

Clinico-Demographic Profile and Hematological Pictures of Childhood Leukemia in a Tertiary Care Hospital

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Background: Leukemia is the most common childhood malignancy worldwide. It accounts for approximately 35-40% of all cancers under the age of 15 years.

Objectives: The aim of the study was to evaluate the clinico-demographic profiles and hematological pictures of childhood leukemia in a tertiary care hospital.

Methods: This cross-sectional study was conducted at Hematology and Oncology unit of department of Pediatrics of Rangpur Medical College Hospital, Rangpur from October, 2016 to June, 2018. After parental permission and ethical clearance, total 50 hospitalized patients, age between 1-12 years, clinically suspected as leukaemia were selected for the study. Hematological picture and morphological study of bone marrow aspirates were done for each patients. Among them, 37 cases with positive blood picture and bone marrow aspirates of leukemia were finally enrolled into this study.

Results: Analysis revealed that out of all leukemia cases, acute lymphoblastic leukemia(ALL) was the predominant type, 30 (81%) patients and chronic myeloid leukemia(CML) being the lowest, 2 (5.40%) cases. Children belonging to age group 1-10 years were highest, 25 (67.56%) in number. Male patients(23) outnumbered female(14). Out of eight districts of Rangpur Division, most leukemic patients, 11(29.73%) hailed from Rangpur District. Among most frequent clinical parameters, fever was present in 37(100%) cases, pallor, 36(97.29%), hepatomegaly, 24(64.86%), splenomegaly, 21(56.75%), both hepatosplenomegaly, 15(40.54%), lymphadenopathy, 25(67.56%), bony tenderness, 12(32.43%), bleeding manifestation, 08(21.62%), bone pain, 04(10.81%) and bodyache in 03(8.10%) patients. Hematological pictures revealed, Hb% <7 gm/dl in 22 (59.45%) cases, WBC count(<50000/cmm) in 18(48.64%) ALL cases and in 05(13.51%) AML cases. WBC count (>50000/cmm) was found in 12(32.43%) cases of ALL and in 02(5.40%) CML cases, p<0.041. Platelet count was <20000/cmm found in 10(27.02%) and blast cell(>25%) in 35 (94.59%) cases. Low platelet count was statistically significant (p < 0.001).

Conclusion: This study concluded that ALL was the predominant type of childhood leukemia and male patients belonging to age between 1-10 years suffered more than female. In all cases, fever was present, pallor being the next common clinical sign. Thrombocytopenia, leucopenia and significant blast cell in bone marrow were found in most of the leukemia cases.

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Key words : Children, Leukemia, Clinical profile, Haematological picture

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Introduction

Leukemia is the most common malignancy of children worldwide.^{1,2,3} The expected incidence of cancer under 15 years of age is 110-150/1,000,000 children a year.⁴ It accounts for approximately 35-40% of all cancers under the age of 15 years. It is the most common childhood malignancy (28%) in Bangladesh.⁵ The proportion of leukaemias varies across different countries ranging from 27 to 35%. In US, for instance, leukaemias account for 31% of all pediatric cancers, while it is approximately 37% in Kolkata, a neighboring Indian state and nearly 26% in Pakistan with similar culture and socioeconomic status to Bangladesh.⁵ Leukemia is a clonal disease of bone marrow stem cell (originating in a single cell) and evolves by the accrual of mutations within a clone. This results in progressive genetic diversification followed by a “natural selection” of dominant mutant subclones.⁶ It has been recognized that childhood leukaemia is not one homogeneous disease. The major morphological classification into acute lymphoblastic leukaemia (ALL), acute myeloblastic leukaemia (AML) and chronic myeloid leukemia (CML) is supplemented by the identification of a range of subsets based on gene expression, antigens that delineate cell type or differentiation status and chromosomal and molecular abnormalities.⁶ The early presentation of pediatric leukaemia, with non-specific symptoms often mimicking the common, self-limiting illnesses, complicates the diagnostic challenges faced by frontline clinicians.^{7,8} In general, diagnosis should be suspected in any child with anemia not associated with bleeding, fever associated or not with pallor, visceromegaly and CBC with anemia and or neutropenia (sometimes leukocytosis), bone pain not associated with trauma, and CBC with cytopenias.⁴ ALL is defined by the presence of more than 20% lymphoblasts in bone marrow.^{9,10} It represents the most common type of leukemia in childhood, accounting for 80% of all leukemia

cases. It predominates in men and occurs most often between the ages of 2 and 5 years.^{10,11} AML represents 17% of all types of leukemia.⁹ Occurrence of AML is similar in both sexes with no predominance for any given age range.¹¹

Methods

This cross-sectional study was conducted at Hematology and Oncology unit of department of Pediatrics of Rangpur Medical College Hospital, Rangpur from October, 2016 to June, 2018. Initially, 50 cases, 1-12 years of age of both sex, admitted as clinically suspected leukaemia were selected for the study. Blood picture and morphological study of bone marrow aspirates was done for every patients. Positive blood picture and bone marrow aspirates of leukemia was positive in 37 cases who were finally enrolled into this study. Informed written consent was obtained from parents after explaining the purpose of the study. Clinical details including age, sex, duration of illness, address, associated clinical conditions, concomitant illness, blood pictures, morphological picture of bone marrow aspirates were recorded on a standard questionnaire. Data were collected and enrolled into Microsoft Excel Software that were later analyzed using SPSS version 21.0. Appropriate statistical tests i.e. percentage calculation, Chi-square test and One Way ANOVA test were performed and significant was set at $p < 0.05$.

Result

During 21 months of study period, total 37 cases of childhood leukaemia were enrolled into the study. Among them, highest, 25 (67.56%) cases belonged to 1-10 years of age group (Table I). Male patients (23) outnumbered female (14) (Figure I). ALL was the predominant type, 30 (81%) cases (Figure II). Out of 8 districts of Rangpur division, majority of leukaemic patients, 11 (29.73%) hailed from Rangpur district (Figure III). Among different clinical parameters, fever was

present in 37 (100%) cases, pallor, 36(97.29%), hepatomegaly, 24(64.86%), splenomegaly, 21(56.75%), both hepatosplenomegaly, 15(40.54%) and lymphadenopathy in 25(67.56%) cases (Table II). Among haematological picture, low platelet count (<20000/cmm) was significant, p< 0.001 (Table III). Hb% (<7 gm/dl) was found in

22(59.45%) leukemia cases. WBC count(>50000/cmm) in 12(40%) ALL and 2(100%) CML cases, WBC count, (<50000/cmm) in 18(60%) ALL and 5(100%) AML cases, p<0.041 (Table IV), platelet count (<20000/cmm) in 27.02% cases and blast cell(>25%) in 94.59% cases (Table V).

Table I: Distribution of leukemia cases according to age(n=37)

Age(Years)	Types of Leukaemia			p
	ALL	AML	CML	
<1	03	01	00	0.609 (NS)
1-10	20	01	01	
>10	07	00	01	

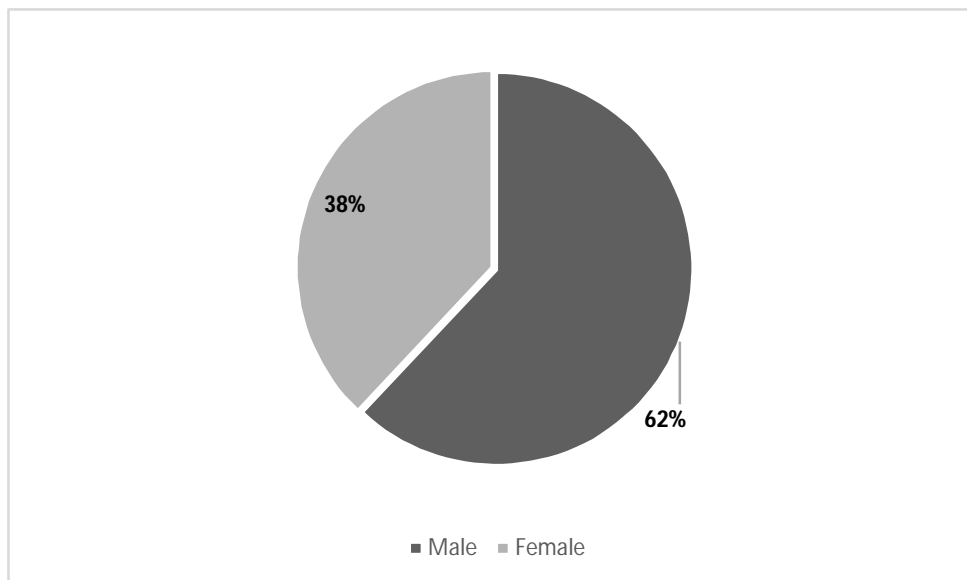


Figure 1. Distribution of leukemia cases according to sex

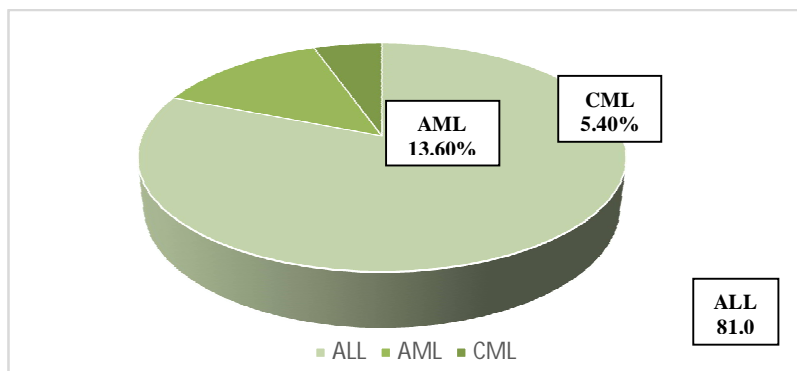


Figure 2. Diifferent types of leukaemia cases

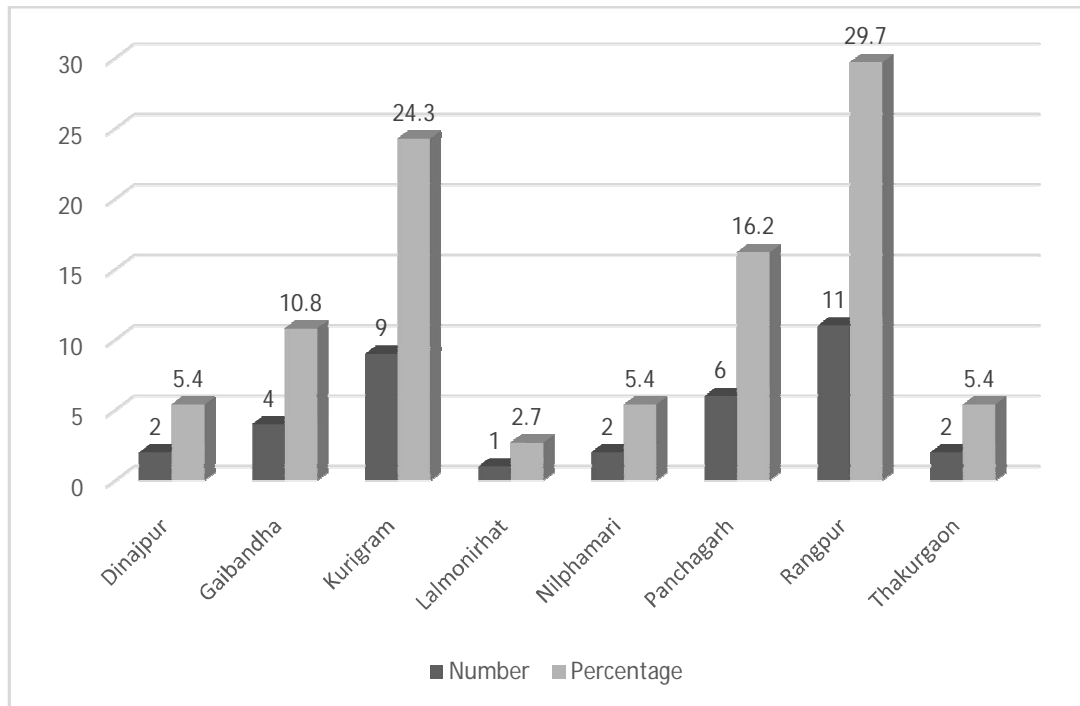


Figure 3. Geographical distribution of leukemia patients

Table II: Clinical parameters of different types of leukemia patients (n=37)

Parameters	Types of Leukaemia cases			Total
	ALL (30)	AML (05)	CML (02)	
Fever	30 (100%)	05 (100%)	02 (100%)	37 (100%)
Pallor	29 (96.66%)	05 (100%)	02 (100%)	36(97.29%)
Gum/ Mucosal bleeding	06 (20%)	00	00	06(16.22%)
Petechiae/ Echymosis	02 (6.66%)	00	00	02 (5.40%)
Bony tenderness	10 (33.33%)	02 (40%)	00	12(32.43%)
Bone pain	04 (13.33%)	00	00	04(10.81%)
Bodyache	03 (10%)	00	00	03 (8.10%)
Hepatomegaly	19 (63.33%)	04 (80%)	01 (50%)	24(64.86%)
Splenomegaly	16 (53.33%)	03 (60%)	02 (100%)	21(56.75%)
Hepatosplenomegaly	11 (36.66%)	03 (60% %)	01 (50%)	15(40.54%)
Lymphadenopathy	20 (66.66%)	40 (80%)	01 (50%)	25(67.56%)
Pleural effusion	01(3.33%)	00	00	01(2.7%)
Proptosis	00	01(20%)	00	01(2.7%)

Table III: Hematological pictures of different types of leukemia patients (n=37)

Parameter	Types of leukemia cases			p
	ALL (n=30) (Mean±SD)	AML(n=5) (Mean±SD)	CML(n=2) (Mean±SD)	
Hb	6.38±2.29	7.98±3.01	7.35±1.90	0.360
WBC	63470.00±84647.97	510100.00±1112449.01	390000.00±84852.81	0.051
Platelet	60866.66±69952.06	194200.00±266351.64	950000.00±311126.98	<0.001
Blast cells %	25.36±15.61	25.80±3.34	00	0.438

Univariate Analysis of Variance (One way ANOVA) test

Table IV: Distribution of different leukemia according to total WBC count (n=37)

Types of Leukemia	No of patient	Total count of WBC		p
		>50000/cmm	<50000/cmm	
ALL	30	12(40%)	18(60%)	0.041(s)
AML	05	0(0%)	05(100%)	
CML	02	02(100%)	0(0%)	

Table V: Highest and lowest levels of different hematological parameters and blast cell in leukemia (n=37)

Parameters	Number	Percentage (%)
Hb(<7gm/dl)	22	59.45
WBC(<50000/cmm)	23	62.16
(>50000/cmm)	14	37.83
Platelet(<20000/cmm)	10	27.02
Blast cells (>25% cases)	35	94.59

Discussion

This study was aimed to evaluate the clinical presentations, demographic profile and haematological picture of leukaemia in children aged 1-12 years .

In the current study, among three types of childhood leukemia, ALL, 30(81%) was the predominant type followed by AML, 5 (13.60%) and CML, 2 (5.40%) cases. Five ALL patients demonstrated FAB ALL L 2 variety and others were FAB ALL L1. Pearce J et al found in a study that ALL represents the most common type of leukemia in childhood, accounting for 80% of cases.¹¹ Hutter J et al showed AML representing 17% of all types of leukemia.⁹ Findings of the present study corroborate with the previous studies.

In current study, male, 23(62%) patients were predominant. Pearce J et al found in a study that male patients belonged to majority in ALL, the most common type of leukemia.¹¹

In present study, among different clinical manifestations, fever was present in 100% cases of all types of leukemia. Clarke RT found in a systematic review and meta- analysis that fever was present only in 53% cases.¹ The probable cause might be due to patients' inclusion in different stages of disease or chemotherapy.

In this study, pallor was present in 97.29% cases of all types of leukemia and among them, pallor was present in 96.66% cases of ALL, 100% of AML and 100% of CML cases. Clarke RT found in a meta- analysis that pallor was present in 54% patients of childhood leukemia.¹ The probable explanation of this discrepancy is attributed to patients' participation in initial stages of leukemia in the later study. Gum and mucosal bleeding were observed in 20% of ALL patients in this study. Clarke RT reported in an analysis that

bleeding tendency was present in 38% of leukemia cases.¹

In this study, hepatomegaly was present in 64.86% cases of all types of leukemia , in 63.33% of ALL , 80% of AML and in 50% of CML cases. Study conducted by Clarke RT also found in a meta-analysis that hepatomegaly was present in 64% cases of childhood leukemia.¹ Splenomegaly was present in 56.75% cases of all types of leukemia and in 53.33% of ALL, 60% of AML cases and in 100% of CML cases in this study. Clarke RT found in a meta-analysis that splenomegaly was present in 61% cases of leukemia.¹ Hepatosplenomegaly was observed in 40.54% cases of three types of leukemia and in 36.66% of ALL cases, 60% AML cases and in 50% of CML cases in this study. Similar observations were reported in a study revealing hepatosplenomegaly in 42% cases of childhood leukemia in a study done by Clarke RT.¹ In a study done by Bhattacharyya D et al in India found hepatosplenomegaly in 53.3% of ALL cases.¹² In another study, Aquino V et al found hepatosplenomegaly in about 50% of AML patients.¹³

In current study, lymphadenopathy, was present in 67.56% cases of all type of leukemia and in 66.66% of ALL cases, in 80% of AML cases and in 50% of CML cases. Doric M et al and Restrepo R et al found generalized lymphadenopathy in 29.5% children followed by cervical in 21.9%, and inguinal or axillar only in 0.8% of leukemia cases.^{14,15} In another similar study Maloney K et al showed that the involvement of cervical, axillary and or inguinal nodes up to 50% of patients with ALL but Aquino V et al found it only in 25% of patients with AML.^{10,13} Echymosis was found only in 2(6.66%) of ALL patients and absent in AML and CML patients in this study. Clarke RT found bruising and petechiae in 42% patients.¹ Bony tenderness was present in 33.33% of ALL cases, 40% of AML and absent in CML cases in this study but bone pain was

reported in only in 13.33% of ALL cases and absent in AML and CML patients. Clarke RT found bone pain in 26% cases of childhood leukemia in a study.¹ An estimated 30% of patients with ALL presented with bone pain in a study by Pearce J et al.¹¹ Body ache was found only in 10% ALL cases and not in other types of leukemia. Pleural effusion was found in 1 case of ALL and proptosis in 1 case of AML among uncommon presentations.

Regarding hematological pictures, Hb (<7 gm/dl) was observed in 59.45% of all cases of leukemia and platelet count (<20000/cmm) in 27.02% cases in current study. Alteration of platelet was statistically significant (p<0.001) among leukemia cases. Amanda Ibagy et al found Hb (<7 gm/dl) in 34.14% of ALL cases, Hb (>7 gm/dl) in 60.97% of ALL patients, platelets (<20000/cmm) in 4.87% of ALL cases and platelet counts (>20000/cmm) in 70.73% ALL patients¹⁶. Pearce J et al found anemia, thrombocytopenia or neutropenia with normal, decreased or increased WBC count in a study.¹¹ Blast cell > 25% was present in 94.59% cases of leukemia in this study. Doric M et al found blast cell >25% in 75% of leukemic patients in one study¹⁴. This finding is in concordance with the present study. In this study, initial WBC count was < 50000/cmm in 62.16% leukemic cases and >50000/cmm in 37.83% of patients. A similar study by de Sausa DWL reported initial WBC <50000/cmm in 74.5% of ALL cases and WBC >50000/cmm in 25.5% of ALL patients.¹⁷ This dissimilarity in findings in previous studies was probably due to inclusion of patients' of different subtypes and in different stages of leukemia.

Conclusion

This study concluded that ALL was the predominant type of childhood leukemia and male patients belonging to age between 1-10 years, suffered more than female. In all cases of acute leukaemia, fever was the most frequent clinical sign, pallor being the next common.

Thrombocytopenia, leucopenia and significant blast cells in bone marrow were found in majority of patients with acute leukemia.

Recommendation

This study implies and stresses the importance of early recognition of fever and pallor as an alarming symptom and sign of acute leukaemia in children. Additionally, it is of crucial importance to recognize the disease with simple haematological parameters to ensure good outcome and prevent initial complications. However, larger multicenter studies in large scale are needed to validate the data in Bangladesh perspective.

References

1. Clarke RT, Bruel AV, Bankhead C, Mitchell CD, Phillips B, Thompson MJ. Clinical presentation of childhood leukaemia: a systematic review and meta-analysis. *Arch Dis Child* 2016;101:894-901.
2. Mitchell C, Hall G, Clarke RT. Acute leukaemia in children: diagnosis and management. *BMJ* 2009; 338: 1491-95.
3. Metayer C, Dahl G, Wiemels J, Miller M. Childhood Leukemia: A Preventable Disease. *PEDIATRICS* 2016; 138(s1): s45-s55.
4. Viviana R S, Cristian G B. Imaging studies in early diagnosis of childhood leukemia. *Revista Chilena de Radiología* 2012; 18(1):24-29.
5. Hossain MS, Begum M, Mian MM, Ferdous S, Kabir S, Sarker HK. Epidemiology of childhood and adolescent cancer in Bangladesh, 2001–2014. *BMC Cancer* 2016; 16:104.
6. Greaves M. Science, medicine, and the future: Childhood leukaemia. *BMJ* 2002; 324: 283-87.
7. National Institute for Clinical Excellence. Improving outcomes in children and young people with cancer. 2005.
8. Dang-Tan T, Franco EL. Diagnosis delays in childhood cancer. *Cancer* 2007;110:703-

- 13.
9. Hutter J. Childhood Leukemia. *Pediatr Rev*. 2010; 31: 234-41.
10. Hay W, Levin M, Deterding R, Sondheimer J: Current Diagnosis and Treatment Pediatrics. 20th Edition, 2011, Lange publication, Neoplastic Disease, Chapter 29.
11. Pearce J, Sills R. Consultation with the specialist: childhood leukemia. *Pediatr Rev* 2005; 26: 96-104.
12. Bhattacharyya D, Das S, Sethy S, Singh SC, Mohanty R. Study of clinico-hematological and immunophenotypic profile in adult patients with Acute Lymphoblastic Leukemia in Eastern India. *Journal of Scientific Research & Reports*.x(x):XX-XX,2013; Article No. JSRR.2013.XXX. www.sciencedomain.org
13. Aquino V. Acute myelogenous leukemia. *Current Problems in Pediatric and Adolescent Health Care* 2002; 32: 50-8.
14. Doric M, Benovic N, Lazic J. Correlation between initial blood count and clinical parameters in children with acute lymphoblastic leukemia: *Medicinski Podmladak* June 2015; 66(1):58-64.
15. Restrepo R, Oneto J, Lopez K, Kukreja K. Head and neck lymph nodes in children: the spectrum from normal to abnormal. *Pediatr Radiol* 2009; 39: 836-46.
16. Ibagy A, Silva DB, Seiben J, Winneshoffer APFF, Costa TEJB, Dacoregio JS, Costa I, Faraco D. Acute lymphoblastic leukemia in infants: 20 years of experience. *J Pediatr (Rio J)*. 2013;89(1):64-69.
17. de Sousa DWL, de Almeida Ferreira FD, Felix FHC, de Oliveira Lope MV. Acute lymphoblastic leukemia in children and adolescent: prognostic factors and analysis of survival. *Rev Bras Hematol Hemotor*, 2015;37(4):223-29.