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Acute myeloblastic leukemia: Important clinical and epidemiological facts from Hiwa Hospital in Sulaimaniyah, Iraq

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Abstract:

BACKGROUND: Acute myeloblastic leukemia is the most common acute leukemia in adults, with both diagnostic and therapeutic challenges. It has a poor treatment outcome both locally and internationally. The aim of this study was to investigate some epidemiological aspects and treatment outcome of AML patients treated in single center.

PATIENTS AND METHODS: A retrospective observational study extended from February 2013 to February 2018 and included 98 patients who referred to Hiwa Hematology Oncology Hospital in Sulaymaniyah city. All patients had met the diagnostic criteria by flow cytometry for *de novo* acute myeloid leukemia (AML). Electronic records of all patients were reviewed carefully.

RESULTS: Ninety-eight patients (46 females and 52 males) with a mean age of 42 years were included the study, with new diagnosis of AML, most of the patients were below the age of 60 years (81%), while only 19% were 60 years of age or older. The most frequent subtype is AML M3 ($n = 25$; 25.5%) of patients, followed by M1, M2 ($n = 16$; 16.3%) each, and M5 ($n = 15$; 15.3%) with M4, M0, M6, M7, and acute leukemia of ambiguous lineage comprising the remainder, respectively. The clinical features at the diagnosis of the 98 patients included pallor in 91 patients (92.9%), easy fatigability in 82 patients (83.6%), while bleeding tendency was present in 46 patients (46.9%) in the form of ecchymosis, petechial hemorrhage, epistaxis, or abnormal vaginal bleeding. Fever was present in 85 patients (86.7%), while pain in the form of headache, generalized body ache, or bone pain was initially manifested in 29 patients (29.6%). The survival of our patients at 1 year is (88%) M3 patients, while it was (58%) for non-M3 patient.

CONCLUSIONS: Clinical and epidemiological characteristics were different in some aspect, while comparable in other when compared to published studies. treatment outcome and survival data were comparable to international data.

Keywords:

Acute myeloblastic leukemia, acute myeloid leukemia survival, FrenchAmericanBritish classification

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Introduction

Acute myeloid leukemia (AML) is a heterogeneous disease with wide variation in response to therapy and survival.[1] AML is the most common acute leukemia in adults and stands for about 80% of cases,[2] while in children, AML accounts for <10% of acute leukemias <10 years of age. In the United States and Europe, the incidence is 3–5 cases/100,000 populations.[3,4]

In adults, the median age at diagnosis is approximately 65 years in the United States,[5] while the median age at diagnosis in Iraq was 35 years.[6]

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The symptoms of AML are nonspecific, but they are usually due to the cytopenia. Usually, patients present with symptoms of fatigue, hemorrhage, or infections and fever due to decreases in red cells, platelets, or white cells, respectively. Pallor, fatigue, and dyspnea on exertion are common.[7]

AML is classified either according to the French–American–British (FAB) or The World Health Organization (WHO) classification was developed for better understanding the biological features of AML. FAB subtypes are (M0–M7). According to the available morphological and cytochemical characteristics,[7] the WHO classification of AML was revised in 2008. It incorporates newly recognized entities and emphasizes the essential role of cytogenetic abnormalities.[8,9]

Prognosis plays a key role in clinical decision-making for patients with AML, with the introduction of well-known high-throughput molecular sequencing platforms, assessment of FLT3 and NPM1 mutations has become a standard major determinant in predicting patient outcome, and FAB classification still may expect the outcome in some subsets of AML patient.[10]

Although improvement in the management of AML has led to substantial improvements in outcomes for younger patients, prediction in the elderly who account for the majority of new cases remains poor. Even with recent treatments, as much as 70% of patients 65 years or older will die of their disease within 1 year of diagnosis.[11] Local experience with AML treatment shows poor outcome-related mortality of 34%.[12]

Patients and Methods

A retrospective, descriptive study was conducted at Hiwa Hematology and Oncology Hospital in Sulaimaniyah. Data were collected from electronic records of the hospital and then analyzed statistically. Those data included patient characteristics, chief complain, hematological parameters, diagnostic method, and survival at 1 year.

The diagnosis of AML was based on the morphologic characteristics of bone marrow leukemic blast cells, classified according to the FAB classification and immunophenotyping was performed in all patients. Cytogenetics and molecular studies were not performed in most of the cases, as it was not available regularly.

Ninety-eight patients of 14 years and older (52 males and 46 females) admitted to Hiwa Hospital, from February 2013 to February 2018, with a new diagnosis of AML were included in this study. Patients with previous malignancy of any type and patients who had received chemotherapy prior to the diagnosis of AML were excluded from this study because the clinical presentation and other epidemiological aspects might be changed because of the primary disease or its treatment. Patients with lost records or without immunophenotyping confirmed AML were excluded from the study as well.

The study was approved by the Review Ethical Committee of Hiwa Hospital. Data were entered into Excel sheet and then transferred to SPSS-21 (IBM Company, Armonk, New York, USA). Descriptive analysis (numbers, percentages, median, means, and standard deviation [SD]) was performed for all variables. Analytic analysis was conducted to find any association or differences between compared variables using *t*-test, Chi-square test, and Fisher's exact test. $P < 0.05$ was regarded as statistically significant.

Results

In our study, among 98 patients with AML, most of the patients are below the age of 60 years (81%), while only (19%) are 60 years of age or older [Figure 1]. The minimum age for them was 15 years, while the maximum was 87 years with the median age of 43 years; 52 cases are male (53%) and 46 patients are female (47%), and male:female ratio is 1.1:1 [Figure 2]. The most frequent subtype is AML M3 ($n = 25$; 25.5%) of patients, followed by M1, M2 ($n = 16$; 16.3%) each, and M5 ($n = 15$; 15.3%) with M4, M0, M6, M7, and acute leukemia of ambiguous lineage comprising the remainder, respectively [Table 1].

The least hemoglobin (Hb) level for those 98 patients at diagnosis was 4.1 g/dl, while the upper level was 15.8 g/dl with a mean of 8.51 ± 2.00075 SD. The patients were divided into three groups according to their Hb; normal when Hb is above 11 g/dl 11 patients (11.2%), low when Hb is 7–10 g/dl 67 patients (68.4%), or very low when Hb is <7 g/dl 20 patients (20.4%). The lowest

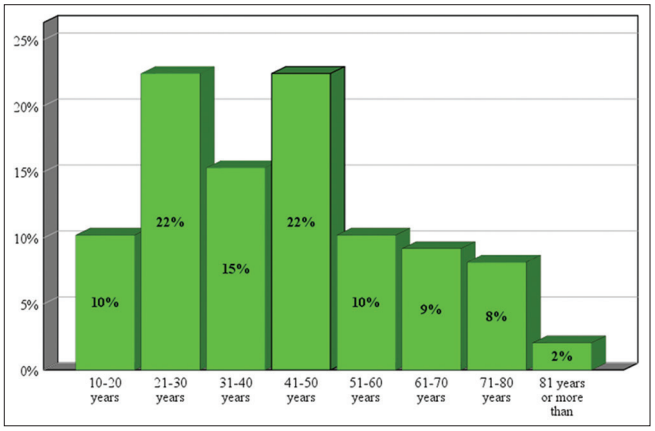

Figure 1: Age distribution

white blood cell (WBC) count was (0.2 × 10^9/l), highest WBC count was (281 × 10^9/l), mean WBC counts was 33,040.82 ± 5,3450.63 SD, 31 patients (31.6%) had WBC count (<4 × 10^9/l), 12 patients (12.2%) presented with normal WBC count (4–11 × 10^9/l), 55 patients (56.1%) had WBC count of (>11 × 10^9/l). While the platelet count range was 3900–238,000 × 10^6/l with a mean of 54,095.92 ± 4,7253.48 SD, 5 patients (5.1%) had platelet count (<40,000 × 10^6/l), 4 patients (4.1%) had low-platelet count (40, 000–100,000 × 10^6/l), and 89 patients (90.8%) had platelet count (>100,000 × 10^6/l) [Tables 2 and 3].

The clinical features at diagnosis of the 98 patients included in this study are summarized in Table 3; majority of patients presented with pallor 91 patients (92.9%), easy fatigability 82 patients (83.6%), while bleeding tendency was present in 46 patients (46.9%) in the form of ecchymosis, petechial hemorrhage, epistaxis, or abnormal vaginal bleeding. Fever was present in 85 patients (86.7%), while pain was initially manifested in 29 patients (29.6%) [Table 4].

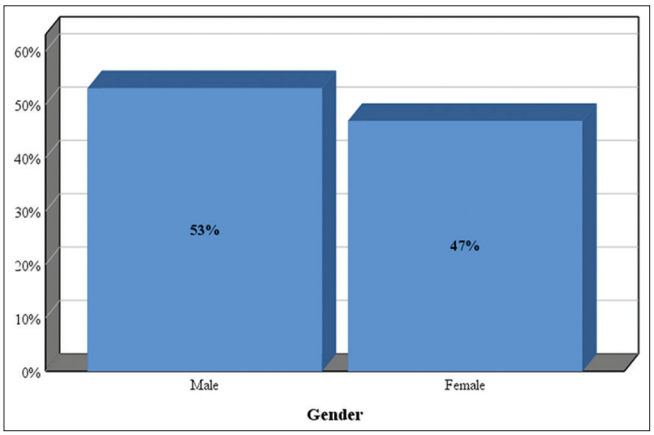

Figure 2: Gender

Table 1: French-American-British subtype frequency

Subtype	Frequency (%)
M0	5 (5.1)
M1	16 (16.3)
M2	16 (16.3)
M3	25 (25.5)
M4	13 (13.3)
M5	15 (15.3)
M6	2 (2.0)
M7	1 (1.0)
AML (ambiguous)	5 (5.1)
Total	98 (100.0)

AML=Acute myeloid leukemia

We prognostically subdivided the patients into two main subgroups: M3 and non-M3 subtypes. We found that 25 patients (25.5%) are M3 and 73 patients (74.5%) were non-M3 [Table 5]. Flowcytometry is considered for the final diagnosis and it was more sensitive in determining lineage and/or subtype in (94%) of the cases.

The survival of our patients at 1 year is (88%) M3 patients, while it was (58%) for non-M3 patient [Figure 3a and b].

Discussion

In this study, we found that acute myeloblastic leukemia has the highest incidence in adolescents and adults aged 14–60 years than older adults and elderly patients, and these findings were comparable with the results of a study on Iraqi patients conducted by Mohammad *et al*.,[13] while in the Swedish acute myeloblastic leukemia patients the highest incidence was reported in elderly patients of 80–85 years.[14] In our study, males are affected slightly more than females which are comparable to local and international studies.[15,16]

In our study, M3 subtype was the most common subtype of acute myeloblastic leukemia that is comparable with local data but differs from the international studies were M2 or M4 subtype were the most common.[16-19]

At presentation, the median WBCs count was 17,850 × 10^6/l, and this is higher than what was described in Egypt and other parts of Iraq.[16,19] The median hemoglobin at diagnosis was 8.5 g/dl, which is close to what was found in Egypt a median of 8.4 g/dl. The median platelet count was 44,000 × 10^6/l. While in Egypt, the median platelet count was higher at 62 × 10^6/l.[19]

The presenting clinical feature was pallor, fever, and easy fatigability in most of the patients, then bleeding tendency and pain less frequently, which is comparable to local studies.[6]

The patients were separated into M3 and non-M3 subgroups, as there is a clear variation in treatment and outcome in favor of M3 patients.[20] Flow cytometry was used for final diagnosis, and it is more popular as

Table 2: Age and some hematological parameters

Variables	*n*	Minimum	Maximum	Median	Mean±SD
Age (years)	98	15	87	43.00	42.73±19.06
Hb (g/dl)	98	4.10	15.80	8.500	8.51±2.00075
WBC count (×10^6/l)	98	200	28,1000	17,850.00	33,040.82±53,450.63
Platelet count (×10^6/l)	98	3900	238,000	44,000.00	54,095.92±47,253.48

SD=Standard deviation, WBC=White blood cell, Hb=Hemoglobin

Table 3: Hematological parameters grouping according to severity

Variables	Frequency (%)
Hb groups	
Very low	20 (20.4)
Low	67 (68.4)
Normal	11 (11.2)
Total	98 (100.0)
Platelet groups	
Very low	5 (5.1)
Low	4 (4.1)
Normal	89 (90.8)
Total	98 (100.0)
WBC groups	
Low	31 (31.6)
Normal	12 (12.2)
High	55 (56.1)
Total	98 (100.0)

WBC=White blood cell, Hb=Hemoglobin

Table 4: Presenting symptoms

Presenting symptom	Frequency (%)
Fever	
Yes	85 (86.7)
No	13 (13.3)
Total	98 (100.0)
Pallor	
Yes	91 (92.9)
No	7 (7.1)
Total	98 (100.0)
Easy fatigability	
Yes	82 (83.6)
No	16 (16.4)
Total	98 (100.0)
Pain	
Yes	29 (29.6)
No	69 (70.4)
Total	98 (100.0)
Bleeding	
Yes	46 (46.9)
No	52 (53.1)
Total	98 (100.0)

Table 5: Subgroups

Variables	Frequency	Percentages
M3	25	25.5
Non-M3	73	(74.5
Total	98	100.0

it is extremely efficacious and sensitive tool to diagnose acute myeloblastic leukemia,[21] although it has some limitations such as difficulty in analysis of uncertain positivity, absence of blasts in dry tap bone marrow aspirate, and rigorous necessity of fresh sample.[22,23]

In our study, we found 1-year relative survival rate of 58% for non-M3 patients for all age groups collectively,

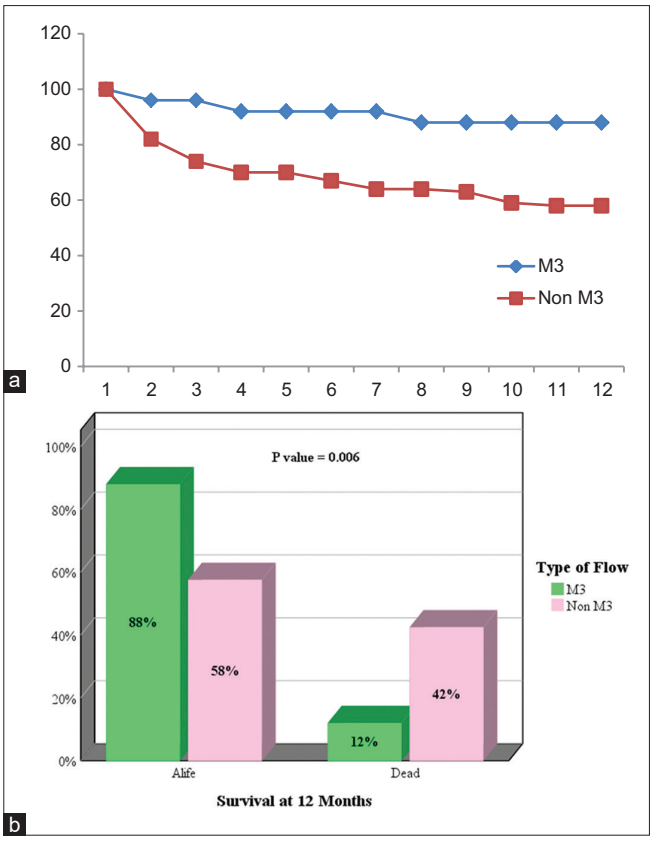

Figure 3: (a) Survival at 12 months, (b) Acute myeloid leukemia survival percentage in months

and this result is also comparable to local data where the survival rate was about 60% at 1 year, although the other study included patients 60 years of age or younger.[6] While M3 patients' survival at 1 year was at 88% in our study, Chinese study showed that this excellent response could be maintained at 3 years with incorporation of arsenic trioxide into the treatment.[24]

Conclusions

The following conclusions were drawn from our retrospective descriptive study: clinical and epidemiological characteristics were different in some, while comparable in other aspects with previously published studies. Median WBC and AML subtypes frequencies were different, while survival data were comparable.

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Conflicts of interest

There are no conflicts of interest.

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