



ACUTE MYELOID LEUKEMIA; DEMOGRAPHIC FEATURES AND FREQUENCY OF VARIOUS SUBTYPES IN ADULT AGE GROUP.

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ABSTRACT... Background: Acute myeloid leukemia (AML) is an aggressive haematological malignancy with highest incidence in older adults. AML accounts for approximately 25% of all leukemias in adults in the Western world, and therefore is the most frequent form of leukemia. **Objective:** The aim of study was to analyze the demographic and clinical features and frequency of various subtypes of acute myeloid leukemia in adult age group in our population. **Study design:** Descriptive Cross sectional survey. **Settings:** The study was conducted in Pathology Department, King Edward Medical University, Lahore. **Study Period:** Five years September 2007 to September 2011. **Material and Methods:** A five year data of patients diagnosed as acute myeloid leukemia was collected from September 2007 to September 2011 in Pathology Department, King Edward Medical University, Lahore. Patients on chemotherapy and radiotherapy were excluded from the study. **Results:** Among the 77 patients of Acute Myeloid Leukemia, Acute myeloid leukemia with maturation AML M2 (37.7%) was the most common subtype and the least common was Acute megakaryoblastic leukemia AML M7 (1.3%). Mean age for AML was 28 years (Range 15-75 years). M:F ratio was 1.5:1. Fever was found be the most frequent presenting feature followed by pallor, bleeding and gum hypertrophy in the descending order. More than 50% patients presented with hepatosplenomegaly. Lymphadenopathy was seen in 30% of patients. Mean peripheral blood blast count was 29%. 12 patients (15.5%) presented with pancytopenia. **Conclusion:** The study showed male predominance in Acute myeloid leukemia with mean age of 28 years and the most common subtype was AML- M2.

Key words: Acute myeloid leukemia, demographic features, subtypes.

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INTRODUCTION

The leukemias are a group of disorders characterized by accumulation of malignant white cells in the bone marrow and blood leading to symptoms caused by bone marrow failure and infiltration of organs. Acute myeloid leukemia (AML) is an aggressive haematological malignancy with maturation arrest in granulopoiesis resulting in accumulation of primitive blast cells in bone marrow with highest incidence in older adults. Incidence of (AML) is 3–4 persons per 100,000 individuals, with a median age at diagnosis of 67 years.¹ AML accounts for approximately 25% of all leukemias in adults in the Western world, and therefore is the most frequent form of leukemia. Worldwide, the incidence of AML is highest in the U.S., Australia, and western Europe.^{2,3} AML in adults has a slight male predominance in

most countries.^{1,4} AML is classified according to French-American-British (FAB) classification which classifies AML into 8 subtypes. The diagnosis by FAB requires assessment of blood and bone marrow smears and cytochemistry. In the recent years, the FAB classification has been superseded by the revised scheme devised by World Health Organization (WHO) which includes cytogenetic and molecular characteristics. The FAB classification system AML is extensively used and is incorporated into the AML, not otherwise specified (NOS) category in the 2016 WHO edition of myeloid neoplasm classification.⁵ Patients with acute myelogenous leukemia (AML) present with symptoms resulting from bone marrow failure, symptoms resulting from organ infiltration with leukemic cells, or both. Symptoms of bone marrow failure are related

to anemia, neutropenia, and thrombocytopenia. Patients usually present with dyspnea, dizziness, weakness, fever and bleeding manifestations. The most common sites of infiltration include the spleen, liver, gums, and skin. Infiltration occurs most commonly in patients with the monocytic subtypes of AML.⁶

MATERIAL AND METHODS

For this case series study a five year data of patients diagnosed as acute myeloid leukemia was collected from September 2007 to September 2011 in Pathology Department, King Edward Medical University, Lahore. Total 77 patients both male and female having age range (15-75years) were included in the study. Demographic data including age, gender etc. was noted. Patients on chemotherapy and radiotherapy were excluded from the study. Relapsed cases of AML were also excluded. Complete blood counts were done by automated blood cell counters (Sysmex KX-21). Bone marrow aspirate and trephine biopsy were done from posterior superior iliac spine under aseptic technique and local anesthesia. Cytochemical stains (Sudan Black B, PAS, Non specific esterase) were performed. Classification of Acute myeloid leukemia was based on morphology of peripheral blood film, bone marrow aspirate and trephine biopsy, cytochemical stains and immunophenotyping where required. Data was compiled and analyzed using SPSS version 18 and the results were expressed as mean and percentage.

RESULTS

Among the 77 patients diagnosed as Acute Myeloid Leukemia (AML). Mean presenting age for AML was 28 years (Range 15-75 years) (Table-I). Acute myeloid leukemia with maturation AML-M2 (37.7%) was the most common subtype and the least common was Acute megakaryoblastic leukemia AML- M7 (1.3%). Frequencies of other subtypes were as follows, AML- M0 (7.8%), AML-M1 (6.5%), AML-M3 (22%), AML-M4 (15.6%), AML-M5 (6.5%) and AML-M6 (2.6%) (Table-II). M:F ratio was 1.5:1 with 62% males and 37% females (Figure-1). Fever was found in 96% of patients. Bleeding manifestations were most frequently associated with AML-M3 (82%) followed by

AML-M2 (34%) and AML-M4 (16.6%). Weakness and pallor were found in 40.7% of the patients. Hepatomegaly was observed in 26.1% patients, while splenomegaly and lymphadenopathy were seen in 28.6% and 27.2% patients respectively. Rare presenting features included gum hypertrophy 5.2%, proptosis 1.3%, malena 4%, bloody diarrhea 2.3% and pleural effusion 2.6%. Mean Total Leucocyte count (TLC) was $7.2 \times 10^3/\mu\text{l}$ with highest mean TLC of $74.5 \times 10^3/\mu\text{l}$ in Acute myelomonocytic leukemia- M4 and lowest mean TLC $0.5 \times 10^3/\mu\text{l}$ in Acute megakaryoblastic leukemia-M7. 23.3% patients presented with normal TLC. This study showed a mean Hb level of 7.2g/dl and mean Platelet count of $38 \times 10^3/\mu\text{l}$. Mean peripheral blood blast count was 29%. 12 patients (15.5%) presented with pancytopenia.

Age distribution of patients		
Age range(Years)	Number of patients (n)	Percentage %
15-25	41	53.2
26-35	14	18.18
36-45	08	10.38
46-55	03	3.89
56-65	08	10.38
66-75	03	3.89

Table-I. Age distribution of patients in Acute Myeloid Leukemia

Frequency of subtypes of Acute Myeloid Leukemia	
AML-M0	7.8%
AML-M1	6.5%
AML-M2	37.6%
AML-M3	22%
AML-M4	15.6%
AML-M5	6.5%
AML-M6	2.6%
AML-M7	1.3%

Table-II. Frequency of various subtypes of Acute Myeloid Leukemia

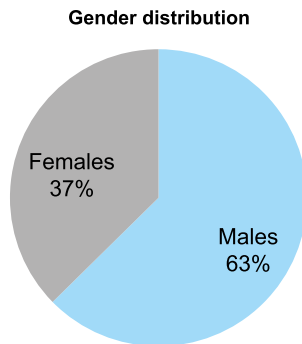


Figure-1.

DISCUSSION

Acute myeloid leukemia (AML) is characterized by a clonal expansion of undifferentiated myeloid precursors resulting in impaired hematopoiesis and bone marrow failure. It can occur at all ages with peak incidence in older age. Incidence of (AML) is 3–4 persons per 100,000 individuals, with a median age at diagnosis of 67 years.⁶ This disease shows male predominance.

In this study demographic features like age and gender, presenting features and frequency of various subtypes of AML were studied. Total 77 patients were included in the study. The mean age of the patients was 28 years. This was comparable to the studies conducted previously in Pakistan showing mean age of 29 years and 34.5 years respectively.^{7,8} This was also comparable to studies conducted in India where median age was 30 years and in Bangladesh where median age was 35 years.^{9,10} However when mean age was compared with studies conducted in western countries, there was difference in the mean age at presentation. In Western countries, AML generally affects older people with a median age of 65-67 years.^{11,12} A study conducted in France showed that 60.6 % of AML was observed in people aged 60 years and above.¹³ This difference might be due to different geographical distribution and genetics.

AML is generally more common in males. In our study there was male predominance shown by M:F of 1.5:1. Studies conducted Pakistan also showed male predominance with M:F of 1.5:1.^{7,8} A study conducted in Fujian China showed male predominance in AML as well.¹⁴

In this study according to FAB classification, AML-M2 (37.7%) was the most frequent subtype followed by M3 (22%), M4 (15.6%), M0 (7.8%), M5 (6.5%), M1 (6.5%), M6 (2.6%) and M7 (1.3%). A study conducted in Pakistan showed AML- M2 followed by M4 and M5. In a study conducted in Morocco, the distribution of AML according to the FAB classification, revealed that M2 was the predominant FAB subtype (46 %), followed by M3 and M5 (17 %), M1 (8 %), M0, M4 and M6 (4 %).¹⁵ A study conducted in China showed the most frequent subtype to be M2.¹⁶ The predominance of M2 was also observed in Iran, India, Germany, USA and Singapore.^{17,18}

Symptoms of AML are attributed to bone marrow infiltration with leukemic cells resulting in bone marrow failure and organ infiltration. In this study, the most frequent symptom was fever (96%) followed by weakness and pallor (31%), bleeding manifestations (31%) and gum hypertrophy (6.4%). Previous studies conducted in Pakistan by Sultan S et al showed the major complaint as fever (72.8%), generalized weakness (60%) and dyspnea (12%) and Asif N et al showed fever (80.4%), pallor (46.4%) bleeding (44.5%) gum hypertrophy (10.7%).^{8,19} In this study, physical examination revealed hepatomegaly (21.6%), splenomegaly (28.6%) and lymphadenopathy (27.2%). A study conducted in Pakistan revealed splenomegaly (16%), hepatomegaly (12.8%) and lymphadenopathy (10.4%).⁸ These findings were consistent with our results. Mean Hb was 7.2 g/dl, mean Platelet count was $38 \times 10^3 \mu\text{l}$ while Mean TLC was $37.17 \times 10^3 \mu\text{l}$. A study conducted by Ehsan A showed mean Hb as 7.22g/dl, mean Platelet count as $27.63 \times 10^3 \mu\text{l}$ and mean TLC as $47.17 \times 10^3 \mu\text{l}$ which were comparable with our results.²⁰

CONCLUSION

It is concluded that AML presents at a younger age in our population as compared to western countries. The disease shows male predominance with the most frequent subtype as AML-M2.

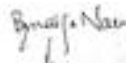

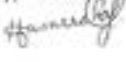
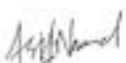
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