Demographic and Prognostic Factors of 455 Patients with Acute Leukemia Admitted to Two Referral Hospitals in Tehran-Iran During Ten Years (2001-2011)

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Abstract

Background: Global death toll of Acute Leukemia (AL), as a heterogeneous group of hematopoietic malignancies, is rather high, i.e. almost 74% of 300,000 new cases die every year. This reflects a poor prognosis of this malignancy in most parts of the world, where contemporary and rather complex remedies are not available. There are a few well documented reports about the epidemiologic features of AL at national level in Iran. This retrospective study demonstrates demographic and laboratory features of Acute Myeloid Leukemia (AML) and Acute Lymphoblastic Leukemia (ALL) patients admitted to the main referral oncology hospitals in the ex-Iran University of Medical Sciences in Tehran (Firoozgar and Rasoul-Akram hospitals) during the last decade (2001-2011).

Methods: Medical records of all patients admitted to the both hospitals diagnosed with AML and ALL were reviewed during the study period for demographic, biological and clinical characteristics at diagnosis.

Results: Four-hundred fifty five patients were diagnosed with AML and ALL, who admitted to the both hospitals during ten years, of whom 59.6 % (271 patients) were male. Fifty five percent of patients had AML and 44.6 % had ALL, both significantly dominated in men ($p<0.001$). AML patients died more significantly ($p<0.05$) and the most deaths occurred in older patients ($p<0.001$). Initial WBC count was significantly related to death ($p= 0.001$), where the least death (13%) occurred in the group with initial WBC between 5-10×10^3/µL and most of deceased had an initial WBC more than 10×10^3/µL. Logistic regression showed that age, fever and WBC were significant prognostic factors.

Conclusion: Demographic characteristics of AL patients were almost the same as other global reports. Most deaths occurred in older patients, those who had fever, and patients with higher WBC count at first admission, which warrants more investigations accurately and also improvements in hospital records.

Keywords: Acute Myeloid Leukemia; Acute Lymphoblastic Leukemia; Epidemiology; Iran

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Introduction

Leukemias are heterogeneous group of hematopoietic malignancies that include diverse and biologically distinct sub-groups [1]. There are four major subtypes of leukemia in most cancer registries including Acute Lymphoblastic Leukemia (ALL), Acute Myeloid Leukemia (AML), Chronic Lymphoblastic Leukemia (CLL), and Chronic Myeloid Leukemia (CML) [2]. Acute leukemias afflict both adults and children while chronic leukemia involves adults mainly [1]. The American Cancer Society estimates that 31,500 individuals are diagnosed with one form of leukemia in the United States each year, of whom approximately 21,500 patients (68.2%) die from their disease [3] , the recent cancer registry in Iran indicated that there were 4393 new cases of hematologic malignancies in 2008, of whom 805

Table 1. Characteristics of AL Patients Admitted to Both Hospitals

Variable		Type of diseases		P value
		AML No. (%)	ALL No. (%)	
Gender	Male	142 (56.3)	129 (63.5)	0.120
	Female	110 (43.7)	74 (36.5)	
	Odds Ratio= 0.74			
Age groups	≤15	5 (2)	54 (26.2)	<0.001
	15-45	129 (51.4)	129 (63.5)	
	≥45	117 (46.6)	20 (9.9)	
Fever	No fever	55 (24.3)	64 (35.8)	0.012
	Fever	171 (75.7)	115 (64.2)	
	Odds Ratio= 0.58			
Hb (g/dl)	<5	12 (4.8)	9 (4.5)	0.394
	5-10	173 (68.9)	126 (63.3)	
	>10	66 (26.3)	64 (32.2)	
PLT ($\times 10^3/\mu L$)	<50	158 (62.9)	98 (49.2)	0.004
	50-100	47 (18.7)	38 (19.2)	
	100-150	18 (7.2)	18 (9.0)	
	>150	28 (11.2)	45 (22.6)	
WBC ($\times 10^3/\mu L$)	<5	98 (39)	101 (50.7)	0.031
	5-10	36 (14.4)	28 (14.1)	
	>10	117(46.6)	70(35.2)	

cases (18.3%) had ALL and 432 cases (9.8%) had AML [4]. Although the incidence of acute leukemia accounts for less than 3% of all cancers, [5] but it is the leading cause of cancer death in children and younger individuals less than 39 years [3].

Acute Myeloid Leukemia (AML) occurs predominantly in adults [6-8], which afflicts the elderly more frequently than the young. Statistics show that more than half of patients with AML are older than 60 years, with a median age of 65 years for newly diagnosed patients [3-10]. Leukemia is the most common cancer and the most common cause of disease-related death in childhood [9,11]. ALL is the most common malignancy in children, accounting for 30% of all cancers in white population and 80% of all leukemias [12-14] , which predominates in male up to twice than female [15]. Leukemias share some major risk factors worldwide, particularly ionizing radiation, though the descriptive etiology of different types and subtypes of leukemias is not identical [1].

Although most patients achieve remission initially, but over 25% of patients will ultimately experience a relapse, and those patients with an early bone marrow relapse have less than 10% survival. Similarly, 50% of patients with AML will relapse [11]. Complete remission with standard induction chemotherapy for ALL patients is 70-90% [16, 17] and for patients with AML ranges from 60% to 80% [18, 19]. However, the majority of patients will relapse and die during 2 years after a remission[19]; so patients with relapse will have a poor prognosis [17, 20]. Statistics from 1996 to 2002 in the United States showed 5-year relative survival rates of 34.4% for adults aged 65 and 4.3% for older than 65 years [6].

A number of factors have been reported as affecting the outcome of the disease, including age, initial White Blood Cell (WBC) count, time to achieve complete remission, immunophenotype (T versus B cell), abnormal karyotypes and cytogenetics [21-23]. Several prognostic parameters have been identified in AML, where the most important factors with respect to survival rate are age and cytogenetics [24]. According to the most recent report of the national cancer registry of Iran in 2008, Age-Standardised incidence Rate (ASR) of leukemia in Iran and Tehran was 8.94 and 7.36 for men and 6.29 and 5.89 for women per 100,000 population, respectively [4]. Acute leukemia constitutes the majority of leukemia whereas about 71 % of lymphoblastic leukemia and 66 % of myeloblastic leukemias have been reported as acute in Tehran metropolitan area [25].

Many factors affect the prognosis of acute leukemia. Risk stratification helps the clinicians to select therapeutic modalities based on prognostic indicators, which has been emphasized in the National Cancer Institute/Rome criteria [26] including age, WBC count at diagnosis, immunophenotype [27] cytogenicity of the disease, [28] and brain status [29]. High WBC count at diagnosis has been

Table 2. Different Variables Among Deceased AL Patients (n=210)

Variable	Sub-groups	Deceased (%)	P value
Gender	Male	121 (57.6)	0.44
	Female	89 (42.4)	
Type of leukemia	AML	128 (61)	0.03
	ALL	82 (39)	
Age groups	≤15	13 (6.2)	<0.001
	15-45	122 (58.4)	
	≥45	47 (35.4)	
Medical Centers	Firoozgar	124 (59)	0.17
	Rasol-Akram	86 (41)	
Fever	No fever	45 (23.6)	0.015
	fever	146 (76.4)	
Hb (g/dl)	<5	10 (4.8)	0.9
	5-10	136 (65.4)	
	>10	62 (29.8)	
PLT ($\times 10^3/\mu L$)	<50	129 (62.3)	0.1
	50-100	38 (18.4)	
	100-150	14 (6.8)	
	>150	26 (12.6)	
WBC ($\times 10^3/\mu L$)	<5	72 (34.8)	0.001
	5-10	31 (15)	
	>10	104 (50.2)	

Table 3. Logistic Regression of Prognostic Factors

Variable	Sub-groups	OR	95% CI	P value
Gender	Male	Ref	-	-
	Female	0.75	0.5-1.1	0.2
Type of leukemia	AML	Ref	-	-
	ALL	0.97	0.6-1.6	0.92
Age groups	≤15	Ref	-	-
	15-45	0.4	0.2-0.9	0.02
	≥45	0.26	0.1-0.64	0.004
Medical Centers	Firoozgar	Ref	-	-
	Rasol-Akram	0.95	0.6-1.5	0.82
Fever	No fever	Ref	-	-
	fever	0.58	0.3-0.94	0.03
Hb (g/dl)	<5	Ref	-	-
	5-10	1.03	0.4-2.7	0.96
	>10	0.7	0.3-1.9	0.51
PLT ($\times 10^3/\mu L$)	<50	Ref	-	-
	50-100	1.34	0.8-2.3	0.28
	100-150	1.53	0.7-3.4	0.29
	>150	1.7	0.9-3.2	0.1
WBC ($\times 10^3/\mu L$)	<5	Ref	-	-
	5-10	0.58	0.3-1.1	0.08
	>10	0.5	0.3-0.78	0.003

considered as a strong prognostic factor for treatment failure, resistance and recurrence [30] ,

and survival rate in childhood ALL [16]. Absolute Lymphocyte Count (ALC) in young patients with AML and ALL has been shown to be a powerful prognostic factor for remission free and overall survival [26]. Different cut points have been used in the literature to categorize initial WBC count for verification of its possible role in AL prognosis, [9, 10, 16, 31-34] however current evidence underscores the strong relationship between higher initial WBC count and higher mortality rates [31, 35]. The purpose of this study was to demonstrate demographic and the most popular laboratory features of AML and ALL patients admitted to the two main referral oncology hospitals in the ex-Iran University of Medical Sciences in Tehran (Firoozgar and Rasoul-Akram Hospitals) between 2001 and 2011.

Materials and Methods

All patients diagnosed with AML and ALL admitted to the two major oncology referral hospitals of ex-Iran University of Medical Sciences (Firoozgar and Rasoul-Akram Hospitals) were included in this retrospective study during the last decade from March 2001 to March 2011. Prognostic factors which were considered in the analysis included demographic, biological and clinical characteristics at diagnosis. Gender, age, type of leukemia, White Blood Cells (WBC), Hemoglobin (Hb), Platelet count (PLT) and fever (axillary>37.5°C) were taken from the medical records to fill a pre-determined checklist. Phone calls were made to spot patients' death.

Data were analysed by SPSS v.17 software. Patients' variables were summarized by frequency tabulation (for categorical variables) or by calculating mean and median for continuous variables. Univariate analysis of the association between each variable and outcome was done using chi-square method. Logistic regression was conducted to find out the most significant prognostic factors.

Results

Demographic features of the patients are shown in Tables 1-2. Four-hundred fifty five patients were diagnosed with AML and ALL, of whom 253 cases were admitted in Firoozgar (55.6%) and 202 cases (44.4%) in Rasoul-Akram Hospitals. Almost 60% (271 patients) were male, 55.4 % of patients had AML and 44.6 % had ALL, both significantly dominated in men i.e. 56.3 % male versus 43.7 % female for AML and 63.5% male versus 36.5% female for ALL. Totally, the mean age at diagnosis was 35.58. The mean age in AML was 44.79 and in ALL was 24.20 years. Most patients (56.8%) were in the age group of 15-45 years, while the younger group (≤15 years) was in the minority (13%). AML was the most common in older people and ALL in youngsters (p=<0.001). AML patients tended to be admitted more in Firoozgar Hospital (p=0.01), while equal number of patients were admitted to both hospitals during the study period. Most of AML (64%) and ALL (75%) patients had fever. Most of AML and ALL patients had PLT less than 50000/µL. The proportion of AML patients who had WBC higher than 10000/µL, was more than ALL patients, while patients with less than 5000/µL were more likely to be AML. There was no significant gender difference in the age, fever and hematologic features.

Amongst 455 patients, 130 deaths were recorded in both hospitals, while the remaining patients were followed by telephone calls. Wrong telephone numbers, vacant or unavailable contact numbers were excluded and amongst 325 patients after follow up, 80 deaths were detected. Survival analysis was performed for 210 patients, of whom 128 patients (61%) had AML and 82 (39%) had ALL. Amongst them 74% survived one year and 26% survived more than 1 year (Results are not shown here).

The relationship between death and AL variables are shown in Table 2. AML patients died significantly more than ALL patients (p<0.05). Compared with patients under 15 years, most deaths occurred in older patients (p<0.001). There was no significant relationship between death and hemoglobin and platelet levels, however most deaths occurred in patients with fever (p =0.01) and high initial WBC count i.e. more than 10×103/µL which was significantly related to death (p= 0.001), while the least death (13%) occurred in the group with initial WBC of 5-10×10^3/µL. Logistic regression showed that age, fever and WBC count were significant prognostic factors (Table 3).

Discussion

Research on epidemiological features of acute leukemia is poorly reported in Iran [36]. This study demonstrates demographic characteristics of a large number of patients with AML and ALL admitted to two hematology-oncology wards during 10 years. Leukemia is moderately common and accounts for almost 3 percent of all cancers in both developed and developing countries [5]. Demographic features in this retrospective study were consistent with other studies, where men were affected more with acute leukemia, [37, 38] ALL occurs more in children under 15 years [12] and AML occurs more in elderly [3, 7, 39, 40]. In this study, 26.7% of AML patients were older than 60 years while only 2% were less than 15

years; also 26.6% of ALL patients were less than 15 years while 3.4% were older than 60 years.

Our results showed that males were more diagnosed with acute leukemia, which is in compliance with other studies [1, 10, 41-43]. Incidence rates are usually higher in males [1]. Kobayashi et al reported 72.4% male dominancy in AML [42] , and Santos et al reported that 62% of AML patients were men [44]. ALL is the most common cancer in children and adolescents, [13, 40] representing almost one-third of all form of cancer during childhood in white population [1], whereas AML is presented mainly in adults [7]. Our findings indicated that 46.6% of AML patients were over 45 years while 9.9% of ALL patients were in this age group, and only 2% of AML patients were less than 15 years.

The mean age at diagnosis for AML and ALL patients were 44.79 and 24.20, respectively, which were less than Giles et al report for AML patients (50 years) [20] , however, almost similar age distributions have been reported in Iran [45] and elsewhere [11, 46]. In the current study, the mean survival rates in total, AML, and ALL patients were 290.7, 280.9 and 303.5 days, respectively. Most deaths occurred in AML patients because age is an important factor in the prognosis of acute leukemia [24, 47] and also the mean age in ALL is less than AML patients. Among studied factors (age, gender, duration of fever, Hb, WBC and PLT) age, fever, and WBC were associated significantly with death. Most deaths occurred in the elderly, patients with fever and those with higher WBC counts at diagnosis, which are in compliance with the body of literature [9, 10, 16, 31, 32, 34]. Although the most employed cut point for initial WBC count are $50\times10^3/\mu L$ [13, 27, 48-52] and $10\times10^3/\mu L$ (53-56), but other cut points close to this study (<5, 5-10, $>10\times10^3/\mu L$) are well accepted in the literature [16, 33]. Yanada et al found that in a series of T-ALL adults, patients with initial WBC count of 3-5 $\times10^3/\mu L$ had longer survival rates than others [16].

This retrospective descriptive study suffers from a number of limitations. First of all, our findings are limited to the two hospitals during the last ten years, secondly, contact details were not available for most of the patients and medical and laboratory records were not complete and last but not the least, the difference in classification might be a source of bias similar to other studies. A population-based study is required to determine an accurate estimation of epidemiological characteristics of acute leukemia. However, our results indicate significant differences between the types of leukemia and demographic, laboratory and clinical features, particularly duration of fever and WBC counts, which warrant further analysis and more studies in stylish design. Simple laboratory tests such as CBC with differentiation (for the purpose of absolute lymphocyte count) are probably more efficient in risk stratification of AL patients [26].

In conclusion, this retrospective study reveals that demographic characteristics of AL patients admitted to the selected referral hospitals in Tehran were almost the same as other global reports. Most deaths occurred in older patients, those who had fever and finally patients with higher WBC count at diagnosis. The prognostic factors need more investigations to find out their influence accurately. Complete hospital records, setting up hospital or population-based registry and more advanced study designs are required to provide better healthcare for acute leukemia patients.

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Conflict of Interest

The authors have no conflict of interest in this article.

Authors' Contribution

Parvin Ayremlou collected and analyzed the data and drafted the manuscript in Farsi, Seyed Mohsen Razavi, Masoud Vakili, had visited all the patients as oncologists and also contributed in design and implementing the study, Masoud Solaymani-Dodaran and Mohsen Asadi-Lari contributed in design and conducting the study, supported data collection and proof read the manuscript. Mohsen Asadi-Lari was the main supervisor and wrote the paper.

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