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Clinical and demographic profile of children with leukemia

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Abstract

Background: Cancer is essentially a disease of adults yet it is one of the common killers in childhood .Among childhood cancers, acute leukemias are the most common and account for 30% of all newly diagnosed cases .Calicut medical college at Kozhikode is catering treatment to six districts of Malabar, a major centre managing childhood cancers, in northern part of Kerala, India .Studies have shown that demographic and clinical profile can be different in different part of the world study of which is useful for planning management locally.

Methods: All children below the age of 12 years admitted consecutively to Institute of maternal and child health (IMCH),Medical college Kozhikode, Kerala, India, diagnosed with child hood leukemia by peripheral smear and/or by bone marrow examination ,confirmed by our pathology department were included .A detailed history, physical examination ,relevant laboratory investigations including CBC, Xray chest,peripheral blood and bonemarrow smears were done in all cases. Trephine biopsy and ultrasound examination were done in selected cases. The data so collected were compared with similar data from other part of the world and was statistically analysed.

Results: some of the demographic factors like age and sex distribution were similar to but with significant difference with literature data. Clinical profile also showed similarities and differences when compared with data from other parts of the world.

Conclusions: The study reaffirms the findings that already known from other parts of the world and in addition, identifies the differences in demographic and clinical profile in this part of the world thus highlighting the need to study this aspect further. This may help to prognosticate and plan management policies locally.

Keywords: Childhood Leukemias, Demography, Clinical Profile, Kerala, India

Introduction

Cancer is essentially a disease of adults, yet it is one of the common killers in childhood. Among childhood cancers, acute leukemias are the most common accounting for approximately 30% of all newly diagnosed cases. Central nervous system tumors are the second most common, followed by lymphomas, and

tumors of sympathetic nervous system, kidney, soft tissue and bone1.

Among childhood leukemias, Acute Lymphoblastic Leukemia (ALL) is the most common (75-80%), followed by Acute Myeloblastic Leukemia (15-20%) and chronic leukemia (2-3%). In western countries, cancer is next only to trauma as a cause of mortality in children under 15 years of age. Excluding the neonatal period, childhood cancer is the most common medical cause of death in persons under the age of 15 years in United States[2]. In India, although infections and malnutrition are the major factors contributing to childhood morbidity and mortality, malignancies are coming into greater focus because of the preventive measures against infections and malnutrition.

In best centres two third or more children with acute leukemia can be cured. The five-year survival of patients of ALL in good centres in India is reported to be 45% to 55%[3]. The mortality and morbidity due to childhood leukemias are higher in India compared to developed countries. This can be attributed to greater incidence of CNS involvement at presentation, higher prevalence of L_2 morphology and T cell leukemia, inadequate treatment and supportive care. Severe complications, poor compliance, loss of follow up and financial hardships[4].

The success observed in last two decades can be attributed to more accurate diagnosis, better supportive care, use of drug combinations to achieve and maintain remission, and use of prophylactic therapy to prevent CNS leukemia.

Advances in molecular biology and imaging techniques has provided new insights into the process of malignant transformation and provided new tools for diagnosis, staging, and classifying the disease into risk groups[3]. Advances in imaging techniques also helped to detect minimal residual disease.

The availability of hematopoietic cytokines and other blood components has improved the quality of supportive care helping more children with leukemias surviving into adulthood[5].

Most of the causes of morbidity in leukemia patients are related to infections, toxicity and side effects of therapy. The present approach of aggressive therapy to maximally eradicate the neoplasm render the child susceptible to infections, as most antileukemic drugs not only destroy the proliferating neoplasm but also effect normal cells, especially that of bone marrow, intestinal mucosa and epithelium.

Complications due to chemotherapy and ionizing radiation may become manifest many years later like disturbances in organ function of liver, heart, kidney, brain and bone, growth and development and most devastating, second malignancies[5].

Study objectives: This study was planned to assess the clinical and basic demographic profile of children of northern districts of Kerala with leukemia ,which is a southern state of India.

Materials and Methods

All children with leukemia below the age of twelve years at the time of diagnosis who received treatment from department of Pediatrics ,Institute of maternal and child health(IMCH), medical college Calicut during the period from 1st January2000 to 31'st December 2000 were included in the study after getting informed consent from parents and approval from departmental research committee.

Inclusion criteria:all the children below 12 years at the time of diagnosis diagnosed to have leukemia were included

Exclusioncriteria:Those children whose parents were not willing to do detailed evaluation and treatment from IMCH and wanted referral.. Children whose caregivers unable to give a reliable history were also excluded.

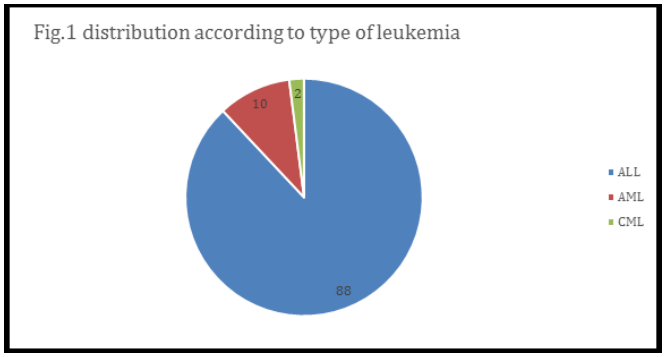
All diagnosed cases were evaluated with detailed history about the symptomatology , educational and financial background of parents followed by thorough physical examination by the principal investigator and were investigated with complete blood count, peripheral smear, chest x-ray, bone marrow examination, renal and liver function tests.All the investigations were done in our own laboratories ..Peripheral blood and bone marrow smears were examined by senior pathologists in the department of Pathology to confirm the diagnosis. Bone marrow trephine biopsy done in doubtful cases or when aspiration was dry. Ultrasonogram of abdomen was done in selected cases. Educational level of mother was assessed because she alone will be allowed to stay with the child during treatment as per hospital policy and majority of them do not salaried jobs.Father is the only source of income for majority of families in our society .hence his income was assessed. .All the data were collected and entered using a proforma and a master chart was prepared.

This data was compared with data from the literature and relevant data statistically analysed using appropriate tests(chi-squire) accordingly.

Since there was no ethical committee at the time of study ,clearance was not possible before the study ,but the present ethical committe has given permission to publish its contents.

Observations

A total of 102 cases of leukemia diagnosed from IMCH, Calicut at or below the age of 12 years were studied. They were distributed as given in the chart below.



The distribution of ALL cases in different age groups is as in table 1.

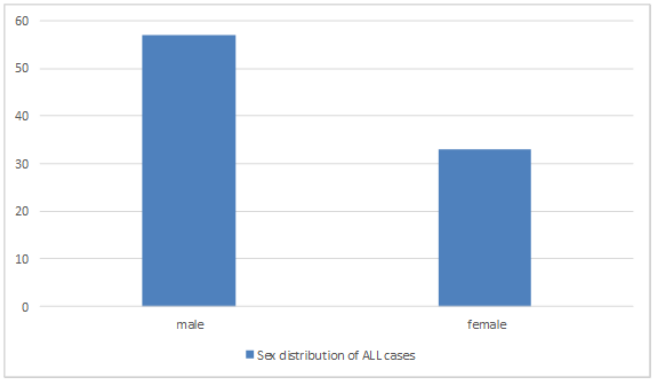
Table 1: Age distribution of ALL cases

Age group	No. of cases	Percentage
≤ 2 yrs	7	8%
2-5 yrs	42	46%
2-9 yrs	63	70%
≥ 9 yrs	20	22%

No significant difference was observed in the distribution of L_1 and L_2 among poor risk and standard risk age groups.

Figure 2: Sex Distribution of ALL

Sex distribution of patients were as in chart below



Education (mother)

Only primary education was there for majority of mothers 51%.44% of them had studied up to secondary school.

Table 2: Educational status of mother

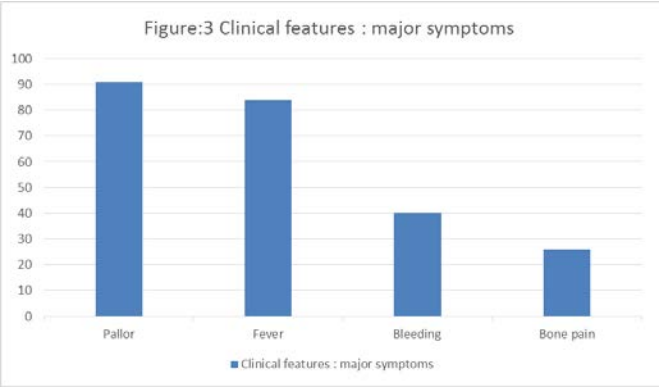
Educational status	No. of mothers	Percentage
Primary	46	51%
Secondary	40	44%
College	4	5%

Table 3: Occupation of father

Occupation (Father)	Total no.	Percentage
Manual labourers	72	80%
Business	15	17%
White collar	3	3%

Clinical Profile

The frequency of major symptoms were as in the chart below



Pallor was the most common presenting complaint (in 91%). In 84% of the patients there was fever at presentation. Bone pain and or arthralgia seen in 23 cases (25%). Skin or mucous membrane bleeds observed in 40% of the cases.

Significant lymphadenopathy was observed in 46.6% of patients, hepatosplenomegaly in 72%. Splenomegaly in 83% and hepatomegaly in 81% of the cases.

Table 4: Major signs

Clinical feature	No. of cases	Percentage
Lymphadenopathy	42	47.6%
Splenomegaly	75	83%
Hepatomegaly	73	81%
Hepatosplenomegaly	65	72%
Splenomegaly alone	10	12%
Hepatomegaly alone	8	9%

Marked Hepatomegaly (span ≥ 15cm) was observed in 3 cases and marked Splenomegaly in one case. 53% of patients had a liver span < 11cm; 24% had 11-15cms.

Table 5: Degree of hepatosplenomegaly

Size	Liver	Percentage	Spleen	Percentage
≤ 5cm	48	53%	57	63%
5-10cm	22	24%	16	18%
≥ 10cm	3	4%	1	1%

2 cases (2.2%) of patients had signs and symptoms of CNS involvement at presentation. One case had testicular enlargement. In both cases of CNS involvement facial palsy and vomiting was the clinical picture.

Two cases had presented with dyspnea secondary to cardiac failure and two cases parotid swellings. One case with proptosis and one case had nasopharyngeal mass hanging down to oropharynx.

Presenting symptom was abdominal pain in two cases, another case presented with back pain and one had fracture vertebra with gibbus deformity at D_{12}. One case had presented with a swelling in the axilla and one with marked hepatomegaly and pedal oedema. Two cases had jaundice at presentation.

A total of 10 children with acute myeloid leukemia were included in our series.one child was an infant;three children in the age group 2-9years, and six cases were above 9 years.

Out of ten, six patients were males and four females(1.5:1)

Pallor was the most common presentation (100%).Fever was there in 90% of them.Bone pain and arthralgia was a major symptom in 3 of them (30%) Four patints had bleeding manifestation at presentation.(40%). significant lymphadenopathy was observed in two cases and gum hypertrophy in one case.Six patients had splenomegaly and seven patients hepatomegaly.(60% and 70% respectively). 75% cases had hepatosplenomegaly. Two cases presented with congestive cardiac failure and two cases with non healing leg ulcer.

Table 6: AML FAB subtypes.

Sub type	No of cases	percentage
M2	7	70
M3	2	20
M6	1	10

There were two cases of juvenile CML. One case was a two month old infant and the other a four year old boy the table 7 summaries the details:

Table 7: Summary of CML patients.

Item	Case 1	Case2
Age	2 months	4 years
Sex	male	male
symptoms	Fever Abdominal distension	Fever cough
signs	Pallor Lymphadenopathy Jaundice Petechiae hepatosplenomegaly	Pallor Lymphadenopathy hepatosplenomegaly

Discussion

Acute leukemia is the most common cause of childhood malignancy. Among leukemias, acute lymphoblastic leukemia is the most common one, which accounts for three-fourth of all newly diagnosed leukemias and one fourth of all cancers.

Out of a total of 102 children with leukemia, enrolled in our study, acute lymphoblastic leukemia[ALL]accounts for 88% followed by acute myeloid leukemia{AML] and chronic myeloid leukemia{CML]10% and 2% respectively, which is comparable to global statistics ie,75-80% being ALL,15-20% AML ,and 2-3% CML[2..]

Out of 10 cases of acute myeloid leukemia ,seven cases belonged to AML-M2,two cases to M3 and one case to M6.

The prevalence of leukemia in patients under 15 years of age increases rapidly after birth and peaks before 5 years of age. This early peak is due to ALL, most evident between 3 and 5 years of age. This peak does not occur uniformly throughout the world ,being absent in Africa and developing countries.[6] our study showed a peak in the age of 2-5 years out of 90 cases of ALL 42 were in the age group 2-5byears.A study in middle east by Hussain J Al Mukharraq,also showed a similar peak[7.]

In contrast to ALL, the incidence of AML is quite constant from birth throughout the first 10 years. There is a slight peak in adolescence. In our study, 6 out of 10 cases of AML,was above the age of 9 years which is comparable to global statistics.

ALL occurs more often in males than in females' is also an important prognostic factor.Our study also shows this male preponderance, with a male: female ratio of 1.72:1 compared to sex ratio of patients in United states which is 1.2:1.Thus we are having higher

number of male patients. As the male sex carries a worse prognosis[8],it affects the final outcome of our patients adversely. Regarding AML,our study revealed a M:F ratio of 1.5:1,literature shows no predilection, which may be insignificant due to small sample size.

Parents have a vital role in the management of children with leukemias. Parental ideas of childhood leukemias, attitudes towards treatment, understanding of information and instructions especially about aseptic precautions to be taken while handling these immunocompromised children; all these are related educational status. Socioeconomic status also has a significant impact on the management and outcome of these as many of them may not be able to buy the costly medicines which is not always freely available in our set up and it involves bringing children on fixed dates and prolonged hospital stay for weeks to months involves financial outlay on food transport and accommodation and loss of day wages. Further it has also reflected in the nutritional status of our children,61% had undernutrition decreasing their tolerance to chemotherapy.

In our study,51% of mothers had formal education only up to primary level. MacDuoudall et all studied the compliance with chemotherapy in childhood leukemia in Africa,by comparing black families with white families. The black families had a lower socioeconomic and educational status. The authors concluded that the reason for the lack of compliance among the black parents was that, many did not appear to understand the nature of the illness or the aims of the therapy. In particular, the need to continue medication, when the child was in remission and appeared to be well ,was not readily understood.[9]

80% of fathers in our study was manual labourers, without any fixed job or consistent income. The study by MacDougall et all also noted that bringing a well-child to a hospital on a specified day did not rank as a high priority ,when it involved financial outlay or loss of days wages. This study reaffirms what has long been known by medical sociologists; the successful administration of modern medical therapy is highly dependent on the socioeconomic milieu in which it is attempted.[9]

Pallor and fever were the most common presenting complaints in our study; present in 91% and 84% respectively. Western literature gives occurrence of pallor in 80% and fever in 75% cases.[10] Limb pain and joint pain were present in 26% of ALL and 30% of AML in our study. This is close to the figures available in western literature that gives a frequency of bone pain in 23%.Bleeding manifestation either from the skin or mucous membrane occurred in 40% of ALL and 40% of AML in our study. Literature has given variable data from 30% to 65% occurrence of this symptom.[10,11]

In our study, generalized lymphadenopathy was observed in 47% of cases of ALL and 20%of AML. Similar studies have documented lymphadenopathy in 50% of cases, which is comparable to our series

Among our ALL patients.83% had splenomegaly and 81% hepatomegaly. It was 60% and 70% respectively in case of AML. The study by Reginald et al showed splenomegaly in 73% and hepatomegaly in69%.Both these data are identical[10.]17% of our patients did not have any enlargement of spleen and 20% of them had either the liver or spleen but not both[12]..It is comparable to the data available from literature which shows a 30% of patients without enlargement of spleen and 25% without the spleen or liver but not both. This stresses the need for general practitioner, to keep in mind the possibility of leukemia even in cases without hepatosplenomegaly.

Leukemic cell burden as measured by initial white cell count, degree of adenopathy and degree of hepatosplemegaly used to be an important determinant of prognosis.[11].Marked hepatomegaly was seen in 3 cases and marked splenomegaly in one case, both poor prognostic factors. Central nervous system involvement at presentation is a bad prognostic featue. Infants and older children with large leukemic cell burden are particularly at risk. In our study, two cases had overt CNS symptoms and signs representing 3% of cases. This figure is comparable to literature data that shows CNS involvement at presentation as <5%.[10,,13]Testicular involvement at presentation is very rare,even though occult testicular involvement can occur in 10-30%.One child had testicular involvement clinically at presentation in our series.

A significant percentage of leukemic children can have rare manifestations which include swelling of parotid glands, symptoms secondary to nasopharyngeal tumours, ulceration of mouth, proptosis, cranial nerve palsies, skin infiltration, dyspnea, rectal bleeding. Very rarely a gouty toe, backache, swellings involving vulva or bone, hemiplegia or priapism can be the presenting problem. Reginald et al in his series of 100 cases observed dyspnea in 5 cases, backache in 5 cases, swelling of vulva and parotid gland in one case each. In three cases there was proptosis.[10]

In our series, four children presented with dyspnea secondary to anemia and consequent cardiac failure. Other causes of dyspnea in leukemia at presentation can be due mediastinal mass of thymic or lymph node enlargement. Two children had parotid swellings. Abdominal pain was the presenting symptom in two cases and another case presented with back pain alone. Another child presented gibbus deformity of thoracic vertebra due to fracture. Western literature also describes similar finding, like anterior wedging and progressive collapse of vertebral bodies.[10]Two cases of AML in our series presented with a non healing ulcer one of them to the dermatology department initially. One child had proptosis and another had nasopharyngeal mass hanging down to oropharynx. One child had presented with a swelling in the axilla and another with marked hepatomegaly and pedal oedema.

Two children in our series had jaundice at presentation. Bogg's et al in their series of 322 cases has noted jaundice as an unusual observation[14]

Conclusions

Our study confirmed the percentage distribution of childhood leukemia as similar to global statistics so also the age distribution. But there was male female ratio was higher in our population of ALL.

Clinical presentation was almost similar in our series when compared to literature data, and we too had patients presenting with unusual manifestations.

Almost half of parents of children enrolled in our study had formal education up to primary level only and the other half up to secondary level that emphasizes the importance of health education and parental counseling especially in poor countries like India.

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