplenomegaly and lymphadenopathy are common presenting signs in these cases.¹ In more than half of the patients hepatomegaly and splenomegaly are present. 1 Less than 10% of patients have symptomatic central nervous system (CNS) involvement and T cell mediastinal mass. Testicular involvement is rare in adults.¹¹

Rarely (5% of cases) bone pain, and limping may be the only presenting symptom which is due to leukaemic infiltration of periosteum or joints, and may cause delay in the diagnosis.¹⁹ In our study bone pain was seen in 9% of patients.

A minor percentage of patients of ALL presents with pancytopenia and are labelled as subleukaemic leukaemia cases. These patients usually do not have significant visceromegaly; hence mimicking aplastic anaemia. The peripheral blood in these patients usually do not show the presence of blast cells. Therefore they can only be diagnosed by bone marrow aspiration/trephine biopsy. About 12% of our patients fall in this category which is in agreement with a study conducted by Tariq et al.²⁰ This incidence is higher as compared to western study reported by Patthak et al.²¹

Childhood ALL cases have much better prognosis than the adults. Infants and children age 10 years and older tend to have a poorer outcome than young children with ages 1 - 9 years.²² Infants with MLL gene

rearrangement have very high (WBC) counts and increased incidence of central nervous involvement with poor outcome.²⁸ Some studies indicate a better prognosis for girls than boys. This may be partly due to boys' risks for testicular cancer.²³

The survival of adults with acute lymphoblastic leukemia (ALL) is inferior to that of paediatric patient²⁴ because a higher proportion of adults have unfavourable cytogenetic abnormalities such as t(9;22) translocation.²⁵ Many patients over the age of 60 years do not tolerate intensive chemotherapy, hence the outcome remains poor for older patients.²⁶ Younger patients especially those younger than age 50 years have a better prognosis than older patients.⁷ About 54 (73%) patients in our study fall in age group below 50 years.

A WBC count of $50 \times 10^9/l$ is used as a cut off limit between better and poor prognosis.²⁷ Hence People diagnosed with a WBC count below 50,000 tend to do better than people with higher WBC counts. Nine patients in our study showed WBC count $>50 \times 10^9/l$. Three patients showed WBC count $>100 \times 10^9/l$. Two of our adult patients and one of our patient aged 4 yrs died with WBC count; $>50 \times 10^9/l$ and $100 \times 10^9/l$ respectively. Two of these patients had ALL-L2 morphology and one patient had L3 morphology. The subtype of T and B cell, also affects the prognosis. Patients with T cell ALL tend to have a better prognosis than those with mature B cell ALL i.e Burkitt Leukaemia.²⁸

Conclusion

We found that ALL is a frequent childhood hematological malignancy in our setting and is more prevalent in males both in children and adults. In childhood ALL cases ALL-L1 is more common than other ALL subtypes. Considering the prognostic factor of age, WBC count, lymphadenopathy, T immunophenotyping and FAB classification; most of our patients constitute

a better prognostic group. Another important finding of this study is that about 12% of the patients presented with pancytopenia. This is an ongoing study and includes as a second stage, remission response of our patients to standard induction therapy.

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