Original Research Article

Clinico-hematological study of leukemias in a hospital-based setup

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ABSTRACT

Background: Leukemia, the malignant proliferation of hematopoietic cells, accounts for a major portion of cancer globally. Types of leukemia are necessary for effective therapy as prognosis, and survival rates are different for each type of leukemia. The objective of the study was to know the relative incidence of leukemia in Silchar Medical College and Hospital, Assam. This study also aims to know the clinical manifestations of leukemia and their hematological correlation.
Methods: It was a retrospective study of 60 patients carried out in the Department of Pathology in SMCH, Assam, over a period of 2 years from April 2019 to March 2021. Diagnosis was based on peripheral blood count, peripheral blood smear and bone marrow examination for morphology, along with cytochemistry study whenever required.
Results: In this study, acute leukemia was more prevalent than chronic leukemia. The most common form was CML followed by AML, ALL and then CLL. Male predominance was observed in this study with male: female ratio = 1.7:1.
Conclusions: In our study, Acute leukemia was more prevalent than chronic leukemia. Leukemia affected male more than female. In this study, the frequency of AML is more than that of ALL but number of cases of CML exceeds that of AML.

Keywords: Leukemia, AML, CML, ALL, CLL

INTRODUCTION

Leukemia is a malignant proliferation of hematopoietic cell (immature cells) originating in the bone marrow replacing other marrow cells.

Acute leukemia is said to be >20% blasts in peripheral blood or bone marrow according to World Health Organization (WHO) criteria.

Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm characterized by predominant proliferation of granulocytic cells. It's a clonal hematopoietic stem cell disorder.

In India, CML constitute 40%, ALL 35%, AML 15% and CLL 10%.[1] CLL is common in the Western countries.

ALL usually occurs in young children and adolescents, whereas CML and AML usually occurs in older people, and CLL in elderly.

Leukemia is the 11th most common cancer worldwide with about 257,000 new cases each year.[2] Leukemias form a significant percentage of hematological disorder and affect individuals of all age groups throughout the world, but the incidence of disease frequency of various morphological types and sub-types have been found to be differing in different countries.[3]

A number of recurrent genetic abnormalities play an important role in malignant transformation of leukemic cells. Diagnosis of leukemia is done by genetic study either molecular or cytochemistry but commonly by peripheral blood study and bone marrow study.

Complete blood count and differential leukocyte count is important for initial diagnosis. Morphology of immature blast cells are taken into account through peripheral blood smear and bone marrow aspiration study. For knowing genetic abnormalities, flowcytometry and immunophenotyping need to be done.

Objectives

To know the relative incidence of leukemias among patients coming to the OPD and Casualty wards in Silchar Medical College and Hospital, Assam. To know the clinical manifestations of leukemias and their hematological correlation for appropriate diagnosis. To study hematological parameters in different types of leukemias.

METHODS

The study was conducted in Silchar Medical College and Hospital, Assam for a period of 2 years from April 2019 to March 2021.

A total of 60 patients with acute and chronic leukemias were included in the study period. The present study was a retrospective, cross-sectional descriptive study conducted in the Department of Pathology, SMCH, Assam. The data were collected from the records maintained in the Department of Pathology using stratified random sampling technique. The study was approved by the Institutional Ethics Committee. The whole blood samples of the patients were collected with informed consent for hematological analysis. Red blood cell indices, white blood cell indices, amount of hemoglobin, total platelet count and percentage of blasts were determined according to standard laboratory procedures. Slides for peripheral blood smear were prepared and stained with Leishman stain for viewing the morphology of blast cells and counting blasts percentage. Bone marrow aspirations were done and morphology of blasts were better appreciated in stained slides and along with that cytochemical stains were done in aspirated smears. MPO (myeloperoxidase) stain, SBB (Sudan Black B) stain, and PAS (Periodic acid- Schiff) stains were done in case of acute leukemias.

Acute Myeloid Leukemias were classified based on FAB criteria.

Inclusion criteria

All clinically suspected cases presenting with short duration of anemia, bleeding, persistent fever, joint pain, hepatosplenomegaly, lymphadenopathy which were later diagnosed as leukemia in peripheral blood examination were included in this study.

Exclusion criteria

All previously diagnosed cases of leukemia and those who got treatment for the same were excluded.

Statistical analysis

All the data were analyzed using Microsoft excel 2019 and figures were drawn using Microsoft word 2019.

RESULTS

In our study, a total of 60 cases were diagnosed as leukemia. Among these, 53% cases were evaluated as acute leukemia, while 45% patients had chronic myeloid leukemia and only one case was diagnosed as chronic lymphocytic leukemia. Cytochemistry stains were performed in acute leukemia cases. MPO and SBB stains positive in acute myeloid leukemia and PAS stain positive in acute lymphoid leukemia. CML and CLL were diagnosed by morphological study on peripheral blood smear. In CML, 'myelocyte-buldge' was seen in PBS along segmented neutrophil, whereas in CLL small, mature-lymphocyte like cells were present in PBS along with smudge/basket cells.

Table 1: Percentage of acute/chronic leukemia.

| Type of leukemia	Total no. of cases	Percentage
Acute leukemia	32	53
Chronic leukemia	28	47
Total	60	100

Table 2: Prevalence of different types of acute/chronic leukemia.

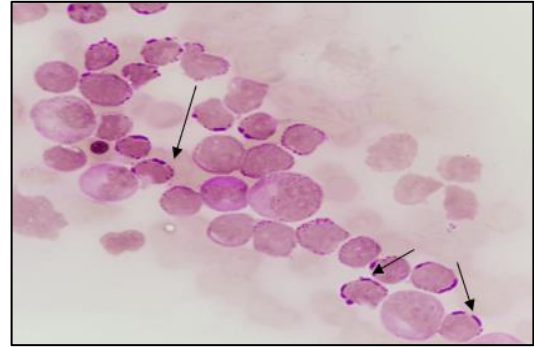| Types of leukemia	Total no. of cases	Percentage
AML	19	31.7
ALL	13	21.7
CML	27	45
CLL	1	1.6
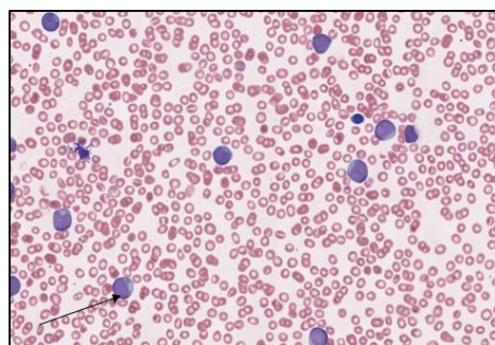
Figure 1: Photomicrograph of AML with predominant blasts showing Auer rods (arrow).

From table 2 it can be seen that a majority of the cases were CML followed by AML > ALL > CLL. But overall it was observed that acute leukemia was more prevalent than chronic leukemia from table 1.
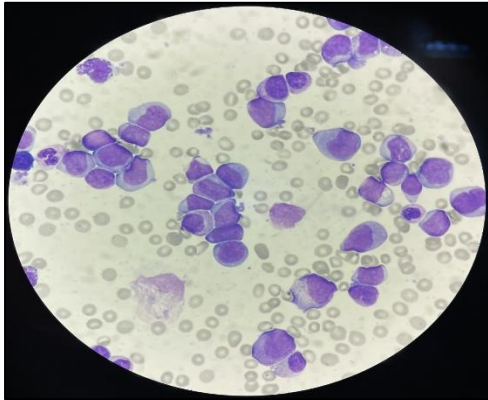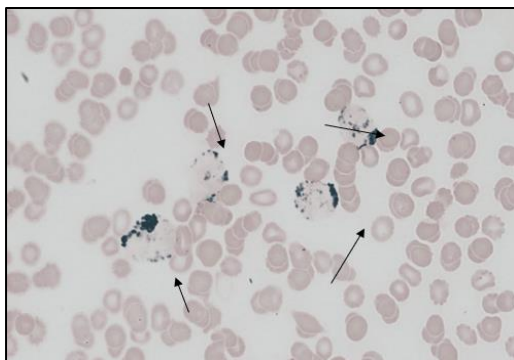

Figure 2: Photomicrograph of AML showing abnormal Promyelocytes and few mature neutrophils and decreased platelet.

Figure 3: Photomicrograph of AML showing MPO positive myeloblasts. (indicated by arrow).

Figure 4: Photomicrograph of ALL shows lymphoblasts – FAB L1.

Overall male preponderance was found with percentage of 63.33% and female population of leukemia includes 36.67%. Male-female ratio = 1.7:1.
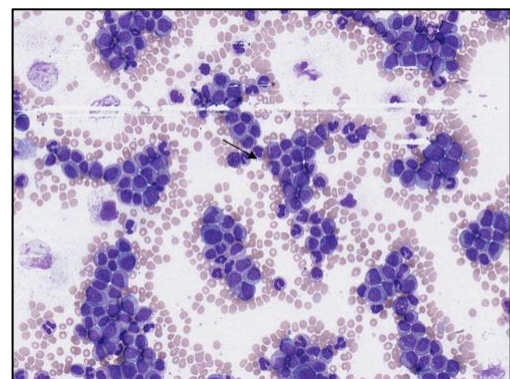
Majority of cases were of 20-40 years of age of which CML precedes, followed by 0-9 years of age. Majority cases of ALL are seen among young children between 0-9 years of age about 18.3%. AML is common in age groups of 20-40 years about 16.7%, while CML in 20-40 years of age but CML about 28.3% precedes AML. CLL is seen in only one case of 80 years of male.
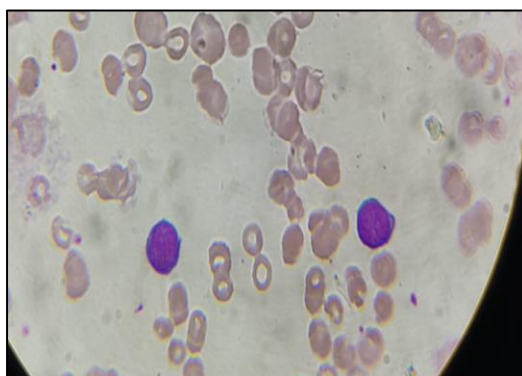

Figure 5: Photomicrograph of ALL showing PAS positive abnormal lymphoblasts.
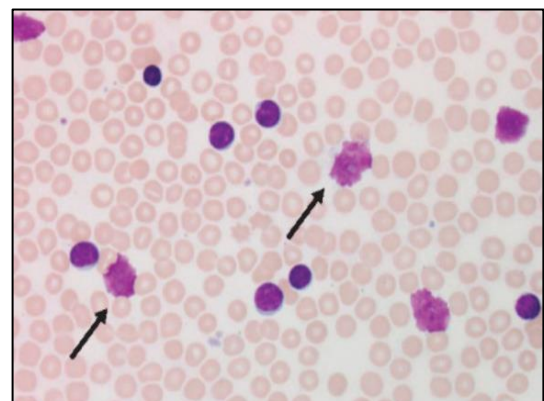

Figure 6: Photomicrograph of CML showing bulge of myelocyte and meta-metamyelocyte and basophilia. (shown by arrow).

Figure 7: Photomicrograph of CLL showing mature lymphocytes and smudge cells (indicated by arrows).

Majority of patients displayed symptoms such as generalized weakness, fever, loss of weight, bleeding

tendencies. Acute leukemia patients present with progressive pallor and gum and nose bleeding along with other features described. This is due to the replacement of normal marrow cells by leukemic cells. Hence, anemia, thrombocytopenia and neutropenia (causing fever) usually occur. On examination, some patients developed hepatosplenomegaly and lymphadenopathy.

Table 3: Age wise distribution of no. of cases of leukemia and types of leukemia.

Age (years)	No. of cases	ALL	AML	CML	CLL
0-9	14 (23%)	11 (78%)	2 (15%)	1 (7%)	0
10-19	5 (8%)	1 (20%)	4 (80%)	0	0
20-40	27 (45%)	0	10 (37%)	17 (63%)	0
40-60	10 (17%)	0	3 (30%)	7 (70%)	0
≥60	4 (7%)	0	3 (75%)	0	1 (25%)

The young patients of ALL usually present with fever, bone pain, pallor and lymphadenopathy.

Whereas, anemia and thrombocytopenia in CML and CLL patients are late manifestation.

In Acute leukemia complete hemogram shows Leukocytosis. In about 80% of patients total leucocyte count are > 1 lac/ cumm and around 20% had TLC ranges between 15,000 – 50,000. RBC population and Hemoglobin counts are severely reduced. In 53% cases, Platelet count usually ranges between 10,000 – 80,000. Blast percentage between 40% - 90%.

In CML complete hemogram shows leukocytosis (TLC >50,000 -1lac /cumm) with increased percentage of basophils depending among stage of CML. RBC population and Hemoglobin counts are reduced but not severely. Blast percentage is usually 2-4% with myelocyte <10% in chronic phase, 10-19% in accelerated phase and ≥20% in blast phase. Among them 70% of patients were found to be in Chronic phase, followed by accelerated phase 22% then blast phase 8%. This differentiation is important for therapeutic purpose. Prognosis of chronic phase is good than blast phase. Without treatment disease progresses from chronic phase to accelerated phase to blast phase.

Further, the patients' samples would be sent for Philadelphia chromosome testing for confirmation. Whereas, in CLL there was leukocytosis with lymphocytosis.

Early diagnosis of leukemia is necessary for proper treatment. The treatment for different types of leukemia is different. It can even vary according to the different stages and subtypes of leukemia. Patients treated early usually have the best prognosis.

Figure 1 and 2 show increased leucocytes with abundant myeloblasts, promyelocytes and few metamyelocyte. Some of the myeloblasts show Auer rods in their basophilic cytoplasm. There is decreased number of mature neutrophils, platelet counts and RBC population. The same is stained with Myeloperoxidase (MPO) and the primary granules in myeloblast and promyelocytes took the stain (MPO positive, Figure 3), confirming the diagnosis.

Figure 4 shows lymphoblasts in Leishman stained smear having smaller size than myeloblast, scanty basophilic cytoplasm, regular nuclear membrane with high Nuclear-cytoplasmic ratio and inconspicuous nucleoli. On staining with Periodic acid Schiff's (PAS) shows PAS-positive 'blocks' in lymphoblasts with clear cytoplasmic background (Figure 5).

Figure 6 shows leucocytosis with peak population of myelocyte and meta-myelocyte, few myeloblasts, increased basophils, few mature forms of neutrophils. In CML, all the stages are present from myeloblast to mature segmented neutrophils. RBC population and platelet count is low to normal. Myelocytes are smaller than myeloblasts, with round eccentric nucleus, condensed chromatin, no nucleoli and secondary specific granules. Metamyelocytes have same features but with cleaved nucleus.

Figure 7 shows neoplastic lymphocytes having small, mature looking, high N/C ratio, clumped chromatin, inconspicuous nucleoli and scant cytoplasm. Smudge cells (indicated by arrow) are characteristic of CLL produced during spreading of blood films due to fragile neoplastic lymphocytes.

DISCUSSION

In the year of 1857, Virchow was probably the first to classify leukemia. Based on the pathologic distribution of tumor, he distinguished splenic and lymphatic forms of leukemia.[4]

The incidence of leukemia has increased considerably and this rise is noticeable because of improved statistics, better case findings with novel technologies leading to better diagnosis and treatment methods. The incidence of leukemia is found to be varying from different geographical areas according to lifestyles, economic conditions, and poverty rate.[5]

In the present study, acute leukemia is more common in about 53% cases out of a total of 60 cases which is in concordance with Singh et al and Nasim et al.[6,7] Singh et

al. in their study at PGIMS, Rohtak, Haryana, India found 66.8% patients had acute leukemia and 33.2% had chronic leukemia. ALL and AML were found in 29.7% and 37.3% of the patients respectively. Of chronic type leukemia, 28.3% had CML and only 4.7% had CLL. In our study, 53% had acute leukemia and 47% had chronic leukemia. ALL and AML were found to be 21.7% and 31.7% of cases respectively. CML and CLL were 45% and 1.67% respectively. Hence, in our study there was a higher percentage of CML cases, followed by AML, and then ALL, and finally, there was only one case of CLL. In our study we got male:female ratio 1.7:1 and in their study got 1.5:1.

Nasim et al in their study conducted in PGMI, Lahore observed that acute leukemia (80%) was more prevalent than chronic leukemia (20%) which was similar to our study. The differences were that they had 49% ALL and 31% AML followed by 16% CML and then 2% CLL. Whereas in our present study we found that AML is more common than ALL which is AML 31.7% and ALL 21.7%. But CML (45%) cases were higher than AML and CLL cases were least (1.67%).

Our present study findings are similar to Jatav et al.[8] Their study was conducted at Gajra Raja Medical College, Gwalior, and they found AML to be more common than ALL which was at 55.4% and 44.6% respectively.

Baviskar et al in her study at Pravara Institute of Medical Sciences, Loni, Maharashtra observed that CML (33.97%) was more common followed by ALL (26.28%), AML (23.07%) and then CLL (15.38%) which vary from our present study where we found overall acute leukemia were more than chronic leukemia but individually CML cases were higher than AML cases followed by ALL and then CLL.[9] In their study, they found ALL was the most common type of leukemia in children and adolescents. Myeloid neoplasm were most common in adults which were in concordance with our present study. Our study was in concordance with from other studies, Vasavada et al, Kushawaha et al, Chatterji et al.[10-12]

Our study was consistent with Humayun et al which showed 90% of acute type and Ali et al and Yasmeen et al proving AML was more prevalent in adults and ALL in children and varied with Shome et al and Menzes et al and Vergehese et al.[13-18]

These differences in studies might be due to geographical variation and public awareness. Acute leukemia is rapidly fatal if left untreated but they are curable with appropriate treatment.[19] Chronic Myeloid Leukemia if diagnosed early in chronic phase is treated with long term therapy of tyrosine kinase inhibitor whereas in later stages may require allogenic hematopoietic transplantation. Nowadays CML is diagnosed earlier for multiple reasons, greater awareness of the disease, and wide availability of cheap but accurate leucocyte and platelet measurements that were not performed in the past.

Limitations

The limitation of the study was that it was a hospital-based study with a small sample size due to COVID period and these cases were not available for follow up. To validate our findings, further research with bigger sample size is needed. Furthermore, flowcytometry set-up is not available in our hospital, so immunophenotypic analysis and subtyping could not be performed.

CONCLUSION

Leukemia is the 10th most common cancer in men and the 12th most common in women. It constitutes 3% of the global cancer burden. In the present study acute leukemia was more prevalent than chronic leukemia. Male predominance was seen in all types of leukemia. Age was an important factor in diagnosis/prognosis of leukemia, as some types of leukemia affected specific age groups only. ALL was more common in children and adolescents and AML and CML in adults, and CLL was seen specifically among the elderly age groups. Majority of the patients had increased leucocyte count, decreased RBC population, decreased hemoglobin count, decreased platelet count presenting commonly with fatigue, fever, purpura, hemorrhages, body ache, lymphadenopathy. Hence, suspecting earlier and early diagnosis of leukemia help with therapy started early causing a better outcome.

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