International Journal Dental and Medical Sciences Research
Volume 5, Issue 2, Mar - Apr 2023 pp 494-499 www.ijdmsrjournal.com ISSN: 2582-6018

Clinico-Hematological Profile of Acute Leukemias With Correlation To Karyotyping – A Case Series

Dr. Swarup Kar
Assistant professor, Department of Medicine, Jorhat medical college and Hospital, Jorhat, Assam Pin: 785001

Date of Submission: 16-03-2023 Date of Acceptance: 28-03-2023

ACKNOWLEDGEMENT:
I am thankful to my guide Lt. Professor R. K. Kotokey, Ex-principal of Assam Medical College and Hospital who helped and guided me in every step of this work.

ABSTRACT:
Leukemia isa common malignancy and commonest among below 15 years. Acute leukemias can be classified as Acute myeloidleukemia (AML) or Acute lymphoblastic leukemia (ALL) depending upon the cell types. AML incidence increases with age, whereas ALL is common in children and elderly. Cytogenetic abnormalities have been shown to be associated with clinical features as well as prognosis in acute leukemias. In our part of Northeast India there are fewer studies showing the correlation of karyotyping withclinico-hematological profile of acute leukemias. This study was conductedamong sixteen (16) patients of acute leukemias; eleven (11) AML patients and four (4) ALL patients over a period of one year.Two out of sixteen patients were found to have abnormal karyotypes, both were AML patients.Clinical and hematological findings of thepatients were correlated with their karyotypes.

KEY WORDS:
Leukemia,AcuteMyeloid Leukemia (AML), Acute Lymphoblastic Leukemia (ALL), Karyotyping

I. INTRODUCTION:

Leukemia is caused by mutation of the bone marrow pluripotent stem cells. The neoplastic expansion results in abnormal leukemic cells and impaired production of red blood cells, neutrophils, and platelets. Among patients less than 15 years, leukemia is the most common malignancy.[1]

On the basis of cell maturity leukemias can be classified into acute or chronic. When blasts or immature cells predominate it is termed as acute, whereas predominance of mature cells is termed as chronic. Acute leukemias can be classified as Acute Myeloid Leukemia (AML) or Acute Lymphoblastic Leukemia (ALL) depending on the cell type.Annual incidence of acute leukemias in the general population is about 4 per 100,000.[2] ALL is approximately five times commoner than AML.[1] Incidence of AML increases with age whereas ALL is primarily a disease of children with a second peak in elderly.[3]

Several studies have confirmed the association between various cytogenetic abnormalities, clinical pattern and prognosis in acute leukemias. Cytogenetics or Karyotyping is the most powerful single indicator of outcome in acute leukemias. There are fewer studies in this part showing the pattern of acute leukemias and their correlation with cytogenetic abnormalities. So this study was conducted to address the issue in this ethnic population.

II. MATERIALS AND METHODS:

The study was a hospital based and observational study, and carried out among 16 patients admitted in Medicine and Pediatrics department of Assam Medical College and Hospital, Dibrugarh, during a period of one year from 1st September 2009 to 31st August 2010.All patients above one year of age and patients diagnosed as AML or ALL in bone marrow analysis were included in the study. Patients below one year and blast crisis cases of CML were excluded. In each patient detailed history, clinical exanimation and investigations like complete blood count, peripheral blood smear, and bone marrow analysis were done. Karyotyping was done from specimens of bone marrow aspirate.

III. RESULTS AND OBSERVATIONS:

Out of the 16 cases, 11 were AML and 5 were ALL. Among AML patients, age

International Journal Dental and Medical Sciences Research
Volume 5, Issue 2, Mar - Apr 2023 pp 494-499 www.ijdmsrjournal.com ISSN: 2582-6018

ranged from 10 to 92 years (median 35 years), whereas ALL patients were from 5 to 45 years (median 14 years). Most of the patients with AML were female (n=8; 72.72%) and ALL were male (n=3; 60%).

The most common symptom in AML was fatigue and weakness which was present in all patients (n=11; 100%), followed by fever (n=9; 81.81%), bleeding manifestations (n=8; 72.72%), pain abdomen (n=6; 54.54%), cough (n=6; 54.54%), bone pain (n=5; 45.45%), visual disturbance (n=2; 18.18%), chest pain (n=1; 9.09%)and nausea/vomiting (n=1; 9.09%). In case of ALL the most common symptom was fever(n=5; 100%), fatigue and weakness (n=5; 100%), followed by bleeding manifestations (n=3, 60%), bone pain (n=3, 60%), cough (n=2; 40%), pain abdomen (n=2; 40%), nausea/vomiting (n=2; 40%) and visual disturbance (n=1; 20%).

AML patients had pallor (n=11; 100%), hepatomegaly (n=8; 72.72%), splenomegaly (n=7; 63.63%), lymphadenopathy, bone tenderness, skin and mucosal infiltration (n=5; 45.45% each), oedema (n=3; 27.27%), chloroma and icterus (n=1; 9.09% each). Among ALL patients common signs were pallor(n=5; 100%) and hepatomegaly (n=5; 100%),followed by lymphadenopathy (n=4; 80%), splenomegaly and bone tenderness (n=3; 60% each).

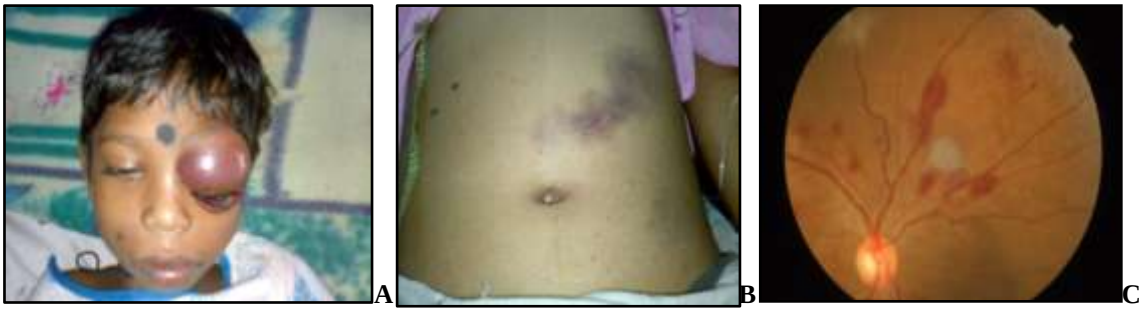

Fig. A) Case no. 15: Patient with AML-M2 with chloroma of left orbit
Fig. B) Case no. 10: ALL patient with echymosis and petechiae in the abdomen
Fig. C) Case no. 13: Fundus of patient with AML-M2 showing retinal haemorrhages

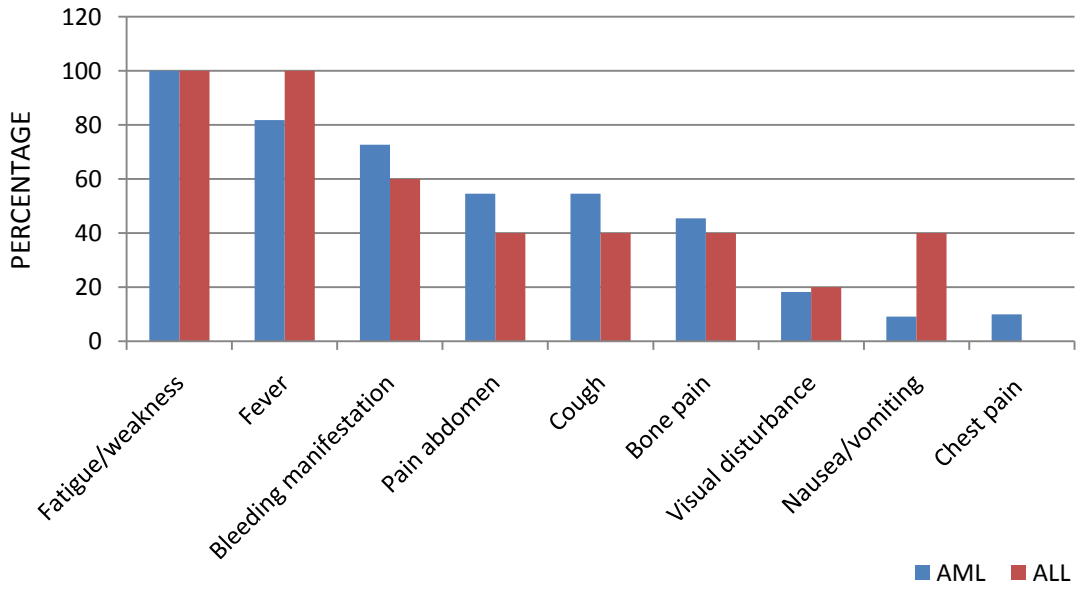

Fig. 1) SYMPTOMS OF ACUTE LEUKEMIAS

International Journal Dental and Medical Sciences Research
Volume 5, Issue 2, Mar - Apr 2023 pp 494-499 www.ijdmsrjournal.com ISSN: 2582-6018

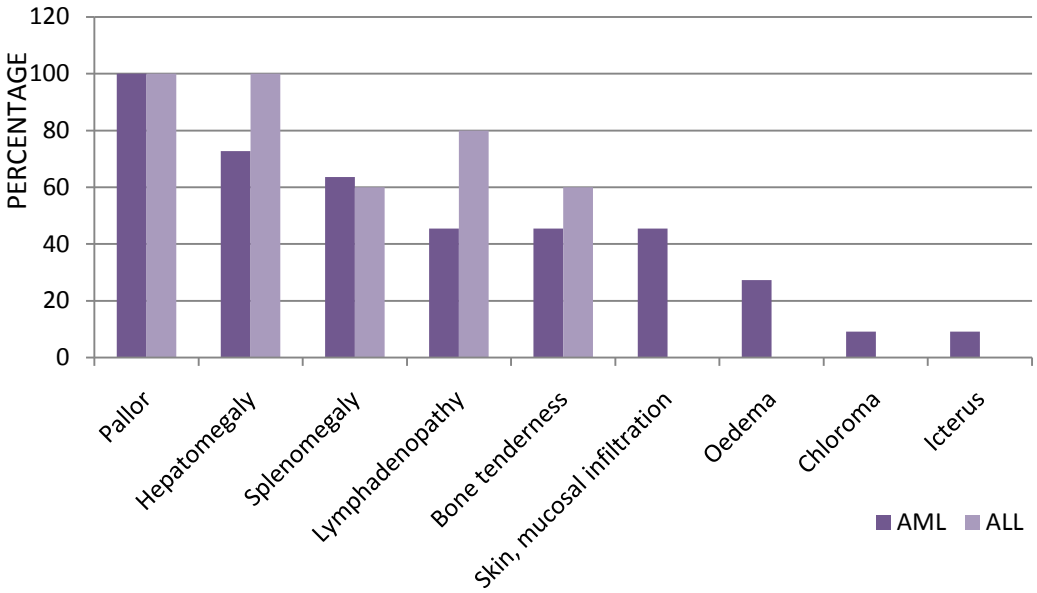

Fig. 2) SIGNS OF ACUTE LEUKEMIAS

The mean hemoglobin inAML was 5.05 g/dl and in ALL was 2.87 g/dl. The mean total count in AML was 91,681.8/mm^3,and in ALL was 67,240/mm^3. The mean platelet count in AML was 45,463.6/mm^3,and in ALL was 36,600/mm^3. The mean bone marrow blast count in case of AML was 81.63% where as it was 88% in case of ALL.

Out of 11 cases, abnormal karyotype was found in two (n=2; 18.18%) cases of AML. All other cases of AML and ALL were having normal karyotype. The abnormalities detected were:

(A) 47,XX,+8,add(17)(p13)[10]/48,XX,+8,add(17)(p13),+21[10]

(B) 46,XX,t(8;21)(q22;q22)[10]/Near tetraploidy>90 Chromosome[10]

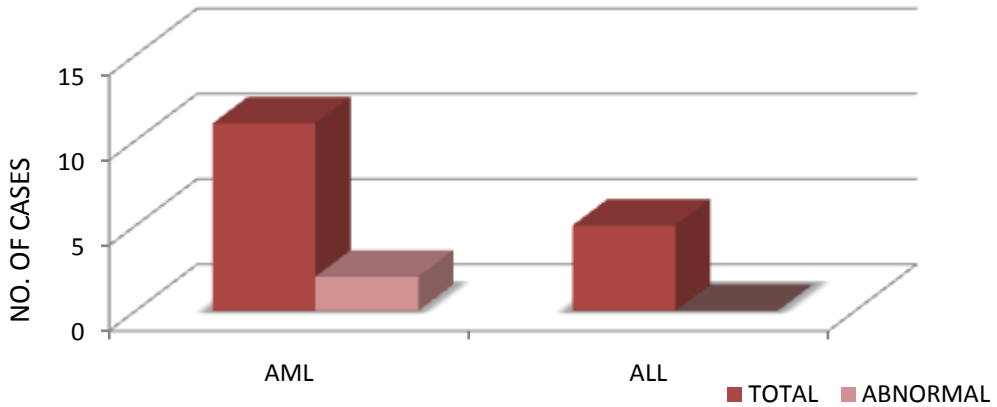

Fig. 3) ABNORMAL KARYOTYPE IN ACUTE LEUKEMIAS

The patient with 47,XX,+8,add(17)(p13)[10]/48,XX,+8,add(17)(p13),+21[10] abnormality was a 54 year old female who presented with fatigue, bone pain, pallor and bleeding manifestations. She was diagnosed as acute promyelocytic leukemia (AML–M3). Unlike other cases she was afebrile, did not have hepato-splenomegaly or lymphadenopathy. There was leucopenia and 57% bone marrow blasts. The patient with 46,XX,t(8;21)(q22;q22)[10]/Near tetraploidy>90 Chromosome[10] abnormality was a 10 year old female who presented with fever, fatigue, nausea-vomiting, pain abdomen , bleeding manifestations, pallor, hepatomegaly, chloroma of the eye and gum hypertrophy. Unlike other cases there was no splenomegaly, lymphadenopathy or

International Journal Dental and Medical Sciences Research
Volume 5, Issue 2, Mar - Apr 2023 pp 494-499 www.ijdmsrjournal.com ISSN: 2582-6018

bone tenderness. She was diagnosed as acute myeloid leukemia with maturation (AML-M2). The total count was 54,000/mm^3 and platelet count was only 5000/mm^3 with 53% bone marrow blasts.

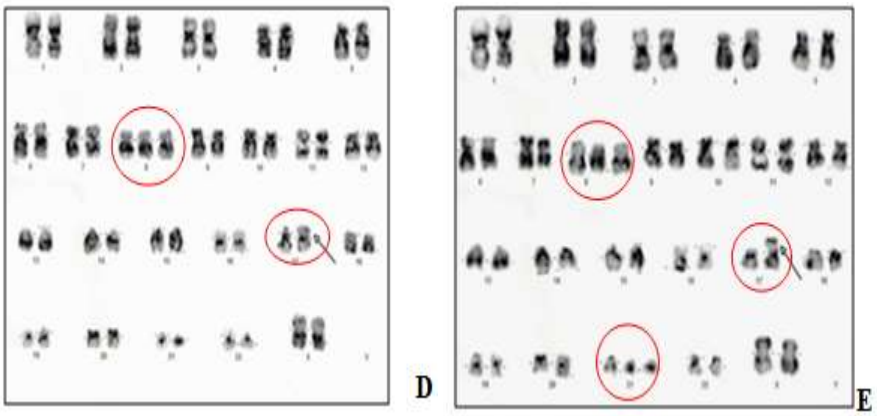

Fig. Dand E)Case no. 6: Karyogram showing:
47,XX,+8,add(17)(p13)[10]/48,XX,+8,add(17)(p13),+21[10]

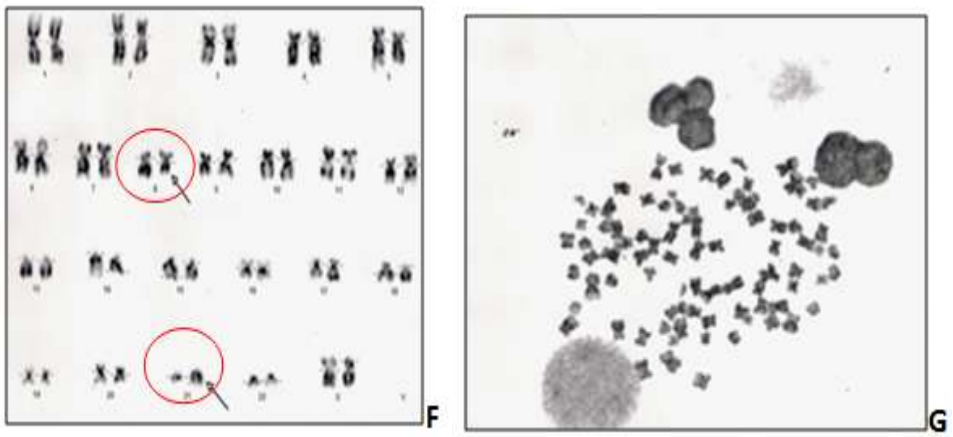

Fig. F and G)Case no. 15: Karyogram showing:
46,XX,t(8;21)(q22;q22)[10]/Near tetraploidy>90 Chromosome[10]

Out of 11 patients of AML five (n=5; 45.45%) expired and out of 5 patients of ALL two (n=2; 40%) expired.

IV. DISCUSSION:

In a retrospective study done by S. Ghosh et al, (2003) among 260 patients of AML it was found that the majority of the patients (82%) had generalized weakness and bleeding was present in 21.9% of patients.[4] In another study done by GG D'Costa et al, (1989) among the patients of acute leukemia, it was observed that fever was the commonest symptom, followed by weakness, bleeding and bone pain. Hepatomegaly was more common in AML.[5] Similarly present study shows that the constitutional symptoms are the prominent features of AML, but bleeding manifestations, hepato-splenomegaly and lymphadenopathy were found to be more. Tropical diseases and hemoglobinopathies are more common in this part of the country which may be a possible explanation.

In a study by M.F.N. Rego et al in Teresina (2003) it was found that in ALL fever was the most common clinical feature found in 59.56% cases, followed by lymphadenopathy in 54.84%, splenomegaly in 51.47% and hepatomegaly in 44.72%.[6] In another study done by S. Advani et al, (1999) in India among patients of ALL, it was found that most patients had hepatosplenomegaly (80%) and/or lymphadenopathy(79%).[7] Thus findings in ALL in this study are similar to that of the earlier studies.

Incidence of anemia was higher (45.45%) in this study as compared to previous reports published by GG D'Costa et

International Journal Dental and Medical Sciences Research
Volume 5, Issue 2, Mar - Apr 2023 pp 494-499 www.ijdmsrjournal.com ISSN: 2582-6018

al, (1989) which showed its presence in 25% patients.[5]Anemia in this part of our country is probably multifactorial and may include nutritional, hemoglobinopathies and more prevalence of tropical diseases.

In a study by A K Siraj et al, (2002) among 259 newly diagnosed children with precursor B-cell ALL from India, it was found that only 23% of the patients presented with WBC >50 $\times 10^9$/l.[8] In another retrospective study by Moe Wakui et al, (2008) in Japan among the AML patients, it was found that the median value of WBC count was 13.7 × 10^9/l.[9]In the present study the total count was higher in both AML and ALL patients than previously reported.In a retrospective study done by S. Ghosh et al, (2003), it was found that the mean value of bone marrow blasts was 57.6% in AML.[4] In case of ALL, studies show that 81% of children and 71% of adults have bone marrow blasts more than 90%.[10]Findings in the present study are similar to that of the previous studies.

In a study by Zheng J. et al, (2008) in China it was found that abnormal karyotype was present in 56.55% of the patients of AML and the most common abnormality was t(8,21) seen in AML-M2.[11] This studyshowed similar results, as t(8,21) was seen in AML-M2. In another study by G.Kerndrup it was found that 77.14% of the AML cases and 77.8% of the ALL cases had abnormal karyotype. 38.23% of these abnormal karyotypes had a simple clonal chromosome aberration, and the remaining cases had a complex karyotype.[12] In the present study, out of 11 patients of AML, 2 were having abnormal karyotype and both of them had complex karyotype.

In a retrospective analysis of children with ALL by KeizoHoribe et al, (2000) among 528 patients, 56.43% of patients showed normal karyotypes, 9.2% were hyperdiploids, 4.1% had the Ph1 chromosome, 2.4% had the 11q23 abnormality, and 27.65% had other abnormal karyotypes.[13]In this study out of 5 patients of ALL, all of them had normal karyotypes but findingsmay be limited due to less number of patients.One patient with abnormal karyotype in this study had leucopenia and the other had leucocyte count of 54,000/cumm, which differs from previous reports, as published byJacqueline S. Hart et al, (1971) who found that the frequency of abnormal karyotypes increased with increasing leukocytosis.[14]

Moe Wakui et al, (2008) reported that among AML patients, leucocyte count of patients with t(8;21) was 1.4 × 10^9/l and lower than in other subtypes.[9] This study showed similar results as the patient with t(8,21) presented with lower leucocyte count. Trisomy 8 with complex karyotype was associated with AML-M3 in this study. Whereas Schoch C. et al, (2001) reported that trisomy 8 was a very common abnormality in AML, found in M2, M4, and M5.[15]

In a study by Byrd JC et al, (1997) it was found that t(8;21)(q22;q22) has a high frequency of myeloid sarcoma.[16]In another study by K. Horibe et al, (2001) in Japan it was found that in case of AML t(8;21) was the most frequent abnormality among patients aged 5 to 9 years.[17]Similarly in this study the patient with t(8;21)(q22;q22) was a 10 year old child who presented with chloroma of the eye and was diagnosed as AML-M2.

In previous records published by Hillman et al, (2005) it was shown that even in the presence of a normal karyotype, internal mutations of the tyrosine kinase receptor FLT3 is present in 30-40% of patients with AML.[18] In another study by A. Usvasalo et al, among 27 adolescent ALL patients with normal or failed karyotype at diagnosis, microarray comparative genomic hybridization (CGH) detected cryptic aberrations in 85% of cases.[19]

Therefore the finding of normal karyotype in 9 out of 11 cases of AML and 5 cases of ALL stimulates us for further genomic hybridization studies which may reveal such cryptic abnormalities not detected by conventional karyotyping.

V. CONCLUSION:

Acute luekemia still remains a challenge for treating physicians, both in adults and childrens because of high mortality and morbidity. The present study aimed to evaluate the clinical signs and symptoms, severity of the illness and their correlation with hematological profile and karyotype in patients of Acute leukemia. Karyotyping is donein patients of Acute leukemia by treating physicians. But a methodical study correlating the clinical and hematological features with karyotyping was lacking in this part of the country. In this regard this study may be an eye opener, though the number of

cases was less which might be a limitation. Therefore a study of longer duration comprising a sizeable number of patients will definitely reflect the exact picture of this burning problem.

REFERENCES:

[1]. Dario Campana,Ching-Hon Pui.2008. Childhood Leukemia. Abeloff's Clinical Oncology. 4th edition.Chapter 101

[2]. Douglas C. Tkachuk, Jan V. Hirschmann.2007. Acute Leukemias.Wintrobe's Atlas of Clinical Hematology. 1st Edition. Chapter 2

[3]. Barbara Caldwell.2007. Acute leukaemias. Hematology in practice. Chapter 11. p175

[4]. S. Ghosh et al. 2003.Haematologic and immunophenotypic profile of acute myeloid leukemia: an experience of Tata Memorial Hospital.Indian J Cancer. Apr-Jun. Vol 40(2):71-6

[5]. D'Costa GG, Siddiqui HM, Pradhan RM, Gupte SS. 1989. Pattern of leukemias: a ten-year incidence study of 242 cases. J Postgrad Med. 35:191

[6]. M.F.N. Rego, G.S. Pinheiro, K. Metze and I. Lorand-Metze. 2003.Acute leukemias in Piauí: comparison with features observed in other regions of Brazil.Braz J Med Biol Res. Volume 36(3) 331-337

[7]. S. Advani et al. 1999. AcutelymphoblasticleukemiainIndia**:** An analysis of prognostic factors using a single treatment regimen; Annals of Oncology. 10:167-176

[8]. A. K. Siraj et al. 2003. Frequencies of the major subgroups of precursor B-cell acute lymphoblastic leukemia in Indian children differ from the West.Leukemia.17, 1192–1193. doi:10.1038/sj.leu.

[9]. Moe Wakui et al. 2008.Diagnosis of acute myeloid leukemia according to the WHO classification in the Japan Adult Leukemia Study Group AML-97 protocol.Int J Hematol.87(2): 144–151

[10]. Marshall A. Lichtman. 2007. Acute Lymphoblastic Leukemia. Chapter: 91. part IX- Malignant diseases. William's Haematology. 7th edition

[11]. Zheng J. et al. 2008 Jan.A correlation study of immunophenotypic, cytogenetic, and clinical features of 180 AML patients in China.Cytometry B Clin Cytom; 74(1):25-9.PMID: 18061959

[12]. G. Kerndrup.(n.d). Acute leukemia cytogenetics an evaluation of combining G-band karyotyping with multi-color spectral karyotyping.Cancer Genetics and Cytogenetics. Volume 124. Issue: 1. Pages: 7-11

[13]. KeizoHoribe et al. 2000. Prognostic Factors in Childhood Acute Lymphoblastic Leukemia in Japan.Int J Hematol. 72:61-68

[14]. Jacqueline S. Hart et al. 1971. Cytogenetic Studies and Their Clinical Correlates in Adults with Acute Leukemia. Volume 75. Issue 3. Pages 353-360

[15]. Schoch C, Haferlach T, Haase D, et al. 2001. Patients with de novo acute myeoidleukaemia and complex karyotype aberrations show a poor prognosis despite intensive treatment: A study of 90 patients.Br J Haematol.112:118

[16]. Byrd JC, Weiss RB, Arthur DC, et al. 1997. Extramedullar leukemia adversely affects hematologic complete remission rate and overall survival in patients with t(8;21) (q22;q22): Results from Cancer and Leukemia Group B 8461.J Clin Oncol 15:466

[17]. K. Horibe et al. 2001August. Clinicopathologic characteristics of leukemia in Japanese children and young adults.Volume 15. Number 8. Pages 1256-1261

[18]. Hillman, Robert S, Ault, Kenneth A, Rinder, Henry M. 2005. The Acute Myeloid Leukemias. Part II - White Blood Cell Disorders.Hematology in Clinical Practice. Chapter 17. 4th Edition

[19]. A. Usvasalo et al.(n.d). Acute lymphoblastic leukemias with normal karyotypes are not without genomic aberrations.Cancer Genetics and Cytogenetics. Volume 192. Issue 1. Pages 10-17