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Research Article

Acute Myeloid Leukemia among Patients at the National Oncology Center in Sana'a, Yemen: Prevalence, Subtypes and Hematological Features

Mohammed Abdulkader Al-Nuzaili[1*], Khaled Saad Al-Khamesy[2], Osama Muzher Yahia[3]

[1]Department of Hematology, Sana'a University, Sana'a, Yemen; [2]Department of Medical Physiology, Sana'a University, Sana'a, Yemen, [3]Department of Hematology, Institute of Health Sciences, Sana'a, Yemen

ABSTRACT

Background: Acute Myeloid Leukemia (AML) is a malignant condition that affects the bone marrow's myeloid cell lineage. Genetic abnormalities result in an accumulation of myeloblasts in the BM and peripheral blood. This study aimed to identify the prevalence, subtypes, and hematological characteristics among AML patients at the National Oncology Center (NOC) in Sana'a.

Methods: In this cross-sectional study, 747 patients with hematological malignancies were investigated. There had been 275 females and 472 males, whose ages ranged from 1 to 75. During March 2020 and May 2022, the NOC in Sana'a, Yemen, provided the registered data. The NOC received these patients from a variety of Sana'a hospitals and clinics in addition to those from other governorates. These patients came to NOC to get an accurate diagnosis and suitable treatment. Giemsa-stained blood/BM films, the CBC, and immunophenotypic testing using flow cytometry were used to reach the final diagnosis of AML, if necessary. The data were analyzed using the SPSS 26 program.

Results: Of the 747 patients, 175 (23.4%) had been identified as having AML. It had 98 (56%) men and 77 (44%) women, whose ages ranged from 1 to 75. There were 543 (79.7%) patients with acute leukemia (ALL and AML) as well as 138 (20.3%) patients with chronic leukemia (CML and CLL). ALL, AML, CML, and CLL were the most common types of leukemia, with a prevalence rate of each of 49.30%, 23.43%, 11.65%, and 6.83% for all patients, respectively. FAB-M2 was observed in 48.57% of patients, followed by M5 (17.72%), M1 (15.43%), M3 (11.43%), M4 (5.71%), and the less common M0 (0.57%), M7 (0.57%), and M6 (0%). Hematological characteristics included decreased Hb, increased WBC, and decreased platelets in 96.6%, 81.7%, and 100% of patients, respectively. Age and Hb and WBC had strong positive relationships (p=0.009 and p=0.002, respectively), as did Hb and WBC (p=0.001).

Conclusion: Leukemia was the most common type of hematological malignancy. AML accounts for about 25% of all cases of leukemia. Half of the AML patients had the most frequent FAB subtype, AML-M2.

Keywords: Acute Myeloid Leukemia (AML); Anemia; Thrombocytopenia; Hematological Malignancies (HMs).

INTRODUCTION

Leukemia is a heterogeneous cluster of hematological malignancies characterized by excessive, abnormal proliferation and accumulation of malignant white blood cells within the Bone Marrow (BM) and peripheral blood [1]. It is a clonal neoplasm of hematopoietic cells that results from arrays of factors resulting in somatic mutations in pluripotent stem cells and progenitor cells [2,3].

The incidence of leukemia increased round the world [4,5]. Leukemia ranked thirteenth among all cancers worldwide, whereas its deaths increased by 16.5% [6]. Globally, from 1990 to 2018, the number of cancer cases increased from 297,033 to

Correspondence to: Mohammed Abdulkader Al-Nuzaili, Department of Hematology, Sana'a University, Sana'a, Yemen, E-mail: malnuzaily@yahoo.com

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437,033 [6]. In 2018, there were 437.0 thousand new cases of and 309.0 thousand cancer deaths from leukemia worldwide [7]. In Yemen, the distribution of Hematological Malignancies (HM) increased in south-west Yemen [8]. The incidence rate of cancers increased in South Yemen [9]. The prevalence of leukemia increased at oncology centers in Aden, Hadramoot, and Taiz [10].

Leukemia is classified by 2 classification systems, the French-American-British (FAB) and the World Health Organization (WHO) [11,12]. The FAB system relies on morphology and cytochemistry to outline specific kinds of leukemia [11], and the WHO system relies on morphology, immunophenotypic, cytogenetics, and clinical features to outline and categorize important disease entities [12]. Consistent with the FAB classification, leukemia is divided into myeloid and lymphoid leukemia. Myeloid leukemia is divided into Acute Myeloid Leukemia (AML, with subtypes M0 through M7), Chronic Myelocytic Leukemia (CML), and Myelodysplastic Syndromes (MDS) [11]. Lymphoid malignancies are divided into four categories: Acute Lymphoblastic Leukemia (ALL), Chronic Lymphocytic Leukemia (CLL), malignant lymphoma and Plasma Cell Neoplasms (PCN), and Hairy Cell Cancer (HCL) [13].

The causes of leukemia include many risk factors, like genetic mutations, hereditary inheritance, ionizing radiation, epigenetic lesions, chemical and alternative occupational exposures, smoking, therapeutic medication, and a few viral agents [14,15].

Acute Myeloid Leukemia (AML) is a malignant disorder of the myeloid cell lineage within the Bone Marrow (BM). It is caused by chromosomal abnormalities resulting in the accumulation of myeloblasts within the BM and infiltration of peripheral tissues [16]. The infiltration of tumor cells into the bone marrow causes symptoms of bone marrow failure like anemia, infections, bleeding, and pallor. Also, the infiltration of neoplasm cells into the liver and spleen [1].

The incidence of AML is 3-4 cases per 100,000 people worldwide [1,17]. The incidence of AML is increasing even in developed countries like Canada and Australia [18]. The incidence of AML increases with increasing age, and it's more common in males than females, with a male-to-female ratio of 2.5:1 [4,16].

Acute Myeloid Leukemia (AML) is classified by the French-American-British (FAB) and the World Health Organization (WHO) systems [11,12]. The FAB system divides AML into 8 subtypes, i.e., from M0 to M7, on the basis of the morphology of myeloblasts and cytochemistry [11,16]. In certain cases, when the definitive diagnosis cannot be made by morphology, help is taken from immunophenotypic [16]. The WHO classifies AML on the basis of morphology, immunophenotypic, and cytogenetics [12]. According to the WHO, the diagnosis of AML is confirmed if the bone marrow has more than 20% myeloblasts [12]. However, WHO additionally suggests that if certain genetic alterations specific for AML are present within the patient, the 20% blast criteria isn't necessary [19]. The WHO classification cannot be used widely for patients in developing countries like Yemen due to the price and availability of facilities for cytogenetic and immunophenotypic analysis. On the opposite hand, FAB classification needs no advanced technology and may simply be practiced in most laboratories in Yemen.

In Yemen, there are four cancer registries: The one at the National Oncology Center (NOC) in Sana'a, the Aden Cancer Registry (ACR), the Hadhramout Cancer registry, and the Taiz Cancer registry. The insufficient data and information on cancer patterns can lead to inadequate health services, transient populations, a lack of funding and a shortage of trained personnel. Because there were insufficient data on leukemia patterns at NOC, the aim of this study was to determine the prevalence, subtypes, and hematological features of acute myeloid leukemia among patients at NOC in Sana'a, the capital of Yemen.

MATERIALS AND METHODS

Site of the registry

This cross-sectional study was carried out on 747 patients diagnosed with Hematological Malignancies (HMs) at the National Oncology Center (NOC). It included 472 (63.2%) males and 275 (36.8%) females, aged 1 to 75 years. The registered data was collected from the NOC in Sana'a, Yemen, between March 2020 and May 2022. These patients came to the NOC from different hospitals and clinics in Sana'a as well as from other governorates. The patients came to NOC for a better diagnosis and appropriate treatment. Among 747 patients, there were 175 (23.43%) patients diagnosed with Acute Myeloid Leukemia (AML). Diagnosis of AML was performed by Complete Blood Count (CBC) using the Advia 2120 hematology analyzer (Siemens, Germany), by Giemsa-stained blood/BM films for morphology of cells, and by immunophenotyping using flow (Becton Dickinson Immunocytometry Systems, 2350 Qume Drive, San Jose, California, Model FACSCalibur, USA). Immunophenotyping was used in certain cases to confirm the diagnosis and subtypes of AML that showed myeloid marker positivity. The data regarding sex, age, hematological parameters (hemoglobin, total leukocyte count, and platelet count), subtypes of AML, and years of diagnosis were obtained and registered.

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 26 (IBM corporation., New York, USA). Descriptive data were given as mean ± Standard Deviation (SD), frequency, and percentages. Pearson correlation coefficients (R) were calculated to quantify the relationship between parameters, and $P<0.05$ was considered statistically significant. Tables were used for the presentation of the data. Percentages of the various categories of HMs and AML subtypes with demographic variables were explored using percentages in tables.

RESULTS

Among 747 patients with Hematological Malignancies (HMs), there were 472 (63.2%) males and 275 (36.8%) females, and the M:F ratio was 1.7:1. Leukemia was the most common

hematological malignancy seen in 681 (91.2%) patients. Acute leukemia (ALL and AML) was the more common type than chronic Leukemia (CML and CLL). Acute leukemia was seen in 543 (79.7%) of patients, while chronic leukemia was seen in 138 (20.3%) of patients. The relative frequencies of them were as follows: ALL was the first prevalent type diagnosed in 368 (49.30%) of patients with a M:F ratio of 1.9:1, followed by AML, which was 1.9:1, followed by AML, which was seen in 175 (23.43%) of patients with a M:F ratio of 1.3:1, followed by CML in 87 (11.65%) of patients with a M:F ratio of 1.6:1, and then by Follicular Lymphoma (FL) and Burkitt Lymphoma (BL) (0.26% each), Mantle Cell Lymphoma (MCL) and Hairy Cell Leukemia (HCL) (0.13% each) (Table 1).

The pattern of AML subtypes in 175 AML patients, included 98 males and 77 females. The age of the patients ranged from 1-75 years, with a mean ± SD of 28.9 ± 21.9 years. The FAB-M2 was the first frequent subtype of AML that was diagnosed in 85 (48.57%) of patients; among them, there were 43 (50.6%) males and 42 (49.4%) females, the M:F ratio was 1:1, the mean ± SD of age was 32.4 ± 22.8, the minimum and maximum age values were 1 and 75 years. The FAB-M5 (M5+M5a+M5b) was the second frequent subtype of AML that was diagnosed in 31 (17.72%) patients, among whom there were 22 (71.0%) males and 9 (29.0%) females; the M:F ratio was 2.1:1 with mean ± SD of age of 23.8 ± 17.3. It was followed by FAB-M1, M3, M4, M0, and M7. FAB-M6 was not seen in our study (Table 2).

No.	Type of malignancy	Male	Female	Total number	%	M:F ratio
1	ALL	243	125	368	49.3	1.9:1
2	AML	98	77	175	23.43	1.3:1
3	CML	54	33	87	11.65	1.6:1
4	CLL	34	17	51	6.83	2:1
5	MM	17	10	27	3.61	1.7:1
6	MDS	6	2	8	1.07	3:1
7	CMML	4	2	6	0.8	2:1
8	ET	2	4	6	0.8	1:2
9	Lymphoma	4	1	5	0.67	4:1
10	PCL	2	1	3	0.4	2:1
11	MF	2	1	3	0.4	2:1
12	aCML	2	-	2	0.26	2:0
13	FL	-	2	2	0.26	0:2
14	Burkitt L	2	-	2	0.26	2:0
15	MCL	1	-	1	0.13	1:0
16	HCL	1	-	1	0.13	1:0
Total		472	275	747	100%	1.7:1

Table 1: Distribution and prevalence of hematological malignancies according to number and sex (n=747).

CLL in 51 (6.83%) of patients with a M:F ratio of 2:1, followedby Multiple Myeloma (MM) (3.61%), Myelodysplastic syndrome (MDS) (1.07%), Essential Thrombocytopenia (ET) (0.80%), Chronic Myelomonocytic Leukemia (CMML) (0.80%), Lymphoma (0.67%), Plasma Cell Leukemia (PCL) and Myelofibrosis (MF) (0.40% each). Other less common types of HMs were Atypical Chronic Myeloid Leukemia (aCML),

FAB subtype of AML	N (%)	Sex		Age				
		Male	Female	M:F ratio	Mean ± SD	Range	Minimum	Maximum
		N (%)	N (%)					
AML-M0	1 (0.57)	1 (100)	-	1:00	60	-	-	-
AML-M1	27 (15.43)	13 (48.1)	14 (51.9)	0.9:1	32.8 ± 22.4	10.4-55.2	2	70
AML-M2	85 (48.57)	43 (50.6)	42 (49.4)	1:01	32.4 ± 22.8	9.6-55.2	1	75
AML-M3	18 (10.29)	11 (61.1)	7 (38.9)	1.6:1	18.9 ± 13.6	5.3-32.5	1	52
AML-M3v	2 (1.14)	2 (100)	-	2:00	19 ± 8.5	10.5-27.5	13	25
AML-M4	9 (5.14)	5 (55.6)	4 (44.4)	1.25:1	38.5 ± 26.7	11.8-65.2	6	70
AML-M4e	1 (0.57)	-	1 (100)	0:01	23	-	-	-
AML-M5	21 (12.0)	16 (76.2)	5(23.8)	3.2:1	11.9 ± 11.1	0.8-23	1.5	40
AML-M5a	7 (4.0)	5 (71.4)	2(28.6)	2.5:1	23.6 ± 16.2	7.4-39.8	1.6	48
AML-M5b	3 (1.71)	1 (33.3)	2(66.7)	0.5:1	36.0 ± 24.5	11.5-60.5	11	60
AML-M6	-	-	-	-	-	-	-	-
AML-M7	1 (0.57)	1 (100)	-	1:00	13	-	-	-

Table 2: Pattern of AML subtypes according to the sex and age of patients (n=175).

Hematological parameter	Mean ± SD	Range	Minimum	Maximum
Hb	8.0 ± 1.6	6.4-9.6	4.3	11.7
WBC	97.6 ± 89.4	8.2-187	0.5	320.7
Platelets	41.7 ± 21.2	20.5-62.9	6	0:00

Table 3: Hematological features in AML patients (n=175).

Hematological parameter	Low		Normal	High		
	n	%	n	%	n	%
Hb	169	96.6	6	3.4	-	-
WBC	15	8.6	17	16:48	143	81.7
Platelets	175	100	-	-	-	-

Table 4: Pattern of change in basic hematological parameters in AML patients (n=175).

The hematological features in AML patients (n=175) included Hemoglobin (Hb), White Blood Cells (WBC), and platelets. The mean ± SD for Hb, WBC, and platelets were 8.0 ± 1.6, 97.6 ± 89.4 and 41.7 ± 21.2, respectively (Table 3).

The pattern of change in basic hematological parameters in AML patients (n=175). Anemia was detected in 169 (96.6%) patients, leukocytosis was detected in 143 (81.7%) patients, and thrombocytopenia was detected in 175 (100%) patients (Table 4).

The hematological features in patients with AML subtypes (n=175). For FAB-M1, the mean ± SD of Hb was 7.5 ± 1.3, the minimum and maximum values were 5.1 and 10.3; the mean ± SD of WBC was 35.2 ± 72.7, the minimum and maximum values were 1.5 and 289.4; whereas the mean ± SD of platelets was 29.5 ± 16.9, the minimum and maximum values were 6 and 83. For FAB-M2, the mean ± SD of Hb was 8.4 ± 1.5, while the mean ± SD of WBC was 150.0 ± 79.1, and the mean ± SD of platelet was 43.5 ± 20.7. For FAB-M3, M4, M5, M5a, M5b, M0, and M7, data are shown in Table 5.

AML Subtype	Hb				WBC	Platelets		
	Maximum	Minimum	Range	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD
AML-M0	-	-	-	8.4	-	16.7	-	55
AML-M1	10.3	5.1	6.2-8.8	7.5 ± 1.3	-145.4	35.2 ± 72.7	12.6-46.4	29.5 ± 16.9
AML-M2	16:48	4.6	6.9-9.9	8.4 ± 1.5	70.9-229.1	150.0 ± 79.1	22.8-64.2	43.5 ± 20.7
AML-M3	11	4.3	5.4-9.0	7.2 ± 1.8	-79.8	20.5 ± 39.9	14.6-58.6	36.6 ± 22.0

AML-M3v	14:24	9.5	9.4-9.5	9.5 ± 0.07	182.7-291.9	237.3 ± 54.6	64.7-80.3	72.5±7.8
AML-M4	10.2	6.2	7.0-9.4	8.2 ± 1.2	40.9-198.3	119.6 ± 78.7	34.6-63.0	48.8 ± 14.2
AML-M4e	-	-	-	9.6	-	97.8	-	60
AML-M5	11.2	5.4	5.6-9.4	7.5 ± 1.9	9.7-95.5	52.6 ± 42.9	28.4-65.4	46.9 ± 18.5
AML-M5a	9.2	6.2	7.01-8.9	8.0 ± 0.99	16.1-36.7	26.4 ± 10.3	9.7-43.9	26.8 ± 17.1
AML-M5b	8.4	8.1	8.0-8.3	8.2 ± 0.15	15.5-55.3	35.4 ± 19.9	26.3-80.3	53.3 ± 27.0
AML-M6	-	-	-	-	-	-	-	-
AML-M7	-	-	-	9.8	-	17.7	-	43

Table 5: Hematological features in patients with AML subtypes (n=175).

There were significant positive correlations between age and Hb (r=0.19, p=0.009) and WBC (r=0.237, p=0.002), and a non-significant correlation between age and platelets (r=0.020, p=0.797). There was a significant positive correlation between Hb and WBC (r=0.241, p=0.001) and a non-significant positive correlation between Hb and platelets (r=0.104, p=0.169). There was a non-significant correlation between WBC and platelets (r=0.074, p=0.328) (Table 6).

Variable	Age		Hb	WBC	Platelet			
	R	P-value	r	P-value	r	P-value	r	P-value
Age	1	-	0.197	0.009	0.237	0.002	0.02	0.797
Hb	0.197	0.009	1	-	0.241	0.001	0.104	0.169
WBC	0.237	0.002	0.241	0:01	1	-	0.074	0.328
Platelet	0.02	0.797	0.104	0.169	0.074	0.328	1	-

Table 6: Correlations between variables among AML patients (n=175).

DISCUSSION

In the present study, we found an increased prevalence of HMs in males (63.2%) more than females (36.8%) for all types of HMs except for ET and FL. The distribution and prevalence of Hematological Malignancies (HM) were leukemia (91.2%), followed by Multiple Myeloma (MM) (3.61%), Myelodysplastic Syndrome (MDS) (1.07%), Essential Thrombocythemia (ET) (0.80%), Chronic Myelomonocytic Leukemia (CMML) (0.80%), lymphoma (0.67%), plasma cell leukemia (PCL) (0.40%), and Myelofibrosis (MF) (0.40%). Other types of HMs were less common, such as Atypical Chronic Myeloid Leukemia (aCML) (0.26%), Follicular Lymphoma (FL) (0.26%), Burkitt Lymphoma (BL) (0.26%), Mantle Cell Lymphoma (MCL) (0.13%), and Hairy Cell Leukemia (HCL) (0.13%).

Similar to other previous studies done in Yemen that have reported an increased distribution of Hematological Malignancies (HM) in south-west Yemen [8], an increased incidence rate of cancer in south Yemen [9], and an increased prevalence of leukemia at oncology centers in Aden, Hadramoot, and Taiz [10]. A study done by Saeed et al. in south-west Yemen (Taiz and Ibb provinces) has reported an increased prevalence of HMs. between September 2016 and October 2020. The distribution of HMs was as follows: acute leukemia (45.9%), chronic leukemia (26.2%), Acute Lymphoblastic Leukemia (ALL) (23.6%), Acute Myeloblastic Leukemia (AML) (22.2%), Chronic Myeloid Leukemia (CML) (14.9%), Chronic Lymphocytic Leukemia (CLL) (11.2%), MPN (16.3%), MDS (7.1%), Multiple Myeloma (MM) (1.8%), and lymphoma (2.8%)[8]. Other studies done by Amen B (2018) in South Yemen (Aden, Lahej, Abyan, and Al-Dhale Provinces) have reported the incidence rate of cancers from 1997 to 2011 was 21.6/100,000 populations [9]. The top five cancers among males were leukemia (10.5%), Non-Hodgkin Lymphoma ((NHL), 10.1%), colon cancer (7.5%), Hodgkin Disease ((HD), 6.1%), and stomach cancer (5.1%). For females, breast cancer was the most common (30.0%), followed by leukemia (7.6%), NHL (6.6%), colonic (4.9%) and ovarian cancer (4.5%) [9]. Another study done by Radfan et al. on 1522 Yemeni patients with leukemia registered from June 2010 to December 2014 at oncology centers in Aden, Hadramoot and Taiz, found that ALL was the most common type (33.6%) of the total registered cases of leukemia, followed by AML (26.5%), CML (23.5%) and CLL (16.4%). The most affected age group for ALL was 1-10 years followed by 11-20 years [10].

In the present study, we found that leukemia was the first and most common HM. The prevalence of leukemia was higher (91.2%) than other types of HMs, and higher in males (63%) than females (37%), for all types of leukemia. Acute leukemia (ALL+AML) was the most prevalent type (79.7%), followed by chronic leukemia (CML+CLL), which was seen in 20.3% of patients. Among HMs, we observed that Acute Lymphoblastic Leukemia (ALL) was the first most prevalent type (49.30%), whereas Acute Myeloblastic Leukemia (AML) was the second most prevalent type (23.43%). Chronic Myeloid Leukemia (CML) and Chronic Lymphocytic Leukemia (CLL) were the third and fourth most prevalent types, with prevalences of 11.65% and 6.83%, respectively. Similar findings were reported for an increased prevalence of leukemia in Yemen [8-10].

In the present study, regarding AML subtypes, we found that AML-M2 was the most common subtype seen in 85 (48.57%) AML patients, followed by AML-M5 (17.72%), AML-M1 (15.43%), AML-M3 (11.43%), AML-M4 (5.71%), AML-M0 (0.57%), and AML-M7 (0.57%). AML-M6 was not seen in our study. This finding in our study was in accordance with other studies that reported M2 to be the most common subtype in their studies [1,4,20,21] and in contrast to other studies that showed a predominance of M1 in her study [16]. It is reported that different AML subtypes have different prognostic values [22]. FAB subtypes M0, M5, M6, and M7 are associated with the worst prognosis, while M2 and M4 have a good prognosis. AML-M3 has the best prognosis of all subtypes of AML [22].

In our study, we found that there was a slight male predominance of AML, with a male to female ratio of 1.3:1. Similar previous studies suggest male predominance in AML [1,4,18]. In a study done by Naeem R in 2017, there was male predominance in AML, shown by a male to female ratio of 1.5:1 [1].

In the present study, regarding hematological features among AML patients (n=175), we found high prevalences of anemia (96.6%), leukocytosis (81.7%), and thrombocytopenia (100%) in AML patients. The mean hemoglobin was decreased (mean of 8.0 g/dL), the total leukocyte count was increased (mean of 97.6 × 10^9/L), and the platelet count was decreased (mean of 41.7 × 10^9/L). Similar patterns of changes in hematological parameters were reported in other studies [1,4,16,22]. A study done by Sultan S, where total leukocyte count was increased (mean 43 ± 6.8 × 10^9/L) while hemoglobin and platelet count were decreased (mean 8.2 ± 2 g/dl and 62 ± 7.8 × 10^9/L, respectively) [22].

CONCLUSION

Leukemia was the most common type of hematological malignancy. AML accounts for about 25% of all cases of leukemia. Half of the AML patients had the most frequent FAB subtype, AML-M2. We recommended that further studies be done. Parameters like karyotypes and cytogenetic patterns should be analyzed. More studies should be done in different regions of Yemen to give information that assists in a suitable diagnosis and treatment.

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