

Evaluation of Frequency and Clinico-Hematological Features of Acute Myeloid Leukemia at a Tertiary Care Hospital, Lahore

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ABSTRACT

Objective: To evaluate the frequency and clinic hematological features of AML.

Study design: cross sectional observational prospective study of 5 year duration.

Patients and methods: Newly diagnosed cases of AML of all age groups and both genders were included in the study. The exclusion criteria included patients who were already diagnosed, were on chemotherapy or radiotherapy of AML. A detailed history including age of presentation of the disease and general and physical examination were obtained. History of exposure to drugs, chemicals and occupational history were noted. Laboratory analysis included complete blood counts and bone marrow examination.

Results: In 82 patients of acute leukemia, frequency of ALL was 47(57.3%) and AML was 35(42.7%). Out of 35 AML patients, 21(60%) were male and 7(40%) were female. Of these 35 patients, 24(68.6%) were adults (>15 years of age) and 11(31.4%) were children (<15 years of age). Regarding subtypes of AML, M₃ was most common of all and its frequency was estimated to be about 13(37%) followed in order by M₂ which was 10 (29%), M₁ was 7(20%), M₄ was 3(8%) and M₆ was 2(6%). The most common presenting complaints were pallor, fever and bleeding. The constitutional signs were splenomegaly, hepatomegaly, lymphadenopathy, gum hypertrophy, petechiae and bruises. Infiltration of soft tissues by leukemic cells was common in AML-M₃ and M₁.

Conclusion: Acute myeloid leukemia is more common in adults with a male preponderance. Its clinical manifestations are variable in its different subtypes.

Keywords: Leukemia, AML, Frequency, Clinical Features. AML Subtypes

INTRODUCTION

Acute myeloid leukemia is a clonal hematopoietic disorder that may be derived from either a hematopoietic stem cell or a lineage-specific progenitor cell. AML is characterized both by a predominance of immature forms and loss of normal hematopoiesis. Single or multiple hematopoietic lineages may comprise the leukemic clone. The blast percentage is 20% in the peripheral blood and bone marrow; a lower percentage is acceptable in cases with AML-defining translocations¹.

Acute myeloid leukemias (AMLs) are infrequent, yet highly malignant neoplasms responsible for a large number of cancer-related deaths. AML can occur in patients of any age, but in general, both the overall incidence and the proportion of total acute leukemias that are myeloid increase with age. The incidence of AML increases through adulthood, during which period 70%-80% of acute leukemias are AML. AML affects all age groups. AML is more common in men than in women. The difference is even more apparent in older patients^{2,3}.

Most signs and symptoms of AML are caused by the replacement of normal blood cells with leukemic cells and suppression of normal hemopoiesis resulting in anemia, thrombocytopenia and leucopenia. Some generalized symptoms include fever, fatigue, weight loss or loss of appetite or frequent infections. Enlargement of the spleen may occur in AML. Lymphadenopathy is rare in AML, in contrast to acute lymphoblastic leukemia. The skin is involved about 10% of cases of AML⁴. Some patients with AML may experience swelling of the gums because of infiltration of leukemic cells into the gum tissue. Rarely, the first sign of leukemia may be the development of a solid leukemic mass or tumor outside of the bone marrow, called a chloroma. Occasionally, a person may show no symptoms, and the leukemia may be discovered incidentally during a routine blood test⁵.

METHODOLOGY

This was a cross-sectional study conducted in the Pathology Department of Postgraduate Medical Institute Lahore for a period of 5 years from April 2008 – April 2013. All newly diagnosed cases of AML belonging to all age groups and both genders were

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included in the study. Previously diagnosed or relapsed patients and patients on chemotherapy were excluded.

Acute leukemia was diagnosed in 82 patients, out of which 47 were diagnosed as Acute Lymphoblastic Leukemia (ALL) and 35 as Acute Myeloid Leukemia (AML). A detailed relevant history including age, sex, occupation and duration of symptoms was obtained with special emphasis on constitutional symptoms like fever, pallor, shortness of breath and bleeding. Physical examination was performed which included splenomegaly, hepatomegaly, lymphadenopathy, purpuric or petechial rashes and gum hyperplasia.

Complete blood counts were done on automated hematology analyzer. Bone marrow examination including aspiration and trephine biopsy were performed from posterior iliac crest in all patients except those under 1 year of age in whom aspiration was done from tibia. The peripheral blood and bone marrow smears were stained with Giemsa and Sudan Black B. Trephine biopsy and clot were processed and stained with Hematoxylin and Eosin. Diagnosis of AML was confirmed on the basis of bone marrow aspirate morphology and positivity of granules in the blast cell with special cytochemical stain, Sudan Black B. FAB classification of AML was applied for sub-typing of AML.

RESULTS

Detail of results is given in tables 1, 2, 3 and 4. A total number of 82 patients of acute leukemia were observed in the study. 47(57.3%) were diagnosed as ALL and 35(42.7%) were diagnosed as AML. Out of the 35 patients 21(60%) were males and 7(40%) were females with a male to female ratio of 3:2).

Among the AML sub-types, 13 (37.1%) patients had AML-M₃ and 10(28.5%) had M₂ which were most common sub-types. The lesser common sub-types were M₁: 7(20%) patients, M₄: 3 (8%) patients and M₆ :2(6%) patients (table 1). All the patients belonged to all age groups with an age range of 1 ½ year to 75 years. Among them 9(26%) were below the age of 15 years, 22(63%) were in the adult age group and 4(11%) were in the old age group. So the maximum number of patients was observed in the adult age group (Table 2). The most common presenting symptoms were fatigue (91%), fever (86%) and bleeding from different sites (40%). The less common symptoms were generalized weakness (37%), weight loss (29%), productive cough (11%) and anorexia and vomiting (4%) (Table 3).

Table 1: Frequency of sub-types of AML

AML	M ₁	M ₂	M ₃	M ₄	M ₆	Total
=n	7	10	13	3	2	35
%age	20	29	37	8	6	100

Table 2: Age distribution of subjects (n=35)

Age (Range)	=n	% age
0-15 yrs (Child)	09	26
16-60 yrs (Adult)	22	63
61-80 yrs (Old)	04	11

Table 3: Frequency of clinical symptoms

Symptoms	=n	%age
Easy fatigue	32	91
Fever	30	86
Bleeding	14	40
Generalized weakness	13	37
Weight loss	10	29
Productive cough	4	11
Anorexia/ vomiting	4	11

Table 4: Clinical signs in sub-types of AML

Signs	M ₁	M ₂	M ₃	M ₄	M ₆
Pallor	7(100%)	10(100%)	13(100%)	3(100%)	2(100%)
Splenomegaly	5(71%)	4(40%)	5(38%)	2(67%)	2(100%)
Hepatomegaly	4(5%)	2(20%)	4(31%)	2(67%)	2(100%)
Lymphadenopathy	4(5%)	-----	3(23%)	3(100%)	-----
Gum Hyperplasia	2(29%)	1(10%)	2(15%)	-----	1(50%)
Bruises/ Petechiae	3(43%)	3(30%)	2(15%)	1(33%)	-----
Intraocular swelling	-----	-----	1(8%)	-----	-----
Meningitis	-----	-----	-----	1(33%)	-----

DISCUSSION

In the present study male preponderance was observed in the AML patients and it was consistent with other studies^{6,7,8,9}. The male to female ratio in present study was 3:2 while in the study by Kumar et al it was 2:1¹⁰. AML is primarily a malignancy of adults and its overall incidence increases with age.

The present study confirmed this because maximum number of patients was in the adult age group (63%). These results are consistent with other studies^{7,11} and a study at Armed Forces Bone Marrow transplant Centre¹². The median age for AML is quite high in the West as compared to the studies in Pakistan. In a study in UK from 26 hospitals the median age was 67

years¹³. A study in Spain showed median age of 61 years¹⁴ and in Japan and Australia 51 and 52 years respectively. This higher mean age in the West might be due to overall higher mean age in these countries as compared to the East¹⁵. An overall reduction in hematopoiesis, due to marrow proliferation of abnormal blast cells, results in the common clinical manifestations of anemia, thrombocytopenia and leucopenia with the clinical signs and symptoms of pallor, easy fatigue, dyspnea, bleeding manifestations and fever.

Anemia was the commonest sign (100%) followed in order by thrombocytopenia (86%) and leucopenia (11.4%). The similar features were present in the other studies as well. Ghosh et al., 2003 reported pallor and fatigue in most of their patients, followed in order by bleeding which was common in AML-M₃ and AML-M₅¹⁶. In our study bleeding diathesis was most common in M₁ (43%) followed in order by M₄ (33%), M₂ (30%) and M₃ (15%). Splenomegaly (71%) and hepatomegaly (57%) was observed in the present study. In the study by Naghmi et al., splenomegaly and hepatomegaly were 45% and 48% and the study by Fozia et al., gave the incidence as 27% and 40% respectively. The study by Kumar et al¹⁰ observed that 42% patients had splenomegaly. In the present study 29% patients had lymphadenopathy comparable with the studies by Fozia et al (20%) and Naghmi et al (38%). Gum hyperplasia was present in 17% patients in the present study while Naghmi et al observed it in 10% of the patients, 24% in a study by Kumar et al., and 27% in the study by Fozia et al.

Tissue infiltration was most frequent in M₆, M₁ and M₄, in the present study and it was comparable with other studies, AML-M₄, M₅, M₁¹⁰ and AML-M₅, M₄, M₁⁸. Two patients with AML-M₃ in the present study presented with extramedullary leukemia. One presented with orbital mass and the other with mass at lumbar region with collapse of a lumbar vertebra. To look for the frequency of tissue infiltration in AML subtypes, it was noted that hepatosplenomegaly, lymphadenopathy and gum hyperplasia were the most frequent findings in AML-M₆, M₁, M₄, and M₂. There is geographical variation reported in the distribution of extramedullary leukemia. It is more frequently reported in Uganda, Egypt and Turkey¹⁷. Hence we can conclude that AML is the malignancy of adult age, more common in males and has different subtypes with variable symptoms according to these subtypes.

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