ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 7, Issue – 6, November – 2022 , Page No. : 01 – 08

Clinico-Haemological profile of Acute Leukemias in Kota

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Citation this Article: Dr. Alankrita Madhur, Dr. Neelu Vashist, Dr. Rajeev Saxena, Dr. Nitin Bairwa, "Clinico-Haemological profile of Acute Leukemias in Kota", IJMSIR- November - 2022, Vol – 7, Issue - 6, P. No. 01 – 08.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Leukemias refers to a group of diseases with different bio logical backgrounds and clinical presentation. It is characterized by a malignant trans formation of Hema to poietic cells which produce an abnormal leukemic population (clone) of cells suppressing the production of normal blood cellular components. Leukemias are classified as acute and chronic, according to clinical course. Acute Leukemias generally pursue an aggressive clinical course which, unless modified by treatment**.**

Design: A prospectus study of 2 years

Results: 52 patients were examined out which 23 were Acute Myeloid leukemias and 29 Acute Lymphoblastic Leukemias.

Conclusion: The present case study justified the normal trend of acute leukemias with respect to age, clinical and radiological feature, all Haemological parameters including blast percentage.

Keywords: Acute Myeloid Leukemia, Acute Lympho blastic Leukemia, Throm Bo cytopenia, Leuco cytosis, Lymphadenopathy, Hepato-spenolmegaly.

Introduction

Leukemias refer to a group of diseases with different biological backgrounds and clinical presentation. It is characterized by a malignant Tran's formation of hematopoietic cells which produce an abnormal leukemic population (clone) of cells suppressing the production of normal blood cellular components. Leukemias are classified as acute and chronic, according to clinical course. Acute Leukemias generally pursue an aggressive clinical course which, unless modified by treatment**.**

Leukemia is one of the most commonly seen malignancies both in children and adults. Leukemia is characterized by neoplastic proliferation of hemopoietic stem cells and accumulation of blast and immature cells in the peripheral blood film and bone marrow.

Leukemia is classified into Myeloid and Lymphoid types depending upon the lineage of the progenitor cells involved.

Leukemia is the 10th most common cancer worldwide with incidence of 3, 51,000 new cases and mortality of 2, 57,000 each year. In India, lympho-hematopoietic malignancies constitute 9.5% of all cancers in men and 5.5% in women.

As per available information from population-based surveys, the incidence of leukemia in India varies from 0.8- 5/1,00,000 people. Leukemia is also the most common childhood malignancy. It accounts for 30% of all cancers diagnosed in children under 15 years of age.

Acute Leukemias in children, under 15 years of age, is usually lymphoblastic in type, while in adults it is usually Myeloid. The incidence of acute lymphoblastic leukemia is highest in the first 6 years of life. In adults, it occurs at all ages and is not uncommon in middle-aged and elderly persons. Acute Myeloid Leukemias affect primarily in adults, peaking its incidence between the ages 15 and 39 years.

The rising incidence of leukemia and its possible relationship to background or occupational exposure to ionising radiations in this atomic age have brought the disease increasingly before the public eye.

The presenting features are weight loss, severe pallor and fever. The most common mode of presentation is with symptoms of anaemia or haemorrhages mainly conjunctival, petechiae or ecchymotic patches.

Infective lesion of mouth and pharynx, fever, prostration, headache, and malaise can too be presenting symptoms of disease. The clinical picture reveals gum hypertrophy and ulcerative lesions of the rectum. Lymph node enlargement is more common in lymphoblastic leukemia Gastrointestinal (haematemesis, melena and haemoptysis), renal tract, uterine and nervous system haemorrhages, commonly occur in course of the disease. Tenderness of sternum is a common presentation. Meningeal involvement may also occur. USG finding shows mild to moderate hepatosplenomegaly. Lymph nodes are moderately enlarged especially in Acute Lymphoblastic Leukemia. Tenderness of sternum is a common presentation. Meningeal involvement may also occur.

Acute Lymphoblastic Leukemia

It is a common leukemia in children who present who present with lymphadenopathy, leucocytosis, anemia and bleeding tendency. ALL is characterized by the presence of 30-95% of lymphoblast of total WBC count. It is neoplastic disorder that is rapidly fatal if left untreated.

Incidence of ALL is a most common paediatric malignancy accounting for ¼ of childhood cancers and ¾ of newly diagnosed Leukaemia's. Incidence is about 3-4 patients per 1,00,000 children under 5 years of age. It constitutes 35% of all hematological malignancies in children.

Down syndrome, Li-Fraumeni syndrome or type 1 Neurofibromatosis may be some of the genetic risk factors. Though chemotherapy or selective medicines that directly destroy cancer cells are used as treatments, but exposure to radiation or previous chemotherapy, may add to the environmental risk factors. Children with Down's Syndrome have an increased risk for childhood ALL as well as AML. Exposure to high-energy radiation in early childhood increases the risk of developing ALL.

The clinical onset of Acute lymphoblastic leukemia is increasing in subtle way and is insidious, and presenting signs and symptoms reflect bone marrow as well as extramedullary involvement by leukemia. There is anemia and severe thrombocytopenia in the peripheral blood film. Examination of peripheral blood smear is often sufficient for establishing the diagnosis. In bone marrow examination, 20-50% of all cells of bone marrow are lymphoblasts due to malignant proliferation and suppression of all other lineages of cells. Lymphadenopathy and he pato - splenomagaly are frequent.

Acute Myeloid Leukemia

Acute Myeloid Leukemia is a clonal hematopoietic disorder characterized by impairment of self-renewal,

differentiation, and proliferation of myeloid stem cell compartment due to acquired somatic mutation. It is a neoplastic process with blasts more than 20% to 30% in peripheral blood smear.

Incidence of AML

Annual incidence of Acute Myeloid Leukemia varies from 0.9 to1.5 per 100000 people per year worldwide. It constitutes 15% of hematological malignancies.

Acute Myeloid Leukemia incidence increases with age and sex. It is more men than women. In the patient <65 years incidence is 1.7 patients / 1,00,000 individuals and 15.9 patients /1,00,000 in those aged > 65 years. The median age at diagnosis is 67 years.

Hereditary Factors**,** genetic factors, radiation, chemical, drugs (anticancer drugs) and other occupational hazards are predisposing factors of AML.

Cases of Acute Myeloid Leukemias show a clinical presentation of anemia, easy bruising, infections, and hepato-splenomegaly which due to infiltration of leukemic cells.

Material and methods

In present study, we have taken up all the cases of Acute Leukemias, that have been diagnosed from 1 June 2019 to 30 June 2021. Initially, we have took a detailed history of the patient related to age, sex, epidemiology, and etio-pathogenesis of the patient. Then clinical features too have been observed. Putting all the above, together, we reached a provisional diagnosis.

Once we receive the well-labelled sample of EDTA blood, we have first run the blood samples in coulter-counter then studied their histogram and other values too. After this, a detailed peripheral blood film study was done. The morphological patterns of cell are noted and detailed differential counts have been done. In a few patients bone marrow aspiration, is required which is done along with PBF for a complete diagnosis. The PBF and the bone marrow examined has been stained by Leishman's Stain (Romanowsky). In our present study, we will use PBF and bone marrow aspiration as our diagnostic procedure.

Discussion

Acute Leukemias are malignant clonal disorders of blood-forming organs involving one or more cell-lines in the hematopoietic system. These disorders are marked by the diffuse replacement of bone marrow with abnormal immature and undifferentiated hematopoietic cells, resulting in reduced numbers of erythrocytes and platelets in the peripheral blood. Based on the origin of the abnormal hematopoietic cells involved, such as lymphoid, myeloid, mixed or undifferentiated, these disorders are classified accordingly. In the present study, 52 patients were diagnosed with Acute Leukemias after being subjected to detailed clinical history and examination followed by a complete hematological work up and bone marrow examination.

Acute lympho blastic leukemia is characterized by the unrestrained clonal proliferation of haemo poietic precursor cells coupled with aberrant or arrested differentiation. Clinicians depend on the newer diagnostic modalities to diagnose and recognize the association between the morphology and immune opheno type and specific cytogenetic abnormalities. This has led to the development of added treatment modalities based upon specific genetic defects.

Stratification of patients according to age groups is associated with important clinical and biologic features that might be in part responsible of the marked differences in the outcome witnessed in children and adults with ALL. It accounts for 60-80% of childhood leukaemia. Male preponderance is noted in children with ALL.

In my study, a total of 29 out of 52 patients of Acute Leukaemias were diagnosed Acute Lymphoblastic Leukaemia

The study done by Guru et al (2018) shows male predominance i.e. male: Female is 3.5:1. The study done by Kulkarni KP et al (2013) (3) showed male predominance with Male: Female ratio of 3.1:1

In present study out of 29 children 20 (69%) were male, 9 (31%) were female. The male: female ratio was 2.22: 1.

Male predominance was noted in present study

Sousa DW et al (2015) (4) conducted a study in 76 patients under 19 years of age and diagnosed with ALL. Similar observations were made with Guru FR et al (2018) (5), Arya L Set al (2011) (6) and Ahirwar R et al (2018) (7).

In present study peak incidence of paediatric ALL were reported in the age group of 0-5 years of age

The number of children who were affected in this age group was18 (62%) out of 29 children diagnosed with ALL**.**

Pandian G et al (2018) (8) did a prospective study in GRH Madurai. In his study fever was the most common symptom as similar to my study.

Shalal HH et al (2017), (9) did a retrospective study in 55 patients to

show initial presenting features of ALL. In his study fever and pallor were the most common presenting features similar to present study.

In present study fever and pallor are most common presenting clinical pictures.

In the study of Siddaiahgari SR et al (2015) (10), 4.5% of study population had mediastinal involvement. In the study of Shalal HH et al (2017) (9), 7.2% of study population had mediastinal widening. In our study most of children had Pleural effusion. In the study of Shalal HH et al (2017) (9), 1.8% of study population had pleural effusion**.**

In the present study majority of children do not have any radiological finding. Pneumonitis and hepato-splenomegaly are also seen on ultrasonography.

Sousa DW et al (2015) (4) conducted a study in 76 patients who were under the age of 19 years and positive for ALL. In their study anaemia was found in 85% of patients. The similar observation was noted in my study, anaemia is seen in almost 90.26% of population among which 54.68 %(62 children) were severely anemic.

In present study majority of patients had anaemia at the time of diagnosis.

65% with ALL had severe anaemia (hemoglobin value less than 7gms /dl***)***.

The study of Shalal HH et al (2017) (9) had 16.4% of study population with hyperleukocytosis. Kong SG, et al (2014) (11) did a study regarding hyperleukocytosis in pediatric ALL at Pusan national university hospital.

In present study majority of children had WBC counts in the range of 5900-5,44,430/mm3.

Hyperleukocytosis was observed in majority of cases with ALL.

48% had count above 1,00,000 followed 31% under 50,000 and rest 21% had count in between 50,000-1,00,000.

In the study done by Shalal HH et al (2017) (9) 25.5% of cases had severe thrombocytopenia. Also the study by Pahloosye A et al (2011) (12) 19% of cases had severe thrombocytopenia in their study population.

In present study among 14 out 29 children, had platelet count less than 20,000/mm3 with severe thrombocytopenia.

Acute Myeloid Leukemia

In present study 23 out of 52 case diagnosed with Acute Leukemias were of Acute Myeloid Leukemia

According to SEER statistics patients older than age 65 represent approximately 55% of AML cases, only 37% of the patients entered onto the Southwest Oncology Group trials reported here was older than age 65. (13)

Acute myeloid leukemias affect primarily adult, peaking its incidence between the ages 15 and 39 years. The mean ages of various subtypes of AML in this study correlates with the study conducted by Shome et al. (14)

In the present study 39% (9) of cases of AML lies between age group of 40-60 years age.

Chang et. al. reported that in children and adolescent, female patients with AML t (8), inv(16), or a normal karyotype had better prognosis than males with the same genetic profiles [15].

In present study male: female ratio is 1:22. Male predominance was observed.

Fever and fatique were observed by studies conducted by Advani et al., [16], Shome et al., [14] and Mathur et al., [15].

In the AML patients of present study, the main presenting symptoms in the study was fever (26%).

Incidence of Lymphadenopathy was seen in study of Advani et al. (4%), whereas in other studies done by Shome et al (14) and Mathur et al (15) lymphadenopathy was seen in more than 30% of patients.

In studies conducted by Shome et al., hepatomegaly was seen in 73% of patients and splenomegaly was seen in 52% of patients. In study conducted by Mathur et al. hepatomegaly was seen in 76% and splenomegaly was seen in 73% of patients.

In present study, Hepato-splenomegaly was seen in 26% of patients.

Most of patient studied did not presented with any other complain.

In the study conducted by Mathur et al anaemia was seen in majority of study subjects.

In present study 23 out 23 of patients of AML have Anaemia

n the present study, TLC ranged between 0.6-149 $\times 10^9$/l with a mean of 48.5 $\times 10^9$/l. In studies conducted by Mathur et al the TLC ranged was between 5-100 $\times 10^9$/l with a mean of 38.5 $\times 10^9$/l.

In present study

leucocyte count was more than 1,00,000 in 43% of patients who were diagnosed with AML.

In studies conducted by Mathur et al., mean platelet range was 0-150$\times 10^9$/l with a mean of 58.4$\times 10^9$/l. Thrombocytopenia is an important finding in acute Leukemias.

The present study showed

36% of patients, platelet range from 50,000 to 100,000/mm3

31% showed platelet less than 20,000/mm3 and 27% showed platelets ranging from 20,000 to 50,000/mm3. The majority patients showed thrombocytopenia

last percentage in Peripheral Blood Smear and Bone Marrow

Bone marrow aspiration was done in all cases of AML. Mean blast percentage correlates with the study conducted by Mathur et al.(17)

All the patients with Acute Leukemias in present study have blast above 20%.

Fig1-7 show blast in bone marrow and peripheral blood film.

Results

The study include incidence of Acute Leukaemias according to age, sex and ethnicity of the patient. All possible etiological factors, family history, socio-demographic factor and clinical presentations with haematological picture were studied along with age, sex and incidence were correlated for complete diagnosis. Acute Leukemias were classified according to French

American and British classification. All the findings were compared to other studies after reviewing the literature and following conclusion were drawn

Total 52 cases were studied out of which 29 were Acute Lymphoblastic Leukemias and 23 were Acute Myeloid Leukemias. Acute lymphoblastic Leukemias were seen most commonly in patients less than 5 years of age. Acute myeloid Leukemias were seen in age group of *50-60* years. Male preponderance was seen in both Leukemias .Fever and pallor were most common clinical presentation in Acute lymphoblastic Leukemias. Fatigue was the initial and most common presenting complain of patients with Acute Myeloid Leukemias. Cases of Acute Lymphoblastic Leukemias either do not have any radiological finding.

Pneumonitis and hepato-splenomegaly are also most common radiological findings. In the cases of Acute Myeloid Leukemias hepato-splenomegaly is common radiological finding. Anaemias, leucocytosis and thrombocytopenias was observed on haematological study in both Acute Leukemias last percentage was more than 20% in both peripheral blood film and bone marrow stained slides.

A well-made and well stained peripheral blood film, is the main tool of diagnosis of Acute Leukemias. Most of the time a complete diagnosis is possible by a well stained (Leishman stain) peripheral blood smear or it gives a leading effect towards other methods of diagnosis e.g.; special stain, bone marrow biopsy and bone marrow aspiration.

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Legend Figures

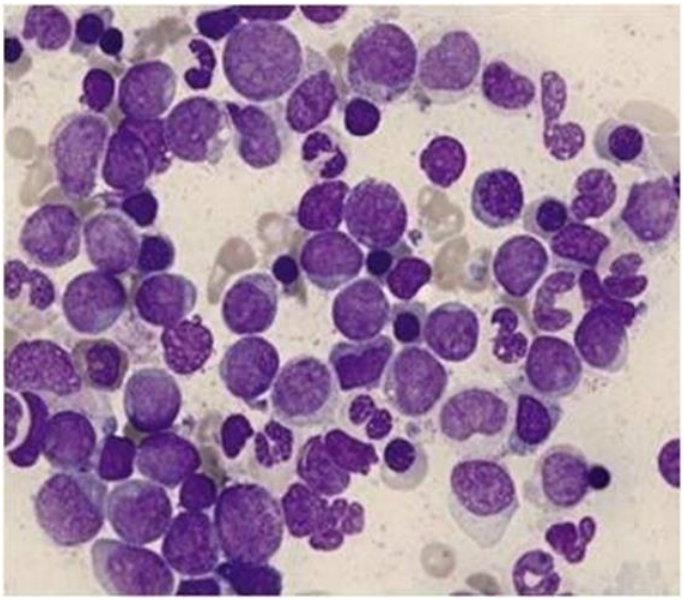

Fig 1: Bone marrow aspirates showing myeloblasts in a case of AML. (Leishman oil immersion 100x)

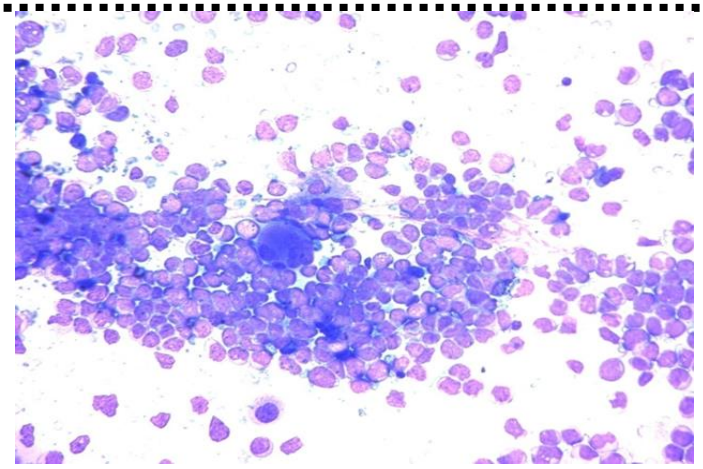

Fig 2: Bone marrow aspirate showing many myeloblasts (40x Leishman stain) PBF

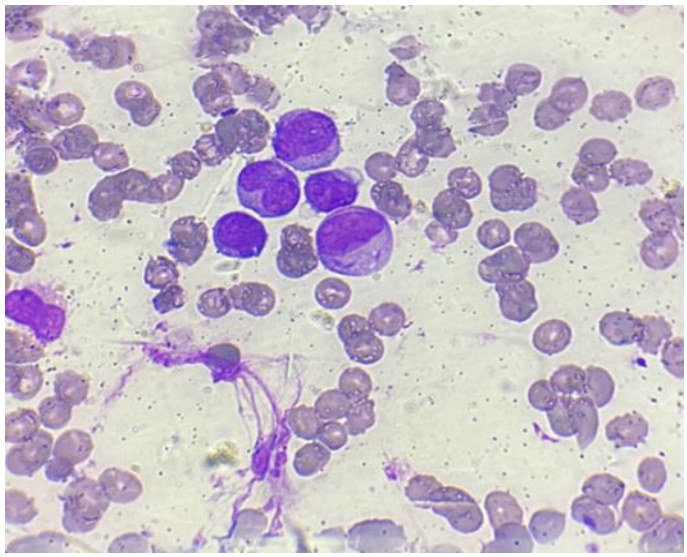

Fig 3: Peripheral blood smear showing myeloblast with Auer rods in a case of AML (100X Leishman stain)

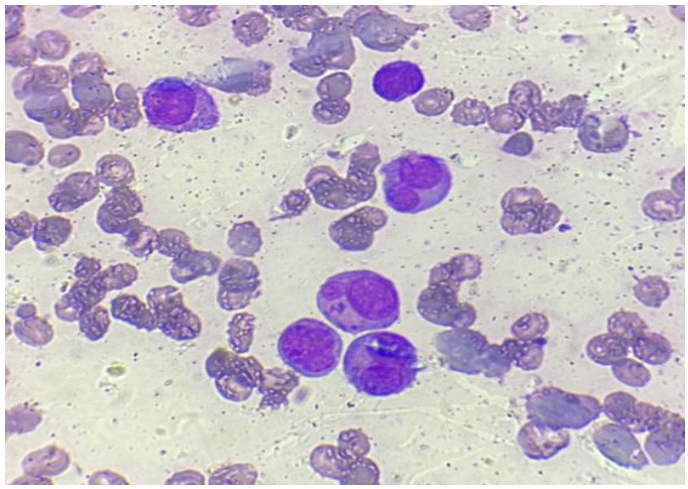

Fig 4: Peripheral blood smear showing myeloblast with Auer rods in a case of AML (100X Leishman stain)

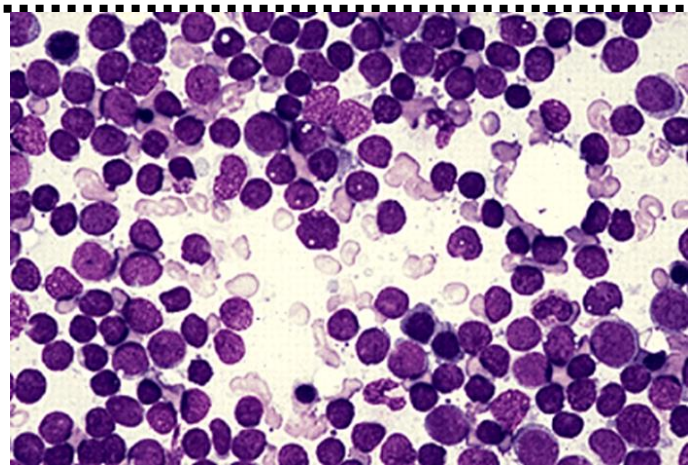

Fig 5: Bone marrow aspirate of ALL showing increased cellularity with many lymphoblasts (100 x Leishman stain)

Peripheral blood smear

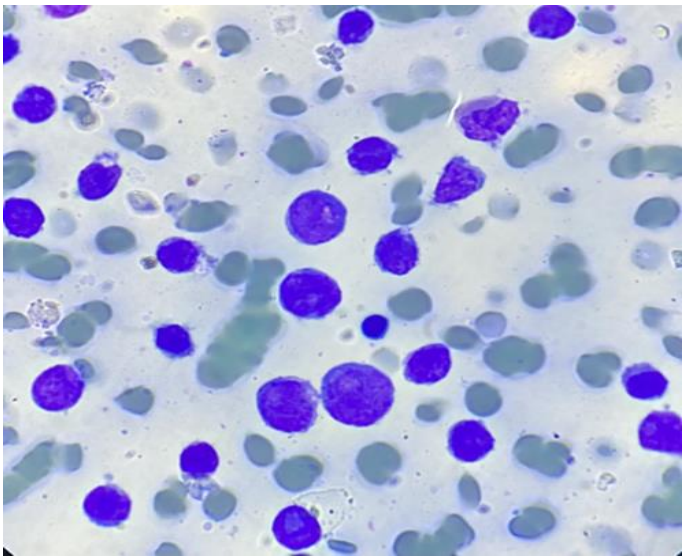

Fig 6: Peripheral blood film showing blasts with prominent nucleoli and ill-defined cell margins (100x Leishman stain)

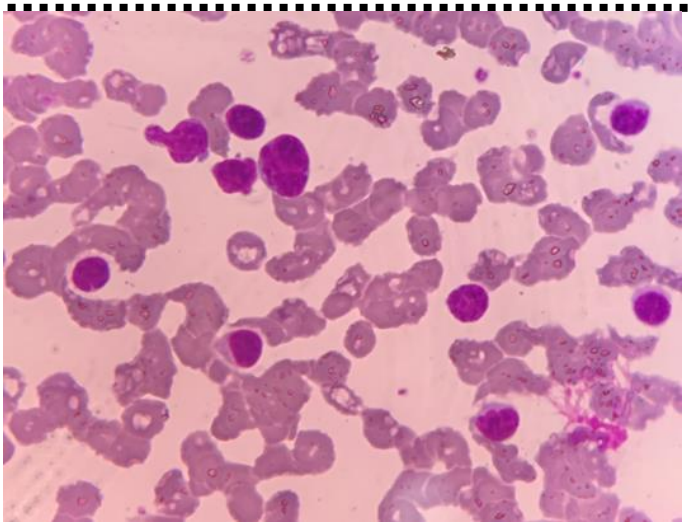

Fig 7: peipheral blood film showing hand mirror cells lymphpblast.