Original Article

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# Clinico-Hematological Study of Acutemyeloid Leukemias

Pathology Section

PREETHI C.R.

## ABSTRACT

**Context:** Acute Myeloid leukemia has been of special interest to innumerable workers in the field of cancer research since the blood and haematopoietic tissue can be easily and repeatedly sampled.

**Aim:**

- To know the relative incidence of Acute myeloid leukemia among the patients referred for complete haemogram at the Department of Pathology, JJMMC, Davangere, India.
- To study the clinical manifestations and their correlation with various types of acute myeloid leukemia.
- To study the haematological profiles in acute myeloid leukemia.

**Settings and Design:** This was a hospital based study conducted at haematology unit, Department of Pathology, JJM Medical College, Davangere, India.

**Materials and Method:** The present study was done during the period of June 2006 to May 2008 at haematology unit department of Pathology, JJM Medical College, Davangere, India. Cases from Chigateri General Hospital, Bapuji Hospital and other private hospitals situated in and around Davangere were included for the study. The case selection was based on the clinical features and supported by laboratory evidence. Bone marrow aspiration was subsequently carried out after obtaining written consent from the patient or the guardian.

**Statistics:** The results were expressed in percentage.

**Results and Conclusion:** A total of 1039 patients who were referred to the Department of Haematology out of which 50 patients were diagnosed as Acute Myeloid Leukemia. The present study highlighted that light microscopic features of peripheral smear and bone marrow will still remain mainstay in the diagnosis of acute leukemias.

**Keywords:** Leukemias, AML, Hospital-based study

## INTRODUCTION

Acute myeloid leukemias affect primarily adult, peaking its incidence between the ages 15 and 39 years. AML is quite heterogenous reflecting the complexities of myeloid cell differenciation [1].

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 [2].

GC DeGruchy defined leukemia as a disease of unknown aetiology characterised by uncontrolled, abnormal and widespread proliferation of haematopoietic cells of the body which infiltrate the bone marrow and other tissues. This proliferation usually but not invariably accompanied by the appearance in the peripheral blood of immature leucocytes which are morphologically abnormal [3]. The most commonly used classification was proposed by the FAB co-operative group in 1976 [4]. The latest WHO classification of the acute leukemias differs from the FAB classification in that greater than or equal to 20% blasts are used for diagnosis of acute leukemias [5].

Leukemia has been of special interest to innumerable workers in the field of cancer research since the blood and haematopoietic tissue can be so easily and repeatedly sampled. A multiplicity of techniques, physical, chemical and biological have been directed to elucidating the nature and fundamental components of the leukemic state [2]. Leukemia is a treatable disease. Most treatments involve chemotherapy, medical radiation therapy, hormone treatments, or bone marrow transplant. The rate of cure depends on the type of leukemia as well as the age of the patient. Children are more likely to be permanently cured than adults.

Acute myeloid leukemia is a complex disease with considerable phenotypic and genotypic heterogeneity. There are more than 100 recurring cytogenetic abnormalities observed in AML and numerous point mutations [6].

The pathogenesis of AML is uncertain but chromosome abnormalities are present in most patients. Cytogenetic translocations result in the formation of fusion proteins, which are a common pathway in leukemogenesis [7].

Patterns of leukemia incidence vary in different parts of the world. In India, under the existing circumstances, population screening for the study of leukemia is extremely difficult and an unrealized dream. Therefore, we have to depend largely on the hospital based data.

## OBJECTIVES

A clinico-haematological study of acute myeloid leukemias was done at the Department of Pathology, JJM Medical College, Davangere, India from a period of June, 2006 to May, 2008 with the following objectives.

- To know the relative incidence of acute myeloid leukemia among the patients referred for complete haemogram at Department of Pathology, JJMMC, Davangere, India.
- To study the clinical manifestations and their correlation with various types of acute myeloid leukemia.
- To study the haematological profiles in acute myeloid leukemia.

## MATERIALS AND METHODS

The present study on “Clinico-Haematological Study of Acute Myeloid Leukemias” was undertaken during the period of June

2006 to May 2008 at Hematology unit, Department of Pathology, J J M Medical College, Davangere, India.

The cases from chigateri hospital, Bapuji hospital and other private hospitals situated in and around Davangere formed the material of the study. Case selection was based on clinical features and supported by laboratory evidences. Bone marrow aspiration was subsequently carried out after obtaining written consent from the patient or the guardian.

### Inclusion Criteria

- New cases of acute myeloid leukemia.

### Exclusion criteria

- Treated cases of acute myeloid leukemia.
- Blast crisis in chronic myeloid leukemia.

**The following investigations were done:**

1. Complete Haemogram was performed and the peripheral smear was stained by Leishman stain for all cases and examined in detail.
2. Bone marrow aspiration and study was done in all the cases and leishman's stain smears were examined.

In all cases, the following cyto-chemical stains were employed for diagnosis and subtyping of leukemias.

1. MPO-Myelo-peroxidase stain
2. SBB-Sudan Black B
3. PAS-Periodic Acid Schiff Stain
4. NSE-Non specific esterase stain

Acute myeloid leukemias were classified based on the FAB (French-American-British) criteria.

## RESULTS

The following results were recorded and analysed. A total of 1,039 patients were referred to the Department of Haematology during the period 2006 to 2008 out of which 50 patients were diagnosed as acute myeloid leukemia. In this study, the age of the patients ranged from five months to 85 years of age and the mean age was 27.75 years of age. The incidence of acute myeloid leukemia year-wise was observed in 2008 to be 4.4 whereas the lowest incidence was observed in 2006 with an incidence of 2.2. Out of 50 patients, 23 were female patients and 27 were male patients. Males were slightly more affected by the disease when compared to females.

| M0 | M1 | M2 | M3 | M4 | M5 | M6 | M7 |
|---|---|---|---|---|---|---|---|
| 0 | 10 (20%) | 22 (44%) | 3 (6%) | 11 (22%) | 4 (8%) | 0<br>- | 0<br>- |

**[Table/Fig-1]:** Distribution of acute myeloid leukemias according to morphological types
AML (Number-50; Percentage-100)

The morphological typing and sub-typing of leukemia was based on peripheral smear examination and bone marrow aspiration studies with cytochemical stains, employing the FAB criteria.

Complete hemogram revealed, anaemia (Hb<8gm/dl) in 47 patients (94%) and 8-10 gms/dl of Hb in 3 patients (6%). The total leucocyte count ranged from 0.6 × $10^9$ to 149×$10^9$/l. 25 (50%) patients had counts between 11-49×$10^9$/l and 9 (18%) patients had between 50-99×$10^9$/l and 5 patients (10%) had TLC above 100×$10^9$/l.

Thrombocytopenia was seen in all patients of AML. Nineteen (38%) of patients showed severe degree of thrombocytopenia (platelet count <50×$10^9$/l) and 19 (38%) had moderate to mild degree (50-100×$10^9$/l) and 12 (24%) patients with lower limit of normal platelet count that is <150×$10^9$/l.

Bone marrow aspiration was performed in all the 50 patients. AML was further subtyped by using the FAB criteria on morphological and cytochemical grounds into 8 subtypes M0 to M7. The demonstration of myeloid lineage was done by positive myeloperoxidase stain and sudan black B stain. The monocytic lineage cells were demonstrated based on morphological grounds.

The distribution of AML patients into various subtypes were;

AML M1 in 10 patients (20%)

AML M2 in 22 patients (44%)

AML M3 in 3 patients (6%)

AML M4 in 11 patients (22%)

AML M5 in 4 patients (8%)

No patients of AML M0, AML M6 and AML M7 were encountered in this study [Table/Fig-1].

### Acute Myeloblastic Leukemia with Minimal Maturation (AML-M1)

The diagnosis of AML-M1 was made in 10 patients constituting 20% of all AML patients. The age ranges 7-50 years with mean age of 22.4 years. The mean age of males and females was 26.2 years and 20.6 years respectively. There were five male patients and five female patients with a male female ratio of 1:1.

The main presenting symptoms of this subtype were fatigue or generalized weakness in five patients (50%) and fever in five patients (50%). Pallor was seen ranging from mild to severe in all 10 (100%) patients. Hepatomegaly was seen in six (60%) patients, splenomegaly was seen in 5 patients (50%).

Anemia was seen in all the patients. The Hb levels ranged from three to 9.8 gm/dl. Total leucocyte count ranged from 0.6×$10^9$/l to 50×$10^9$/l and with a mean 20.86×$10^9$/l. Thrombocytopenia was seen in all 10 patients with platelet counts ranging from 37×$10^9$/l to 140×$10^9$/l with a mean platelet count of 91×$10^9$/l.

Bone marrow aspiration was done in all the ten patients. In all the cases, myeloblast constituted more than 90% of the cells with a mean blast count of 92%. The mature myeloid series of cells accounted for less than 10% of the cells. Cytochemical stains showed MPO/SBB positivity in more than 3% of the blasts.

### Acute Myeloblastic Leukemia with Differentiation (AML-M2)

AML-M2 comprised of 22 patients constituting 44% of the total AML patients. It was the commonest subtype observed in this study. The age ranges 3-85 years. There were 12 males and 10 females with male to female ratio of 1.2:1.

The main presenting symptoms of this subtype were fever in all the 15 patients (68.18%), generalized weakness in 5 patients (22.72%), breathlessness in one patient (4.5%) and bony pain in one patient (4.5%).

Pallor was seen ranging from mild to severe in all 22 patients (100%). Hepatomegaly was seen in 20 patients (90.9%). Splenomegaly was seen in six patients (27%). Lymphadenopathy was seen in one patient (4.5%). Anaemia was seen in all the 22 patients. Haemoglobin levels ranged from 1.7-8gm/dl, with the mean haemoglobin being 5.17gm/dl. Total leucocyte count ranged from 0.6-102.9 ×$10^9$/l. The mean total leucocyte count was 35.75×$10^9$/l.

Thrombocytopenia was seen in all the 22 patients with platelet counts ranging from 0.14-150×$10^9$/l. Mean platelet count was 63.69×$10^9$/l.

Bone marrow aspiration was done in all 22 patients. Bone marrow was hypercellular. Blast percentage was 62%. Auer rods were seen in all the patients.

### Acute Promyelocytic Leukemia (AML-M3)

Three patients were diagnosed as AML-M3 comprising 6%. The age ranges 35-40 years with the mean age being 37.3 years. There

was one male and two female patients, with the male to female ratio of 1:2.

The mean age of male was 40 years and of female, it was 36 years. The main presenting symptoms were fever in two patients (66.6%) and bleeding gums in one patient (33.3%). Pallor was seen in all the 3 patients (100%). Hepatomegaly and gum hypertrophy was seen in one patient (33.3%). Splenomegaly was seen in two patients (66.6%).

Anaemia was seen in all the three patients (100%). The haemoglobin levels ranged from 3.6-8gm/dl and mean haemoglobin being 5.86gm/dl.

TLC ranged from 7.8-80×$10^9$/l. Mean TLC was 33.53×$10^9$/l. One patient had subleukemic count- 7.8×$10^9$/l.

Thrombocytopenia was seen in all the three patients with platelet count ranging from 30-65×$10^9$/l. Mean platelet count was 45×$10^9$/l.

Bone marrow aspiration was done in all the three patients. M:E ratio was 16:1. The predominant cells were myeloblasts and promyelocytes constituting 90%. Some of the promyelocytes showed multiple auer rods (Faggots). Cytochemical stains for MPO/SBB revealed strong positivity.

### Acute Myelomonocytic Leukemia (AML-M4)

The diagnosis of AML-M4 was done in 11 patients. The age ranges 6-80 years with the mean age of 42.3 years.

The mean age of males and females was 43.2years and 41.6 years respectively. There were 5 male patients and 6 female patients, with a male to female ratio of 0.8:1.

The main presenting symptoms of this subtype were fever in seven patients (63.61%), petechial rashes on the skin in two patients (18.18%), bony pain in one patient (9.1%) and breathlessness in one patient (9.1%).

Anaemia was seen in all the patients. Pallor was seen in all the 11 patients (100%). Hepatomegaly was seen in three patients (27.2%). Splenomegaly was seen in four patients (36.4%). Gum hypertrophy was seen in three patients (27.2%), Sternal tenderness in two patients (18.18%) and lymphadenopathy in one patient (9%).

The Hb levels ranged from 3 gm/dl to 7.5 gm/dl, with the mean Hb being 5.43 gm/dl.

TLC ranged from 15-149×$10^9$/l with mean TLC being 63.5×$10^9$/l

Thrombocytopenia was seen in all the patients, with platelet count ranging from 0.27×$10^9$/l to 140×$10^9$/l with mean platelet count being 82.9×$10^9$/l.

Bone marrow aspiration was done in the patients. The average blast count was 75%, which included cells of both myeloid series and monocytoid series. Cytochemical stains showed weakly positive MPO stains. Non-specific esterase stain was positive in most of the cases.

### Acute Monocytic Leukemia (AML-M5)

AML-M5 comprised of four patients constituting 8% of the total AML patients. The age range was 12-50 years and the mean age was 33 years.

There were four male patients and no female patients were encountered in this subtype.

The main presenting symptoms of this subtype were breathlessness in one patient (25%), fever in one patient (25%), hematuria in one patient (25%) and bleeding gum in one patient (25%).

Pallor was seen in all patients. Splenomegaly and gum hypertrophy was seen in three patients (75%). Hepatomegaly was seen in two patients (50%). Sternal tenderness was seen in one patient (25%).

The Hb levels ranged from 3.5-5 gm/dl with the mean Hb being 4.12 gm/dl.

Total leucocyte count ranged from 0.8-30×$10^9$/l with mean TLC being 8.25×$10^9$/l. Three patients had subleukemic count.

Thrombocytopenia was seen in all the four patients with platelet count being 40-95×$10^9$/l with mean platelet count being 58.75×$10^9$/l.

Bone marrow aspiration was done in all the four patients. Bone marrow aspiration showed a hypercellular marrow. Leucopoiesis showed a predominance of monocytoid blasts (> 80%). Cytochemical staining for Non-specific esterase stain was positive in most of the cases and MPO/SBB showed negative staining and PAS stains were also negative.

M6 and M7 subtypes were not encountered in this study.

## DISCUSSION

In the present study, 50 patients were diagnosed with acute myeloid leukemia after being subjected to detailed clinical history and examination followed by a complete hematological work up along with special stains and bone marrow examination.

In the AML patients of our study, the main presenting symptoms in the study were fever and generalized weakness. Similar presenting symptoms were observed by studies conducted by Advani et al., [8], Shome et al., [9] and Mathur et al., [10].

Pallor was seen as a presenting symptom in 100% of the patients. This correlates with the study conducted by Mathur et al.

In our study, incidence of Lymphadenopathy correlates well with study of Advani et al. (4%), whereas in other studies done by Shome et aland Mathur et al lymphadenopathy was seen in more than 30% of patients.

In our study, Hepatomegaly was seen in 64% of patients and Splenomegaly was seen in 40% 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.

Anemia, in the present study correlates well with the study done by Mathur et al.

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

Thrombocytopenia was present in all the cases in the present study. Platelet count ranged from 25-105 ×$10^9$/l with a mean platelet count of 70.6 ×$10^9$/l. In studies conducted by Mathur et al., mean platelet range was 0-150×$10^9$/l with a mean of 58.4×$10^9$/l. Thrombocytopenia is an important finding in acute leukemias.

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

Applying the FAB classification, M2 was found to be the commonest subtype followed closely by M4 variety. Next was M1 which was followed by M5 and M3 was the rarest of all the subtypes. Similar observations were found in the study conducted by Shome et al.,

The mean ages of various subtypes of AML in this study correlates with the study conducted by Shome et al.,

Clinical features in our study correlated well with the study conducted by Shome et al.,

Anemia was a common feature in our study as observed by Shome et al.

The TLC in the present study compares well with Shome et al., except for AML-M2, it is less and AML-M4, it is more.

Thrombocytopenia correlates well with the study conducted by Shome et al., in M1 and M2 subtypes, but it is more in our study in M3, M4 and M5 subtypes.

Bone marrow study is indicated when there is clinical or laboratory

evidence of progressive depression of platelet, granulocyte or haemoglobin levels or in the presence of unexplained splenomegaly, generalised lymphadenopathy or bone involvement.

The observations of bone marrow aspiration was similar to findings of study conducted by Shome et al.,

## CONCLUSION

The present study is to highlight that light microscopic features of peripheral smear and bone marrow still remain mainstay in the diagnosis of acute leukemias, whereas immunotyping and cytogenetics are complimentary procedures at specialised centres.

However, with newer modalities of therapy and rewarding curative results in hematological malignancies, the use of cytochemistry, immunotyping and cytogenetics have become gold standards for arriving at a specific diagnosis.

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**PARTICULARS OF CONTRIBUTORS:**
1. Assistant Professor, Department of Pathology, JJM Medical College, Davangere, India.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**
Dr. Preethi C.R.,
Door No. 3055, 8th Main 3rd Cross, MCC B Block, Davangere, India.
Phone: 9880499151, E-mail: drshanni@gmail.com

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