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Original Article

Clinical Presentation of Leukemia in Children

* Hasan ASMD[1], Mollah DH[2], Hossain MM[3], Aronee NS[4], Khandakar T[5]

Abstract

A thorough medical history, physical examination, and clinical presentation are crucial diagnostic processes for leukemia diagnosis. As a result, fatigue, irritability, and anorexia are common non-specific leukemia symptoms. Fever, pallor, lassitude, purpuric lesions, and bleeding are often the most common clinical observations and symptoms, which are usually indicators of the underlying thrombocytopenia, neutropenia, and anemia. This study aimed to evaluate the clinical presentation of leukemia in pediatric patients. This cross sectional study was conducted in the Department of Hemato-Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, for a period of 6 months from 1st September 2010 to 31st March 2011. A total of 80 diagnosed cases of leukemia among children aged 0 to 15 years who attended the study site were included in the study. The data were analyzed using the Statistical Package for the Social Sciences (SPSS), version 15. The most prevalent (58.8%) age group among the 80 patients was ≤5 years, followed by 30.0% and 11.2% in age group of 5-10 and >10 years respectively. Regarding sex, the male to female ratio was 1.67:1, consisting of 62.5% males. The most frequent clinical symptom observed was fever, occurring in 95.0% of cases, followed by progressive pallor at 43.8%. Other notable clinical presentations included bone pain, lymph node enlargement, and haemorrhagic symptoms, with frequencies of 31.3%, 38.8%, and 25.0%, respectively. Additionally, headache (3.8%), vomiting (3.8%), abdominal distention (16.3%), a history of sore throat (1.3%), weight loss (2.5%), anorexia (3.8%), weakness (2.5%), and proptosis (1.3%) were also reported as presenting complaints. The presence of fever, which is then succeeded by increasing pallor, could be essential in the diagnostic procedures for leukemia.

*1 Dr. A.S.M. Didarul Hasan, Assistant Professor, Department of Paediatrics, US-Bangla Medical College, Dhaka. E-mail: drdidar77@gmail.com.
2 Dr. Delwar Hossain Mollah, Professor, Department of Paediatrics, US-Bangla Medical College, Dhaka.
3 Dr. Md. Musharraf Hossain, Registrar, Department of Paediatrics, Netrokona District Hospital, Netrokona.
4 Dr. Nusrat Sharmin Aronee, Medical Officer, Labaid Cardiac Hospital, Dhanmondi, Dhaka.
5 Dr. Tanjina Khandakar, Registrar, Labaid Cardiac Hospital, Dhanmondi, Dhaka.
* For correspondence

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INTRODUCTION

Leukemia is the most frequent malignancy that occurs during childhood and comprises approximately 30% of all childhood cancers.[1] ALL represents about 75% of all leukemia cases in children.[2] Acute lymphocytic leukemia (ALL) is a disorder characterized by the uncontrolled growth and proliferation of immature lymphoid cells. It is the most common malignancy of childhood. The dramatic advances in its treatment over the past three decades have changed what was essentially a universally fatal but current long-term event-free survival rates are nearly 80%.[3] Many initial clinical manifestations of leukemia (eg, pallor, fever, purpura) are a consequence of decreased production of normal red blood cells, white blood cells, and platelets.[1] The presenting signs and symptoms reflect the degree of bone marrow infiltration with leukemic cells and the extent of extramedullary disease spread.

Leukemia generally presents with non-specific signs and symptoms, including anorexia, fatigue, and irritability. The most common symptoms and clinical findings are usually indicative of the underlying anemia, thrombocytopenia, and neutropenia. Fever, pallor, lassitude, purpuric lesions, and bleeding are frequently observed. As the condition progresses, symptoms such as pallor, a tendency to bleed, hepatosplenomegaly, and localized or generalized lymphadenopathy may arise. Central nervous system symptoms, which signify extramedullary leukemic spread, may also be accompanied by bedsores, vomiting, papilledema, sixth nerve palsy, cranial nerve palsies, and convulsions. However, it is rare for joint pain, proptosis, abdominal pain, melena, diarrhea, dysphagia, etc., to be recognized as initial manifestations, which can confuse both clinicians and pathologists[4]. Mostly, children present with pallor, bleeding manifestations, and hepato-splenomegaly. However, there are instances when the manifestations can be atypical, complicating the attribution to leukemia[2].

Historically, leukemia was classified initially in four groups based on clinical presentation and morphologic appearance of the malignant cells: ALL, acute nonlymphocytic leukemia (ANLL), chronic myelogenous leukemia (CML) and chronic lymphocytic leukemia (CLL). Subsequent research investigations which evaluated the morphologic, immunologic, growth regulation, cytogenetic and molecular abnormalities in leukemia cells, further established that the leukemia represent a much more heterogeneous group of malignancies than initially suggested by the four-group classification. However, the designations of the initial classification still are used clinically and it remains useful to consider how the classification pertains to childhood leukemia.[1]

Results of various investigations are decisive for the diagnosis of leukemia. However, a thorough history taking and physical examination are valuable tools in the diagnosis of any disease. Hence, one should remember both the common as well as uncommon signs and symptoms of leukemia for rapid and appropriate diagnosis and management. The objective of this research was to determine the clinical manifestations of leukemia in pediatric patients.

MATERIALS AND METHODS:

This descriptive study, which was cross-sectional in nature, involved 80 diagnosed cases of leukemia in children aged 0-15 years, regardless of sex, and was carried out in the Department of Paediatric Hemato-Oncology at Bangabandhu Sheikh Mujib Medical University (BSMMU) in Dhaka from September 1, 2010, to March 31, 2011. Children who were critically ill and required ICU support were excluded from the study, and a purposive sampling technique was employed to select the participants. In consultation with the parents or legal guardians and after reviewing previously published literature, a questionnaire was devloped for the study. Before data collection commenced, the parents of the children were informed about the study's purpose, and their informed written consent was obtained. Subsequently, the data clinical presentations of the leukemic children were recorded and evaluated.

Statistical analysis:

A window-based computer program called Statistical Packages for Social Sciences (SPSS-15) (SPSS Inc., Chicago, IL, USA) was used to perform statistical analysis on the data. Frequencies were distributed for each of the variables as shown in the tabular and graphical results of the data analysis.

Ethical consideration

Prior to initiate this study, the research protocol was approved by the ethical committee of the Bangladesh College of Physicians and Surgeons in Dhaka. The study's aims, objectives, procedures, alternative methods, risks, and benefits were communicated to the patient's parent/ legal guardian in a clear and comprehensible local language. Subsequently, written informed consent was obtained from the patients or their parents. It was guaranteed that all information and records would remain confidential, and the procedure would assist both attending physicians and patients in making management decisions.

RESULTS:

Table I provides an overview of the age distribution among the patients. Mean age ± SD was 5.78 ± 3.37 years and age range was 1.5 to 14.00 years. From the total of 80 patients, 47 (58.8%) belonged to the age group of ≤5 years, 24 (30.0%) were in the 5 to 10 years, and 9 (11.2%) were in >10 years of age group.

Table- I: Age distribution of the patients (n=80).

Age (in year)	Frequency	Percentage
≤5	47	58.8%
5-10	24	30.0%
>10	09	11.3%
Total	**80**	**100.0%**

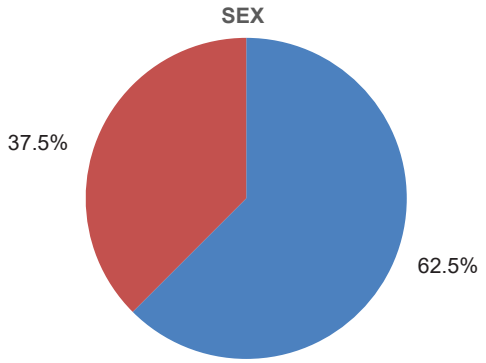

Figure- 1: *Distribution of sex of the patients (n= 80)*

Figure 1 illustrates the sex distribution of 80 patients, with 50 (62.5%) were male and 30 (37.5%) were female, and male-to-female ratio was 1.67:1.

Table II details the distribution of patients who came forward with complaints. Among these individuals, fever was noticed in 76 cases (95.0%), followed by progressive pallor in 35 (43.8%), bone pain in 25 (31.3%), lymph node enlargement in 31 (38.8%), and haemorrhagic manifestations in 20 (25.0%). Furthermore, abdominal distention was reported in 13 patients (16.3%), headache in 3 (3.8%), vomiting in 3 (3.8%), a history of sore throat in 1 (1.3%), weight loss in 2 (2.5%), anorexia in 3 (3.8%), weakness in 2 (2.5%), and proptosis in 1 (1.3%) as presenting complaints.

Table-II: Distribution of patients presented with complaints (n=80).

Presenting complaints	Frequency*	Percent
Fever	76	95.0
Progressive Pallor	35	43.8
Haemorrhagic manifestations	20	25.0
Abdominal distention	13	16.3
Headache	03	03.8
Vomiting	03	03.8
Sore throat	01	01.3
Bone/Joint pain	25	31.3
Lymph node enlargement	31	38.8
Weight loss	02	02.5
Anorexia	03	03.8
Weakness	02	02.5
Proptosis	01	01.3

*Multiple responses

Table III states the distribution of findings from the physical examination. Among the patients, pallor was observed in 62 individuals (77.5%), followed closely by hepatomegaly in 61 patients (76.3%). Additional findings from the physical examination included lymphadenopathy in 44 patients (55.0%), splenomegaly also in 44 patients (55.0%), bony tenderness in 29 patients (36.3%), and petechiae, purpura, or bruises in 21 patients (26.3%). Proptosis and abnormalities in the respiratory system examination were noted in 1 patient (1.3%) each.

Table- III: Distribution of the findings of physical examination

Physical examination	Frequency	Percent
Pallor	62	77.5
Petechiae, purpura, bruises	21	26.3
Lymphadenopathy	44	55.0
Bony/Joint tenderness	29	36.3
Hepatomegaly	61	76.3
Splenomegaly	44	55.0
Any abnormalities in respiratory system examination	01	01.3
Proptosis	01	01.3

Table IV presents the distribution of results from laboratory tests. The Mean±SD values for Neutrophil (N) and Lymphocyte (L) counts were found to be 10.79±7.47% and 35.16±28.89%, respectively. The Mean±SD for blast cell count was 54.54±30.46%, with a range of 5.00- 100.00cmm. The Mean±SD for platelet count was 25556.25 ±19691.84/cmm, with a range of 3000.00- 90000.00/cmm.

Table- IV: Distribution of results from laboratory tests (DC of WBC and Platelet count)

	Mean ± SD	Range
N	10.79±7.47	.00-40.00
L	35.16±28.89	.00-100.00
Blast cell	54.54±30.46	5.00-100.00
Platelet count	25556.25±19691.84	3000.00-90000.00

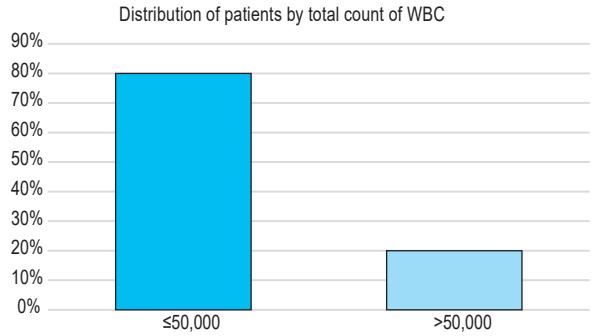

Figure- 2: Distribution of patients based on the total white blood cell (WBC) count.

Figure 2 depicts the distribution of patients based on the total white blood cell (WBC) count. Among the 80 patients, 64 (80.0%) exhibited a total WBC count of ≤

50,000/cmm, while 16 (20.0%) had a total WBC count ≤ 50,000/cmm. The mean ± standard deviation (SD) of the total WBC count was 32052.96 ± 34085.35/cmm, with a range spanning from 2100.00 to 258640.00/cmm.

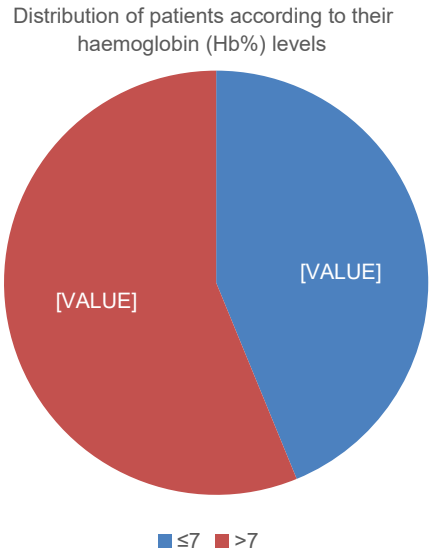

Figure-3: Distribution of patients according to their haemoglobin levels

Figure 3 illustrates the distribution of patients based on their haemoglobin (Hb) levels. Among the 80 patients, 35 (43.8%) exhibited a Hb level of ≤7 gm/dl, while 45 (56.2%) had a Hb level exceeding 7 gm/dl. The mean ± SD for the haemoglobin level was 7.48 ± 2.65 gm/dl, with a range of 2.80 - 17.80 gm/dl.

Table V details the distribution of diagnoses for the patients. Of the 80 respondents, 73 (91.2%) were diagnosed with Acute Lymphoblastic Leukemia (ALL), whereas 7 (8.8%) were diagnosed with Acute Myeloid Leukemia (AML).

Table- V: Distribution of diagnosis of the patients

Diagnosis	Frequency	Percent
ALL	73	91.2
AML	07	08.8
Total	80	100.0

DISCUSSION:

Out of 80 patients, most common age group was <=5 years (58.8%) followed by 5 to 10 years (30.0%). Rest of the patients was > 10 years old (11.2%) (Table 1). The incidence of acute lymphoblastic leukemia peaks in children aged 2-5 years and subsequently decreases with age.[5] Among the patients 50 (62.5%) were male and 30 (37.5%) were female. Male to female ratio was 1.67: 1. Acute lymphoblastic leukemia occurs slightly more frequently in boys than in girls.[5]

Fever is the most common clinical presentation (95.0%) followed by progressive pallor (43.8%). Other common clinical presentation bone pain, lymph node enlargement and haemorrhagic manifestations were 31.3%, 38.8% and 25.0% respectively. Abdominal distention (16.3%), headache (3.8%), vomiting (3.8%), sore throat (1.3%), weight loss (2.5%), anorexia (3.8%), weakness (2.5%), and proptosis (1.3%) also found the as presenting complaints (Table 2). Leukaemia is a systemic disease and involves all organs and tissues of the body.[6] Common constitutional symptoms include fever (60%), fatigue (50%), pallor (25%), and weight loss (26%).[6,7]

The clinical presentation of acute leukemias is quite variable.[8] Children with ALL develop symptoms related to infiltration of blasts in the bone marrow, lymphoid system, and extramedullary sites, such as the central nervous system (CNS).[7] Infiltration of blast cells in the marrow cavity and periosteum often lead to bone pain (23%) and disruption of normal hematopoiesis.[7] Infiltration of the lymphoid system may cause lymphadenopathy and hepatosplenomegaly. CNS involvement is found in less than 5% of children at presentation. When present, the signs and symptoms include headache, vomiting, papilledema and sixth- nerve palsy.[9–11]

Thrombocytopenia with platelet counts less than 100,000 are seen in about 75% of patients. Approximately 40% of patients with childhood ALL present with hemoglobin levels less than 7 g/dL.[7] In the present study the mean ± SD of nutrophil and lymphocyte count were 10.79 ± 7.47% and 35.16 ± 28.89% respectively. Mean ± SD of blast cell was 54.54 ± 30.46 with a range of 5.00-100.00%. Mean ± SD of platelet count was 25556.25 ± 19691.84 with a range of 3000.00-90000.00/cmm (Table 6). In the present study 35 (43.8%) had haemoglobin level ≤7 gm/dl and 45 (56.2%) had haemoglobin level >7 gm/dl. Mean ± SD of haemoglobin level was 7.48 ± 2.65 with a range of 2.80-17.80 gm/dl (Table 7). Bashir et al. (2010) studied to assess the hematological and clinical presentation where they found all patients were anemic at the time of diagnosis their hemoglobin level was 2.8 -12 g /dl. The TLC was quite variable ranged from <4000/cmm to >6,30,000/mm3. Similarly the platelet count was <10,000 to >100000/mm.[8]

Although leukocyte counts greater than 50,000/mm^3 occur in 20% of cases, neutropenia defined as an absolute neutrophil count less than 500 is common at presentation and is associated with an increased risk of infection.[12, 13] Sixty four (80.0%) patients had total count of WBC ≤ 50,000 cmm and 16 (20.0%) had total count of WBC >50,000 cmm. Mean ± SD of total count of WBC was32052.96 ± 34085.35 with a range of 2100.00-258640.00.

In the present study 73 (91.2%) were diagnosed as cases of ALL and 7 (8.8%) were diagnosed as cases of AML. Study showed that in children, acute lymphoblastic leukemia (ALL) is significantly more prevalent than acute myeloid leukemia (AML). ALL accounts for approximately 80% of childhood leukemia cases, while AML represents about 15-20%.[14]

CONCLUSIONS:

In the study, fever is identified as the predominant clinical manifestation, succeeded by progressive pallor. Additional prevalent clinical presentations included bone pain, lymphadenopathy, and hemorrhagic symptoms. Furthermore, patients exhibited vomiting, petechiae, abdominal swelling, sore throat, joint discomfort, fatigue, loss of appetite, and weight reduction.

LIMITATIONS

The present study has some limitations. The study conducted in a single centre in Dhaka city on small sample size which may not be representative for the whole country.

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