

Prevalence of the different FAB sub type of Acute Myeloid Leukemia related to hematological parameters in Sudanese

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Abstract

Background: Acute myeloid leukemia (AML) is a heterogeneous disease. Therefore, various parameters are needed to classify this disease into subtypes. The commonly used method for diagnosis and classification is based on FAB criteria using morphology and cytochemical stains. For some of the categories, immunopheno typing is necessary. The aim of present study is to determine the frequency of various sub types in acute myeloid leukemia using FAB criteria in our Sudanese population. This will aid in the correct diagnosis of acute leukemia and hence proper management of the patients.

Materials and Methods: This is retrospective study conducted at RICH & Fadiial Hospital from January 2014 to December 2016. The total number of subjects was 140 that included both adults and children. The patients were diagnosed on the basis of bone marrow morphology using FAB classification. Cytochemistry was done in all cases, while immunophenotyping was considered only in those cases that were found to be problematic.

Results: Among 140patients, 70 were males and 70 were females with male to female ratio 1:1. The age ranged between 3 years to 101 years with a mean age of 33 years. AML-M3 was the predominant French-American-British (FAB) subtype (29.3%) followed by M2 (19.3%), M4 (15%), M0 (12.9%), M1 (10%), M5 (6.5%), M7 (5%) and M6 (2.1%).

Conclusion: The most common FAB subtype observed in our study was Acute promyelocyticleukemia (M3).the incidence of male to female ratio are equally with medium age 33 years old.

Keywords: French-American-British (FAB) classification; Acute myeloid Leukemia (AML) subtypes;

Introduction

Acute leukaemia can be classified in many ways. An ideal classification is one which recognizes real entities with fundamental biological differences. The FAB classification of ALL and AML is based on morphology and cytochemical staining of blasts. However, the recent classification schemes proposed by the World Health Organization (WHO) require the additional evaluation of the leukemic blasts by molecular analysis and flow cytometry. The results of these 4 methods of evaluation (i.e., morphology, staining, molecular analysis, flow cytometry) not only differentiate ALL fromAML, but also categorize the subtypes of acute leukemia.

Acute myeloid leukemia (AML), also known as acute myelogenousleukemia or acute nonlymphocytic leukemia (ANLL). It is a group of neoplastic blood disorders characterized by the proliferation and accumulation of immature haematopoietic cells in the bone marrow and blood. AML accounts for approximately 20% of acute leukaemias in children and 80% of acute leukaemia in adults [1]. The incidence of AML progressively increases with age; in adults over the age of 65 years, the incidence is approximately 30 times the incidence of AML in children [2]. The underlying pathophysiology in acute myeloid leukaemia (AML) consists of a maturational arrest of bone marrow cells in the earliest stages of development. The mechanism of this arrest is under study, but in

many cases, it involves the activation of abnormal genes through chromosomal translocations and other genetic abnormalities [3]. There has not been any previous study addressing adult and children AML in Khartoum City. Accordingly this study was designed with the intent of providing preliminary data on different haematological and FAB subtype of adult and child AML patients in Khartoum City.

The French- American –British (FAB) classification system divides AML into eight subtypes, M0 through to M7, based on the type of cell from which the leukemia developed and its degree of maturity. This is done by examining the appearance of the malignant cells with light microscopy and/or by using cytogenetic to characterize any underlying chromosomal abnormalities. The subtypes have varying prognoses and responses to therapy. Although the WHO classification may be more useful, the FAB system is still widely used.

Eight FAB subtypes which was subsequently revised in 1985 [3]

- **M0:** Undifferentiated acute myeloblastic leukemia
- **M1:** Acute myeloblastic leukemia with minimal maturation
- **M2:** Acute myeloblastic leukemia with maturation (the most common subtype of AML in children)
- **M3:** Acute promyelocytic leukemia (APL)
- **M4:** Acute myelomonocytic leukemia (more common in children less than 2 years of age)
- **M5:** Acute monocytic leukemia (more common in children less than 2 years of age)
- **M6:** Acute erythroid leukemia
- **M7:** Acute megakaryoblastic leukemia

Subtypes M0 through M5 all start in immature forms of white blood cells. M6 AML starts in immature forms of red blood cells, while M7 AML starts in immature forms of cells that make platelets.

Patients and Methods

140 diagnosed patients with AML treated at RICH (the only hospital that treats acute leukemias in the region) and fadial specialist Hospital. Khartoum from December 2013 to September 2015 was enrolled in this retrospective study. It included patients of all age groups and both sexes. Exclusion criteria were the absence of complete medical records or bone marrow smears for review. Secondary leukemias (cases with a past history of chemotherapy or radiotherapy or myelodysplasia) and chronic myeloid leukemia in blast crisis were also excluded.

The diagnosis of AML was established according to the standard practice, and was based on peripheral blood and bone marrow morphology and cytochemistry. Immunophenotyping was done where considered essential. Hematological parameters were done on Sysmex KX21 autoanalyzer.

Bone marrow aspiration was done from posterior iliac crest under strict aseptic technique and local anesthesia. A written consent was taken from patients at the time of collection. In every case, 6-8 smears were made; two of them with peripheral smears were stained by Leishman's stain. In addition following cytochemical stains were carried out on peripheral blood and bone marrow smears in each case: Sudan blackB (SBB), periodic acid-Schiff (PAS), myeloperoxidase (MPO). The microscopic morphological examination of AML is based on the recommended criteria.

The project was approved by ministry of health in Khartoum and Hospitals Ethics Committee.

Statistical analysis

For statistical analysis excel computer program was used to compare between the results of different subtypes of AML

Results

Of 140 cases, 70 were males and 70 were females with male to female ratio 1:1. The mean age was 33 years (range 3 years –101 years). 47 cases (33.6%) were up to the age of 18 years comprising of 27 males and 20 females and their age ranges between 3 years- 18 years and 93 cases (66.4%) were more than 19 years (Figure 1). Their haematological parameters are given in Table 1. The CBC showed a wide range of variation in hemoglobin concentration and platelets ranging from subnormal to normal. Their Leukocyte count also showed variation from leucopenia to hyper leukocytosis.

Fab Group	< 18 Years n %	> 18 Years n %
M0	03 (23.8)	15 (16.1)
M1	05 (4.7)	09 (9.7)
M2	10 (21.3)	17 (18.3)
M3	17 (36.2)	25 (26.9)
M4	07 (33.3)	14 (15.0)
M5	03 (6.4)	06 (6.5)
M6	01 (2.1)	02 (2.2)
M7	03 (0)	04 (4.3)

Table 1: Distribution of FAB according to age group (n= 140)

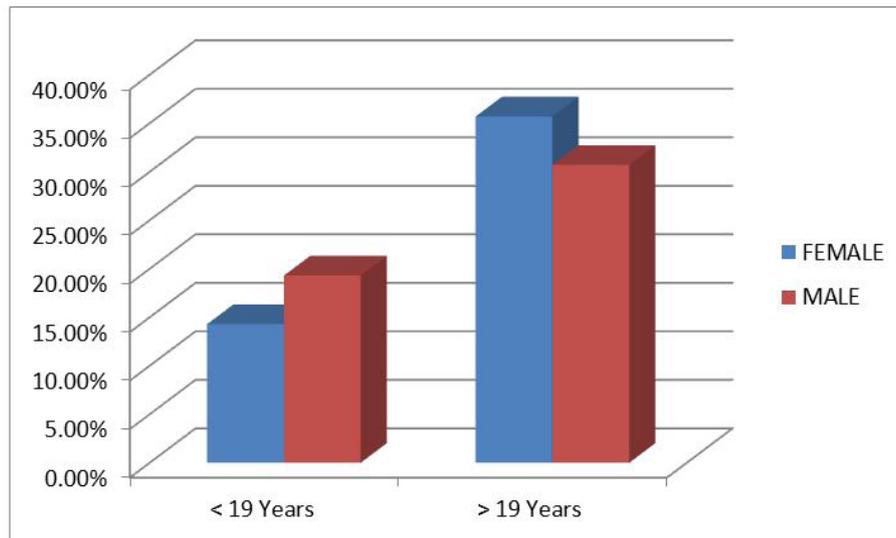


Figure 1: Distribution of gender according to age group

In our study, we found AML (M3 FAB subtypes) to be the commonest comprising 41 out of 140 of total cases (29.3%). The frequency of various AML subtypes according to FAB classification is given in Figure 2.

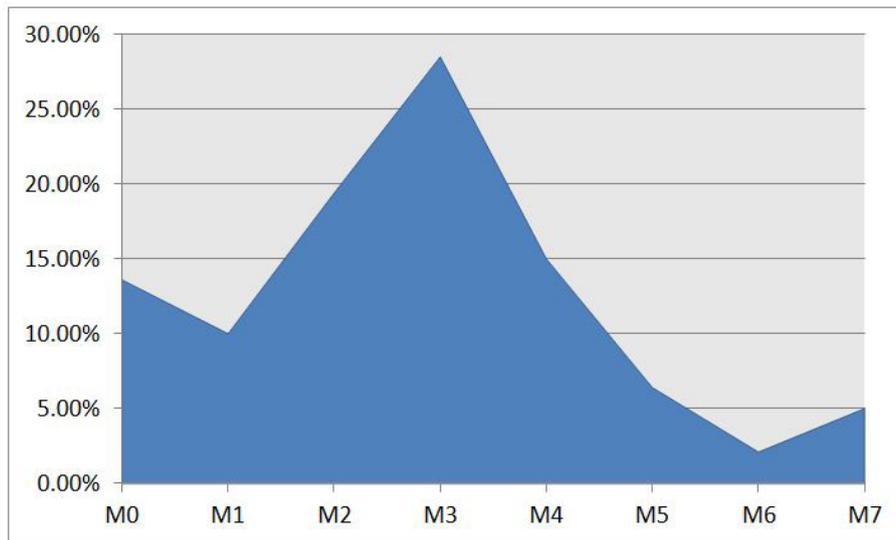


Figure 2: French –American –British (FAB) Sub types in 140 cases of AML

There is no different in pediatrics AML and adult AML in distribution of sub type of AML, which given in Table 1. Hematological parameter with different FAB sub type is seen in Table 1 and mean of hematological parameter in Table 2.

Parameter	Mean	Range
Hemoglobin (gm/dl)	8.4	2.2-14.4
White Cell Count ($10^9/l$)	63.39	0.6-497.4
Platelet count ($10^9/l$)	48.9	1.0-270.0

Table 2: Hematological parameters in AML patients (n = 140)

Discussion

Geographical variations have been described for age and sex distribution as well as FAB (French-American-British classification) subtypes of acute leukemias, possibly due to ethnic and environmental factors. Our study reported Promyelocytic leukemia (FAB-M3) as the most common subtype accounting for 28.5% of cases followed by M2 with 19.4% which similar to result in Iraq that reported the M3 subtype was the commonest one account for 26.9% and followed with M2 with 22.2% [15]. Arber *et al* reported M2 as the commonest subtype followed by M5 [4]. Most published data indicate the predominance of M2 as a most common subtype [5]. In figure (1) below the results are compared with other series.

D'Costa GG *et al* [6] reported M1 and M2 as the most common types followed by M4 with no reported cases from M5 and M7 subtypes. Nakase *et al* showed AML-M4 as common subtype in Australian population compared to Japanese, where AML-M2 is

common [7]. Kakepoto *et al* reported M4 to be the commonest followed by M2 [8].

Many of the differences in AML subtypes may be due to the subjectivity of morphologic diagnosis together with variable nature of acute myeloid leukemia

Subtypes, with no real demarcation. Some genetic factors may be responsible for a particular FAB subtypes distribution of AML in our population. The other reason for this discrepancy may be patients of different ethnic group and or geographical variation. Blast cells were seen in peripheral blood in all of our patients with mean of 65%.

Male to female ratio in present study is 1:1, other studies [9] reported 1.5:1. The medium age 33 years similar to that found in the southeast of Brazil and studies in Saudi Arabia [9] and Pakistan [10] but lower than the median age reported in western countries where AML peaks in incidence after the 6th decade of life [11] (Table 3).

Country	FAB subtype
United kingdom (UK) [12]	M4
Saudi Arabia (KSA) [13]	M4
Libya [14]	M2
United states of America (USA) [5]	M2
Australia [7]	M4
Pakistan [8]	M2
Iraq [15]	M3
India [12]	M2
Japan [7]	M2
Our study	M3

Table 3: Incidence of AML subtype in various countries

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