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Clinicopathological study of acute myeloid leukemia in a tertiary care hospital

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***Abstract*---**Background- The diagnosis of acute myeloid leukemia is based on peripheral blood smear and bone marrow examination. Immunophenotyping characteristics and cytogenetics have clinical relevance besides morphological features in these cases. Present study aims at clinicohematological evaluation of cases of acute myeloid leukemia diagnosed at hematology unit of our tertiary care hospital. Objectives –Present study aimed to diagnose and classify cases of acute myeloid leukemia with clinicohematological correlation. Material and methods- newly diagnosed cases of acute myeloid leukemia within a period of 1 year from May 2020 to May 2021 were included in this cross sectional and prospective study. In addition to hematological work up, flow cytometry, cytogenetics and molecular studies were taken into consideration for clinicohematological evaluation.Result- The study included 14 cases of acute myeloid leukemia which were classified as per FAB classification as AML M1- 7 cases, M3 – 3 cases and M4 and M5 – 2 cases each.

***Keywords*---**acute myeloid leukemia, FAB classification, clinicohematological correlation.

Introduction

Acute myeloid leukemia is a clonal expansion of myeloid blasts in the bone marrow, blood or other tissue. The WHO classification of the acute leukemias incorporates morphologic, immunophenotypic, genetic, and clinical features in an attempt to define entities that are biologically homogenous and that have clinical relevance [1]. The FAB classification system can be useful, but it doesn't take into account many of the factors that are now known to affect prognosis [2]. The World Health Organization (WHO) system, most recently updated in 2016, includes some of these factors to try to better classify AML [3]. The present study is a clinicopathological evaluation of cases of acute myeloid leukemia with special emphasis on clinical features, morphology and immunophenotypic characteristics.

Aims and Objectives

To diagnose cases of acute myeloid leukemia and their evaluation with specific reference to clinical features, morphology and immunophenotypic characteristics.

Materials and Methods

The study was a 2-year cross-sectional prospective study of clinicohematological evaluation of cases of acute myeloid leukemia with special reference to morphology and immunophenotypic features. The study was carried out in hematology section of our hospital which is a tertiary care center from May 2020 to May 2021. Ethical clearance was obtained from institutional ethical committee. All the newly diagnosed patients of AML were included in the study. Clinical details were obtained from the case record. EDTA sample was collected for hematological work up [9]. Bone marrow aspiration was performed with informed consent [10]. For immunophenotyping, blood samples were sent to reference lab. On bone marrow aspiration, cases of AML were classified as per FAB classification based on morphology of blasts, clinicohematology evaluation was done with specific to morphology and immunophenotypic characteristics.

Observations and Results

A total of 14 cases of AML were diagnosed using bone marrow aspiration in the present study. AML was most prevalent in the age range of 11-20 years (Table 1). Males (57.15 %) were predominant than females in this study (42.85 %) with ratio of 1.3:1 (Figure 1).

Table 1: Age distribution in AML

Age	Cases	Percentage
0-10	0	0%
11-20	4	28.6%
21-30	2	14.28%
31-40	1	7.14%
41-50	2	14.28%
51-60	3	21.42%

61-70	2	14.28%
>70	0	0%
Total	14	100%

Figure 1: Sex distribution in AML

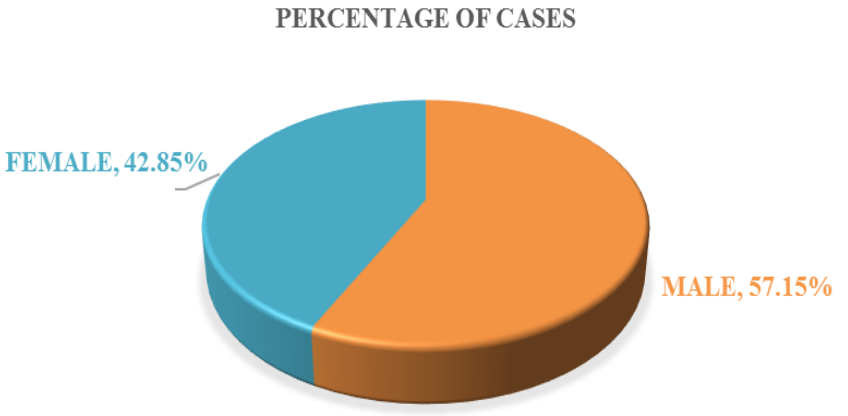


Figure 2: Clinical features of AML cases

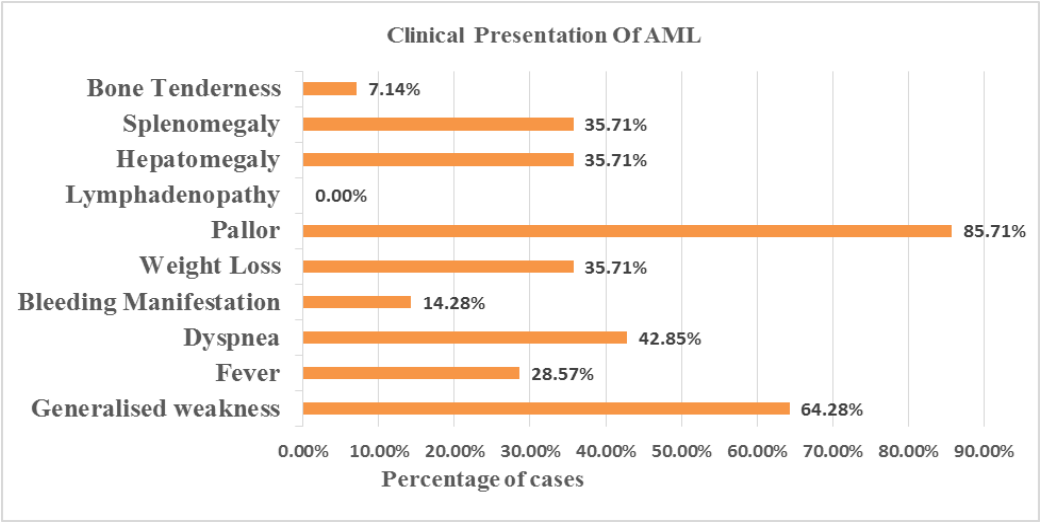


Figure 2 summarizes the clinical presentation of patients in this study. In 9 (64.28 %) cases of AML , generalized weakness was observed followed by dyspnea in 6 (42.85 %) cases. Pallor was seen in the majority of cases 12 (85.71 %) and hepatosplenomegaly was present in 5 (35.71 %) cases.

Table 2: Hemoglobin distribution in AML

Hemoglobin percentage	No. Of cases	Percentage

1 - 3	0	0%
3.1 - 5	1	7.16%
5.1 - 7	2	14.28%
7.1 - 10	9	64.28%
10.1 – 13	0	0%
13.1 – 16	2	14.28%
>16	0	0%
Total	14	100%

Table 3: Total leucocyte count distribution in AML

WBC count	No. Of cases	Percentage
500 - 4000	2	14.28%
4001 – 11000	0	0.0%
>11001	12	85.72%
Total	14	100%

Table 4: Severity of thrombocytopenia in AML

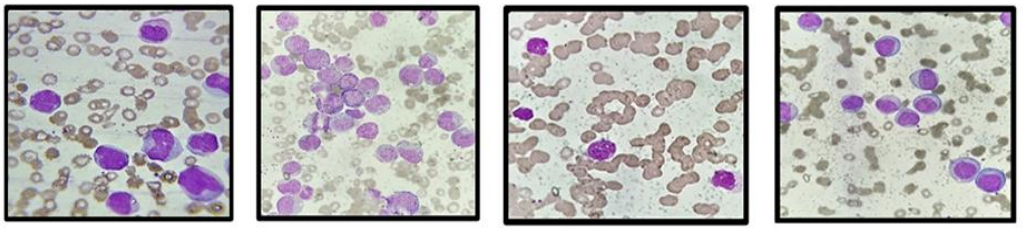
Platelet count	No. Of cases	Percentage
Mild >1 – 1.5l	2	14.29%
Moderate 50,000 - <1.0l	5	35.71%
Severe <50,000	7	50%
Total	14	100%

The hemoglobin concentration varied between 3.1 and 16 gm%. Nine (64.28%) patients showed hemoglobin values between 7.1 and 10 gm%. Leukocytosis was seen in 12/14 patients of acute leukemia in the study. Two (14.28 %) patients were classified as sub leukemic leukemia. The platelet count was between 50000 and 1.50 cells L/mm^3. Seven (50%) patients had severe thrombocytopenia (Tables 2-4).

Peripheral Blood Picture

The erythrocytes were normocytic normochromic with nRBC.The leukocyte count was increased with a presence of immature cells i.e., myeloblast. Myeloblasts with fine chromatin, 2-3 nucleoli and occasional Auer rods were seen. Platelets were decreased (Figure 3, a-d).

Figure 3: Peripheral smear in AML



a. PS- AML M1 - Myeloblast, Leishman Stain (1000X)

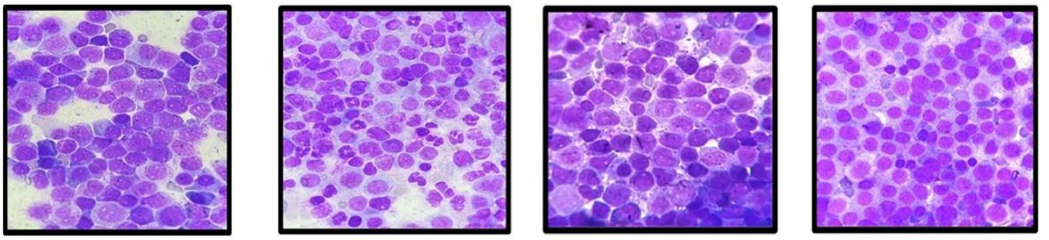
b. PS- AML M3, Leishman Stain (400X)

c. PS- AML M4, Leishman Stain (400X)

d. PS- AML M5, Leishman Stain (400X)

Bone marrow

In all cases, bone marrow was found to be hypercellular. Erythroid series were suppressed. Myeloid hyperplasia was observed with more than 20% blasts in all cases. Megakaryocytes were reduced. Cytomorphology revealed MPO positivity (Figure 4, a-d).



a. BMA- AML M1 with blast, Leishman Stain (1000X)

b. BMA- AML M3, Giemsa Stain (400X)

c. BMA- AML M4, Giemsa Stain (400X)

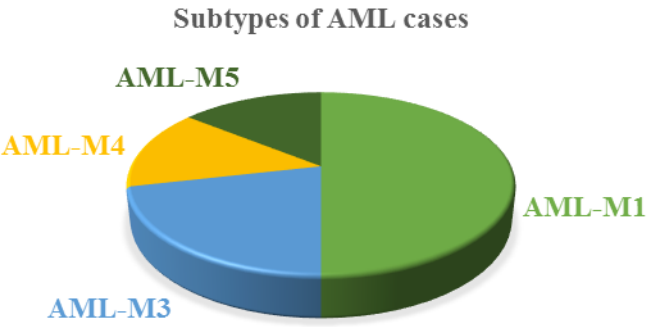
d. BMA- AML M5, Giemsa Stain (400X)

Table 5:FAB classification of AML

Subtype of AML	No. of cases	Percentage
AML- M1	7	50%
AML-M3	3	21.44
AML-M4	2	14.28
AML-M5	2	14.28
Total	14	100%

There are 7 subtypes of AML. Among cases studied , seven (50%) patients were found to be AML- M1 subtype , 3 (21.44%) cases of AML- M3 subtype and 2 (14.28%) cases each of AML- M4 and AML –M5 subtype (Table 5 & Figure 3).

Figure 5: FAB classification of AML



Immunophenotyping in cases of AML

In 8/14 (57.14 %) of the patients, immunophenotyping revealed positive for CD 45, CD 11b, CD 13, CD 15, CD 34, CD 117 and HLA-DR. In one case of AML-M1, cytogenetics revealed a 7q deletion along with numerous abnormalities/complex karyotype, all of which contributed to the patient's bad prognosis. AML FISH Panel was performed in one case of AML-M1 which revealed +21q and resulted in a bad prognosis.

Discussion

In this study, 14 cases of AML were identified with a male predominance (1.3:1). The highest prevalence was seen in the age group of 11-20 years at 28.6 %. Girish Taori et al. found 18.01 % cases with a male preponderance of 1.01:1[4]. Kulshrestha R et al. found a comparable prevalence with the highest incidence (22.92 %) in children under the age of 20 and a male to female ratio of 1.07:1[5]. A study done by Amita Yadav found that 9.4 % of patients were identified with AML, with the highest prevalence occurring in the age group of more than 15 years but less than 34 years with a male predominance (1.76:1) (Table 6) [6].

Table 6: Comparison of age and sex distribution in cases of AML with other studies

Study	Peak age incidence	Sex preponderance
Kulshrestha R (2009) [5]	Below 20 years	Male (1.07:1)
Amita Yadav (2017) [6]	More than 15 years but less than 34 years	Male (1.76:1)
Girish Taori (2019) [4]	15-25 years	Male (1.01:1)
Present Study (2021)	11-20 years	Male (1.3:1)

The majority of patients in this study had pallor, generalized weakness and breathlessness. Hepatomegaly and splenomegaly were seen in 35.71 % of cases in

this study which was concordant with the findings of a study done by I. Sreelakshmi[7]. The majority of patients (64.28 %) had Hb range between 7.1 - 10 gm%, leukocytosis was common (85.72 %) and two patients had leucopenia which was identified as sub-leukemic leukemia. In 50% of patients, severe thrombocytopenia (50,000/mm^3) was seen. Kulshrestha R and Shweta Joshi observed similar results [5] [8]. Present study had 50% of the AML in M3 subtype of FAB classification whereas Kulshrestha R had found 53.57% in M2 subtype of FAB classification (Table 7) [5].

Table 7: Correlation of FAB classification of AML with other studies

AML subtype	M0	M1	M2	M3	M4	M5	M6	M7
Kulshrestha R (2009)[5]	0%	8.93%	53.57%	23.21%	5.36%	7.14%	1.79%	0%
Present study (2021)	0%	50%	0%	21.44%	14.28%	14.28%	0%	0%

Although in the present study, we have focused on immunophenotyping and cytogenetic abnormalities in cases of AML, prospective study with large sample size and longer follow up period are needed for further validation of results.

Conclusion

AML cases are classified on the basis of cytogenetics and immunophenotyping as per WHO guidelines which helps to determine the best treatment options. The use of this updated WHO classification for AML provides consistency in reporting as well as aids in targeted therapy and prognosis prediction. However, the high cost and need for specialized reference laboratories is a disadvantage.

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