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Prognostic and Demographic Characteristics of Acute Myelogenous Leukemia Patients: a Five-Year Study in Mashhad, Iran

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ABSTRACT

Background: Acute myeloid leukemia (AML) is a disease in elderly patients, with a mean age of diagnosis of 70 years. We evaluated the clinicopathological features and experimental variables in AML patients in Northeastern Iran as well as the correlation between survival and FAB subgroups of AML.

Methods: From 2009 to 2014, 98 patients with AML were recruited in a retrospective study. Most of the patients only received the chemotherapy regimen of "7+3" and none of the patients underwent radiotherapy. Also, one-third of the patients underwent bone marrow transplantation. The mean follow-up period was 40 months and during this time, 58 deaths were found.

Results: The mean age of the patients at diagnosis was 40.6 ± 15.4 years (range, 17-77 years) and 40 patients (40.4%) were male. AML-M5 and M3 were the most frequent subgroups in patients with 29.5% and 26.1% frequencies, respectively. Twenty patients (20.4%) had lymphadenopathy. Weakness and lethargy were the most common complaints. The 5-year survival rate was 39.6% and mean survival was 27.3 months. Prevalence of females was higher in AML-M5 and M3 compared to other subgroups.

Conclusions: The mean age in Iran is lower than many countries; also, the frequency of females was higher in our study compared to many previous studies. Overall survival of our patients was higher than other studies which can be due to the difference in types of treatment. The prevalence of AML-M5 in our study was higher than other studies.

Keywords: Acute myeloid leukemia, Survival, Age, FAB subgroups

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Introduction

Acute myeloid leukemia (AML) accounts for about 8% of all malignancies and approximately 50% of known patients with leukemia present with the acute type, from which 90% are AML[1]. AML is a clonal hematopoietic disorder resulting from genetic alterations in normal hematopoietic stem cells[2] and is a disease of elderly patients, with a mean age of diagnosis of 70 years[3]. The mean age of patients in Iran has been reported lower than other areas in the world in many studies[4]. As the disease progresses, blast cells accumulate in the bone marrow, blood, and organs and interfere with the production of normal blood cells. Unless treated, this leads to fatal infection, bleeding, or organ infiltration within 1 year of diagnosis[2]. AML adverse cytogenetic abnormalities increase with age, and within each cytogenetic group, prognosis with standard treatment worsens with age[3]. Neutropenic fever is one of the most serious complications after induction chemotherapy in AML. Survival in AML has improved in younger patients over the last decade[5]. AML is divided into subgroups that are distinguished by the morphology of the leukemia cells, specific chromosomal abnormalities, gene rearrangement patterns, and different clinical courses and response to therapy[6]. The FAB group has classified AML cases into eight subgroups (M0-M7)[7]. Many previous studies have reported AML-M2 as the predominant FAB subtype of AML[8]. Herein, we analyzed the clinicopathological features and experimental variables in AML patients in Northeastern Iran as well as the correlation between survival and FAB subgroups of AML.

Methods

Patients

In a retrospective study from 2009 to 2014, from all AML patients referred to the Clinic of Hematology, Emam Reza Hospital, Mashhad, Iran, 98 patients with AML were selected for this study, because the AML patients with systemic and infectious diseases were censored from the study. The variables age, sex, location, complaints, duration of hospitalization and fever, lymphadenopathy, organomegaly, French-American-British (FAB) subgroups of non-Hodgkin lymphoma (NHL), the count of WBC, RBC, neutrophil, lymphocytes, Hb, platelet and survival were checked in the patients. Most of the patients (78%) only received the chemotherapy regimen of "7+3"(cytarabine (100 mg/m2 for 7 days plus an anthracycline or anthracenedione [most often daunorubicin, 45 mg/m2 in older adults, 90 mg/m2 in younger adults, but other options include idarubicin or mitoxantrone 12 mg/m2] for 3 days) and none of the patients underwent radiotherapy. Also, one-third of the patients underwent bone marrow transplantation. The mean follow-up was 40 months and during this time, 58 deaths were found. Overall survival (OS) was defined from the date of diagnosis until death from any cause or the date of the last follow-up.

Statistical Analysis

Analysis of data was performed using IBM SPSS software version 19 and survival diagrams were plotted using GraphPad Prism software version 5.

Results

The mean age at diagnosis for the patients was 40.6 ± 15.4 years (range, 17-77 years) and 40 patients (40.4%) were male (Table 1). The mean and range of WBC, neutrophil, lymphocytes, RBC, Hb and platelet at diagnosis are shown in Table 1. Out of 98 patients, 20 (20.4%) and 27 (27.6%) patients had lymphadenopathy and organomegaly, respectively. AML-M5 and M3 were the most common subgroups in patients with 29.5% and 26.1% frequencies, respectively. Twenty patients (20.4%) had lymphadenopathy. Weakness and lethargy were the most common complaints (45.9%) on the first visit

Table 1. Baseline variables in patients with acute myelogenous leukemia (n=98)

Variables	n(%)	Mean±SD	Range
Age, years		40.6±15.4	17-77
Sex			
Male	40(40.4)		
Female	58(58.6)		
WBC×103/µL		29.4±38.7	0.2-202
Neutrophil, %		37.7±29.1	1-100
Lymphocytes, %		45.4±28.4	1-99.8
RBC×106/dL		2.9±0.8	0.9-6.2
Hb, g/dL		8.4±1.9	2.3-14.1
Platelet×103/µL		49.4±46.5	1.4-198
Lymphadenopathy			
Yes	20(20.4)		
No	78(79.6)		
Organomegaly			
Yes	27(27.6)		
No	71(72.4)		
Subgroup of AML, n=88			
M2	15(17.1)		
M3	23(26.1)		
M4	15(17.1)		
M5	26(29.5)		
M6	4(4.5)		
MDS transfer to AML	4(4.5)		
M7	1(1.2)		
Complaint in the first visit			
Weakness and Lethargy	45(45.9)		
Fever and Headache	8(8.2)		
Bone pain	7(7.1)		
Bleeding from the gums	5(5.1)		
Others	33(33.7)		

in the patients.

The 5-year OS for all AML patients is shown in **Figure 1**. The survival rate was 39.6% and mean survival was 27.3 months.

in AML-M4.

Table 2. shows the percentage of a number of variables in 88 patients with AML based on sub-groups. The mean age in MDS was higher than the other subtypes. The mean count of WBC was the highest in M4 (48.2×103/µl). Prevalence of females was higher in AML-M5 and M3. Lymphadenopathy was more frequent in AML-M2 compared to the

other subgroups, while organomegaly was greatest in AML-M4.

Table 3. shows the OS for subgroups of AML. The highest mean OS pertained to MDS, followed by M3, M4, M6, M5 and M7, in decreasing order.

Discussion

Acute myeloid leukemia is the second most common leukemia among United States adults9 and most patients are older than 60 years10,11. A study on 5,480 AML patients9 showed that the median age was 78 years (range, 65-93 years); in another study on 454 patients, 61% of whom had abnormal cytogenetics,12 the median age was 48 years. Patients in another research13 had a median age of 64 years (range, 16-79 years), and 50% were males. Also, among 116 patients in Pakistan14, 70 were males with a male-to-female ratio of 1.5:1 and a mean age of 32 years (range, 6-85). Three studies have addressed this issue in Iran: in the first study15 on 95 AML patients, the median age was 37 years (range, 15-68 years), and 64.2% were males. In the second study16 on 455 patients, the mean age of AML patients was 44.7 years and 56.3% were males. In the third study17 on 46 patients, the mean age of patients was 35 years (range, 15-63 years), and 36.9% were males. In this study, the mean age was 40.6 years (range, 17-77 years) and 58.6% were females. These results show that the mean age in Iran is lower than many countries. Also, the percentage of females is higher in our study compared to many previous studies.

A few population-based studies have reported 3-year survival rates of only 9-10% and 5-year survival of 3-8% in patients aged 60 years and higher, compared with 5-year survival rates of up to 50% for younger patients18,19. In 76 de novo AML cases of whom 53 patients were treated with combination chemotherapy for remission induction20, the median OS was 16 months and 3-year OS rate was

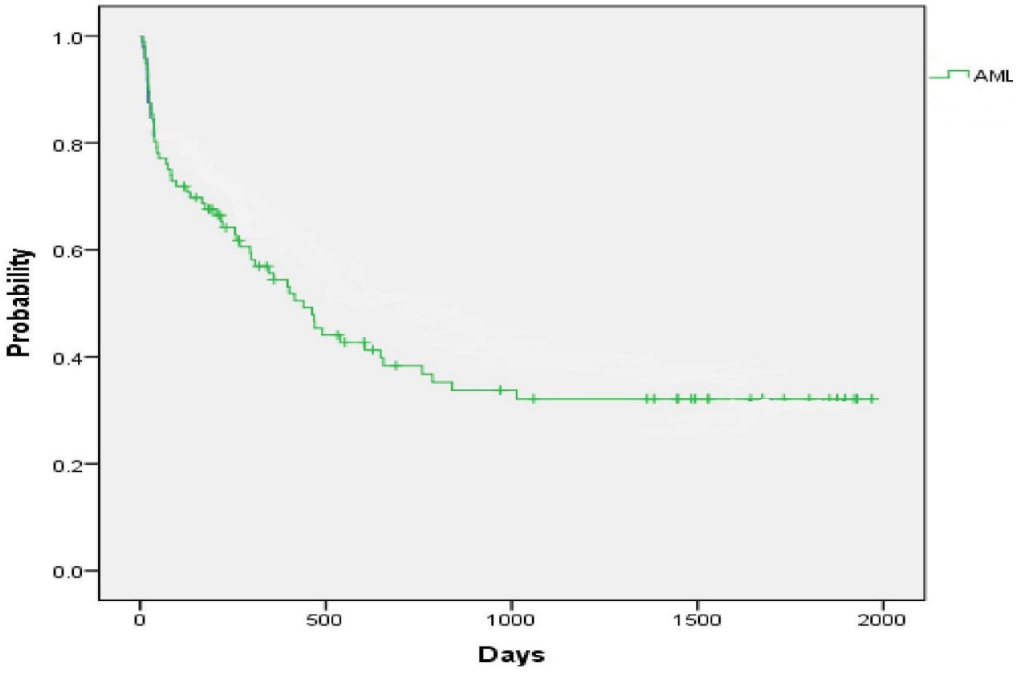

Figure 1: Five-year overall survival for all patients with AML

28%. In our study, 5-year OS rate was 39.6% and mean OS was 27.3 months. Therefore, the OS in our patients is higher than other studies, which might reflect the chemotherapy regimen, radiotherapy and bone marrow transplantation in these patients. These protocols can affect OS as well as side effects.

A total of 113 AML patients were evaluated in a study; the distribution of AML subtypes was 0.8% for M1, (28.4%) for M2, 50.5% for M3, 12.5% for M4, 0.8% for M5, 0.8% for M6 and in 6.2% cases, the morphological subtype could not be classified21. In another study22, AML-M2 was the most common FAB type (32.26%), followed by M1 and M4 (22.58% each), M5 (8.6%) and M6 and M7 (1.61% each), in decreasing order. The mean age of M1, M2, M3 and M5 cases was between 25 and

Table 2. Percentage of a number of variables in patients with acute myelogenous leukemia based on subgroups (n=88)

Variables, n(%)	M2 N=15	M3 N=23	M4 N=15	M5 N=26	M6 N=4	MDS N=4	M7 N=1
Mean age, years	35.3	38.8	41.4	42.7	42.2	50.5	44.0
WBC×103/μL	26.5	11.0	48.2	45.3	8.8	26.5	5.2
Sex							
Male	8(53.3)	8(34.8)	8(53.3)	8(30.8)	2(50)	1(25)	1(100)
Female	7(46.7)	15(65.2)	7(46.7)	18(69.2)	2(50)	3(75)	0
Lymphadenopathy							
Yes	8(53.3)	2(8.7)	2(13.3)	5(19.2)	0	0	0
No	7(46.7)	21(91.3)	13(86.7)	21(80.8)	4(100)	4(100)	1(100)
Organomegaly							
Yes	2(13.3)	2(8.7)	8(53.3)	9(34.6)	2(50)	2(50)	0
No	13(56.7)	21(91.3)	7(46.7)	17(65.4)	2(50)	2(50)	1(100)

Table 3. Overall survival for subgroups of acute myelogenous leukemia

Subtype	**Mean survival (months)**
M2	9.6
M3	28.9
M4	20.5
M5	17.2
M6	20.4
MDS	29.9
M7	13.6

29 years, whereas it was 45.6 years for M4 patients. AML-M2, M4 and M5 were more common in males, M1 was more common in females and M3 was equal in both sexes. AML-M4 was the predominant FAB subtype (36.2%) followed by M2 (30.25%), M3 (10.4%), M1 (8.7%), M0 (7.7%), M5a (3.5%), M5b (2.5%) and M6 (0.8%)14. In 62 patients with AML23, the FAB subtypes were as follows: M1 (27.4%), M2 (21%), M3 (9.7%), M4 (30.6%), M5 (9.7%), and M6 (1.6%). The median OS was 23.5 months for M0, M1 and M2, 97.7 months for M3 and 7.4 months for M4, M5, M6, and M724. In our study, AML-M5 and M3 were the most common subgroups in patients with 29.5% and 26.1% frequencies, respectively. Also, AML-M7 had the lowest prevalence (1.2%). Based on the results, the prevalence of AML-M5 in our study is higher than other studies and also the percentage of M2 is lower compared to other studies. The mean age for MDS (50.5 years) was higher than the other subtypes, followed by M7, M6, M5 and M4 (between 40 to 44 years) and also M3 and M2 (between 35 to 39 years). AML-M2, M4 and M7 were more common in males, M3, M5 and MDS in females and M6 was equal in both genders. In our study, the mean 5-year OS was the highest for MDS (29.9 months) and M3 (28.9 months).

Conclusions

The mean age in Iran is lower than many countries; also, the percentage of females was higher in our study compared with many previous studies. The OS was higher in our patients than other studies which may be due to the difference in types of treatment. The prevalence of AML-M5 was higher in our study than other studies.

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