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Acute Myeloid Leukemia among Patients attending Sana'a Hospitals, Yemen: Prevalence, Subtypes and Hematological Patterns

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ABSTRACT

Objectives: Acute myeloid leukemia (AML) is malignant disorder of cells of myeloid lineage in the bone marrow due to chromosomal abnormalities, leading to accumulation of myeloblasts in the bone marrow and infiltration to peripheral tissues. The aim of this study was to determine the prevalence, subtypes and hematological patterns of AML among patients attending Sana'a hospitals, Yemen.

Materials and methods: This cross-sectional study was carried out on total 257 patients with hematological malignancies (HMs) during the period from November 1, 2023 to March 31, 2024. Among HMs, there were 79 patients diagnosed with AML by complete blood count (CBC), by Giemsa stained blood/BM films, and by immunophenotyping using flow cytometry. Data was analyzed using SPSS-26.

Results: Among 257 patients with HMs, AML was found in 79 patients with prevalence of 30.7%. AML patients included 53 (67.1%) males and 26 (32.9%) females., with M:F ratio of 2:1 and aged between 4 and 80 years, FAB-M2 was the most common subtype of AML in 30 (37.97%) of patients; among them, there were 19 (24.05%) males and 11 (13.92%) females, the M:F ratio is 1.7:1. FAB-M2 was followed by M1 (26.58), M5 (17.2), M3 (7.59), M4 (5.06), M0 (3.8) and M7 (1.26). The hematological patterns included decreased Hb, increased WBC and decreased platelets in 97.5%, 82.3% and 96.2% of patients, respectively.

Conclusion: Leukemia was the most prevalent type among hematological malignancies. The prevalence of AML was high and represent the second leukemia type. AML-M2 was the common subtype of AML.

CONTENTS

1. Introduction:

The leukemias are a group of malignant disorders characterized by the accumulation of malignant white blood cells in the bone marrow and peripheral blood [1,2].

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 [3,4].

Leukemia ranked thirteenth among all cancers worldwide [5]. The incidence of leukemia increased round the world [6,7], whereas its deaths increased by 16.5% [8]. Globally, between 1990 to 2018, the number of leukemia cases markedly increased from 297,000 to 437, 033 [8]. In 2018, it is estimated there were a total of 437.0 thousand new cases of and 309.0 thousand cancer deaths from leukemia worldwide [9].

In Yemen, the distribution of Hematological Malignancies (HM) increased at National Oncology Center in Sana'a [2], increased in south-west Yemen [10]. The incidence rate of cancers increased in South Yemen [11]. The prevalence of leukemia increased at oncology centers in Aden, Hadramoot, and Taiz [12].

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 [13]. 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].

Acute myeloid leukemia (AML) is classified by the French-American-British (FAB) and the World Health Organization (WHO) systems [14,15]. The FAB system divides AML into 8 subtypes, i.e., from M0 to M7, on the basis of the morphology of myeloblasts and cytochemistry [13,14]. In certain cases, when the definitive diagnosis cannot be made by morphology, help is taken from immunophenotypic [13]. The WHO classifies AML on the basis of morphology, immunophenotypic, and cytogenetics [15].

The causes of AML occur sporadically as a de novo malignancy in previously healthy individuals but it can arise in patients with an underlying hematological disorder, exposure to chemicals (benzene), radiation or tobacco smoke, previous chemotherapy and inherited conditions such as Down's syndrome [16].

The global incidence of AML is 3–4 cases per 100,000 populations [1,17,18]. Its incidence increases with increasing age [6]. The reported age of diagnosis of AML is about 60-67 years [1,17,18]. It occurs commonly in males, with male to female ratio of 2.5:1. The incidence of AML is increasing even in developed countries like Canada and Australia [19].

In Yemen, previous studies suggest that acute myeloid leukemia (AML) is the most common type of leukemia among adults in Yemen, with a prevalence varies between 23.43% [2], 22.2% ([10], 26.5% [12], 45.1% [20] and 39.1% [21]. Alhadi *et al.* (2021) reported that AML prevalence was 15.6% among childhood leukemia [22].

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 types in different Sana'a hospitals, therefore, the aim of this study was to determine the prevalence, subtypes, and hematological patterns of acute myeloid leukemia among patients attending some hospitals in Sana'a city, Yemen.

2. Materials and methods

- **Study population**

This cross-sectional study was carried out on total 257 patients with hematological malignancies. Among of them, there were 79 patients diagnosed as acute myeloid leukemia (AML) included 53 males and 26 females and aged between 4 and 80 years. This study was conducted during the period from November 1, 2023 to March 31, 2024. The patients were attended the hematology and oncology clinics at some government and private hospitals as well as medical laboratories centers in Sana'a city, Yemen. It included Al-Gomhori Teaching Hospital Authority, National Oncology Center (NOC), University of Science & Technology

Hospital and Al-Mamoon Diagnostic Medical Center.

- **Sample collection**

Two milliliters and half (2.5 ml) of blood sample was collected in EDTA tube from each patient., Blood samples were carried out for measurment of complete blood count (CBC) by automated hematology analyzer, for morphological examination of blood/BM films and for immunophenotiping by flow cytometry.

- **Laboratory investigations**
- **Complete blood count (CBC)**

Complete blood count (CBC) was done by automated hematology analyzer using SYsmex XN 550 (Sysmex, Japan),

- **Morphological examination of blood/BM films**

By using Giemsa stain for study the morphology of cells.

- **Immunophenotyping by flow cytometry**

Immunophenotyping by flow cytometry was done by using (BD FACSLYRIC™, Flow cytometry, USA) using peripheral blood.

- **Statistical analysis**

Data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 26 (IBM Inc., 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-values less than 0.05 were considered statistically significant.

3. Results

As shown in **Table 1**, Among 257 patients with hematological malignancies (HMs), there were 156 (60.7%) males and 101 (39.3%) females with a M:F ratio of 1.5:1. Leukemia was diagnosed in 242 (94.16%) patients. Acute leukemia (ALL and AML) was diagnosed in 173 (67.32%) patients, while chronic leukemia (CML and AML) was diagnosed in 69 (26.84%) patients. ALL was diagnosed in 94 (36.6%) patients with a M:F ratio of 1.4:1, followed by AML, which was seen in 79 (30.7%) patients with a M:F ratio of 2:1, followed by CML in 40 (15.6%) patients with a M:F ratio of 1.5:1, followed by CLL in 29 (11.3%) patients with a M:F ratio of 0,9:1, Then, leukemia was followed by lymphoma and multiple myeloma (MM) (1.6% each), Hairy cell leukemia (HCL), Myelodysplastic syndromes (MDS), Non-Hodgkin lymphoma (NHL) (0.8% each), and Myelofibrosis (MF) (0,4%).

Table 1: Distribution and prevalence of hematological malignancies according to number and gender of patients (n=257)

Type of Malignancy	Female (N)	Male (N)	Total Number	% of Total
ALL	39	55	94	36.6%
AML	26	53	79	30.7%
CLL	15	14	29	11.3%
CML	16	24	40	15.6%
HCL	0	2	2	0.8%
Lymphoma	2	2	4	1.6%
MM	3	1	4	1.6%
MF	0	1	1	0.4%
MDS	0	2	2	0.8%
NHL	0	2	2	0.8%
Total	101	156	257	100.0%

As shown in **Table 2,** the patterns of AML subtypes according to sex and age in 79 patients included 53 (67.1%) males and 26 (32.9%) females with a M:F ratio of 2:1.. The age of the patients ranged from 4-80 years, with a mean ± SD of 36.19 ± 22.07 years. The FAB-M2 was diagnosed in 30 (37.97%) of patients; among them, there were 19 (24.05%) males and 11

(13.92%) females, the M:F ratio was 1.7:1, with mean ± SD of age was 57.41±21.44. The FAB-M2 was followed by FAB-M1 (26.58%), M5 (17.2%), M3 (7.59%), M4 (5.06%), M0 (3.8%) and M7 (1.26%). FAB-M6 was not seen in our study.

Table 2: Patterns of AML subtypes according to sex and age of patients (n=79)

FAB subtype of AML	n (%)	Sex		Age			
		Male n (%)	Female n (%)	Mean ±SD	Range	Min.	Max.
AML – M0	3 (3.8)	3 (3.8)	0 (0.0)	30.67 ±17.21	33	17	50
AML – M1	21 (26.58)	16 (20.25)	5 (6.33)	91.01 ±42.46	119	36	155
AML – M2	30 (37.97)	19 (24.05)	11 (13.92)	57.41 ±21.44	72	30	102
AML – M3	6 (7.59)	1 (1.26)	5 (6.33)	41.17 ±15.62	44	16	60
AML – M4	4 (5.06)	4 (5.06)	0 (0.0)	37.25 ±37.82	66	4	70
AML – M5	14 (17.2)	9 (11.4)	5 (6.33)	38.14 ±22.28	70	5	75
AML – M6	-	-	-	-	-	-	-
AML – M7	1 (1.26)	1 (1.26)	0 (0.0)	5	0	5	5
Total	79 (100)	53 (67.1)	26 (32.9)	36.19 ±22.07	76	4	80

As shown in **Table 3,** the hematological features in AML patients (n=79) included hemoglobin (Hb), white blood cell (WBC) and platelets. The mean ± SD for Hb, WBC, and platelets were 7.94 ±1.67, 89.84 ±93.03 and 48.58±74.81, respectively. The minimum and maximum for Hb values were 4.5 and 13.9g/dl, for WBC values were 0,68 and 464, and for platelets values were 4 and 531.

Table 3: Hematological patterns in AML patients (n=79)

Hematological parameter	Mean±SD	Range	Min.	Max.
Hb (g/dL)	7.94 ±1.67	9.40	4.50	13.90
WBC ($x10^9$/L)	89.84 ±93.03	463.32	0.68	464.00
Platelets($x10^9$/L)	48.58±74.81	527	4	531

As shown in **Table 4,** the pattern of changes in basic hematological parameters in AML patients (n=79). In regard to Hb level, a low Hb level (anemia) was detected in 77 (97.5%) patients, whereas normal level was detected in 2 (2.5%). In regard to WBC count, a high WBC count (leukocytosis) was detected in 65 (82.3%) patients, whereas a low WBC count (leukopenia) was detected in 8 (10.1%) patients, while 6 (5.6%) patients with normal WBC count. In regard to platelet count, a low platelet count (thrombocytopenia) was detected in 76 (96.2%) patients, whereas a normal platelet count was detected in 2 (2.5%), while a high platelet count (thrombocytosis) was detected in 1 (1.3%) patient.

Table 4: Pattern of changes in hematological parameters in AML patients (n=79)

Hematological parameter	Low		Normal		High	
	n	%	N	%	n	%
Hb	77	97.5	2	2.5	-	-
WBC	8	10.1	6	7.6	65	82.3
Platelets	76	96.2	2	2.5	1	1.3

As shown in **Table 5,** the hematological patterns in patients with AML subtypes (n=79). For FAB-M2, the mean ± SD of Hb, WBC and platelets were 15.70 ± 1.56, 69.00 ± 85.25, and 88.62 ± 68.84, respectively. For FAB-M0 to M7, data were shown in Table 5.

Table 5: Hematological patterns in patients with AML subtypes (n=79)

AML Subtypes	Hb				WBC				Platelets			
	Mean±SD	Range	Min.	Max.	Mean±SD	Range	Min.	Max.	Mean±SD	Range	Min.	Max.
AML M0	6.33±1.11	8.12	5.5	7.6	84.06±24.24	125.45	64	111	17.67±10.78	68.53	10	30
AML M1	14.97±3.32	11.5	10.8	19.8	206.88±216.84	619.7	3.3	438.9	119.53±179.72	627	32	553
AML M2	15.70±1.56	8	12.9	20.9	69.00±85.25	462.4	2.28	464.6	88.62±68.84	375	44	419
AML M3	8.61±1.45	3.8	6.2	10	29.33±20.21	51	4	55	21±10.12	27	9	36
AML M4	7.05±1.48	3.4	5.8	9.2	98.7±53.95	104.8	39.8	144.6	37.7±517.93	37	11	48
AML M5	8.04±1.55	6	4.5	10.5	128.57±89.76	300.8	4.2	305	47.64±34.26	119	16	135
AML M6	-	-	-	-	-	-	-	-	-	-	-	-
AML M7	7.9	0	7.9	7.9	33.9	0	33.9	33.9	22	0	22	22
Total	7.94±1.68	9.4	4.5	13.9	89.84±93.03	463.32	0.68	464	48.58±74.82	527	4	531

As shown in **Table 6,** the correlations between variables among AML patients (n=79). There were non-significant correlations between age with Hb, WBC and platelets (P>0.05). There was a significant negative correlation between Hb with WBC (r=-.239, p=0.034) and positive correlation with platelets (r=.307, p=0.006).

Table 6: Correlations between variables among AML patients (n=79)

Variable	Age		Hb		WBC		Platelet	
	R	*P* value	r	*P* value	r	*P* value	r	*P* value
Age	1	-	-.038-	.739	-.003-	.979	-.095-	.407
Hb	-.038-	.739	1	-	-.239-*	.034	.307**	.006
WBC	-.003-	.979	-.239-*	.034	1	-	.135	.235
Platelet	-.095-	.407	.307**	.006	.135	.235	1	-

Pearson correlation, correlation is significant at the 0.05 level (2-tailed)

4. Discussion

In the present study, we found an increased prevalence of Hematological Malignancies (HMs) in males (60.7%) more than females (39.3%), with a M:F ratio of 1.5:1 for all types of HMs except for Chronic Myeloid Leukemia (CML) and Multiple Myeloma (MM). The distribution and prevalence of HMs was leukemia (94.16%), followed by lymphoma and Multiple Myeloma (MM) (1.6% each), Hairy Cell Leukemia (HCL), Myelodysplastic Syndromes (MDS), Non-Hodgkin Lymphoma (NHL) (0.8% each), and Myelofibrosis (MF) (0,4%). Similar findings were reported for an increased distribution and prevalence of hematological malignancies in Yemen [2,10-12].

In the current study, we found that leukemia was the most common type among HMs with a prevalence of 94.16%. Acute leukemia (ALL and AML) was the more common type than chronic leukemia (CML and CLL) with prevalence of 67.32%) and 26.84%, respectively. ALL was the first prevalent type among leukemia and HMs with a prevalence of 36.6%, followed by AML (30.7%). CML (15.6%), and CLL (11.3%). Similar findings were reported for an increased prevalence of leukemia in Yemen [2,10-12]. A recent study reported an increased distribution and prevalence of hematological malignancies at national oncology center (NOC) in Sana'a [2]. Other previous studies reported an increased distribution of hematological malignancies in south-west Yemen [10], an increased incidence rate of cancer in south Yemen [11], and an increased prevalence of leukemia at oncology

centers in Aden, Hadramoot, and Taiz [12]. A recent study done by Al-Nuzaili et al. (2022) on total 747 patients with hematological malignancies at National Oncology Center (NOC) in Sana'a city. His study included 472 males and 275 females and conducted during the period from March 2020 to May 2022. He has reported an increased distribution and prevalence of HMs. The distribution of HMs was as follows: acute leukemia (79.7%), chronic leukemia (20.3%), Acute Lymphoblastic Leukemia (ALL) (49.3%), Acute Myeloblastic Leukemia (AML) (23.43%), Chronic Myeloid Leukemia (CML) (11.65%), Chronic Lymphocytic Leukemia (CLL) (6.83%), Multiple Myeloma (MM) (3.61%), MDS (1.07%), CMML and ET (0,8% each), lymphoma (0.67%), PCL and MF (0,4% each), aCML, FL and Burkitt L. (0,26% each), MCL and HCL (0,13% each) [2].

In our study, regarding AML, we found that AML was the second prevalent type among leukemia and HMs with a prevalence of 30.7% and a male predominance. AML was more common in males (67.1%) than females (32.9%) with a M:F ratio of 2:1. Regarding AML subtypes, we found that AML-M2 was the most common subtype (37.97%) among AML patients, and more common in males (24.05%) than females (13.92%) with a M:F ratio of 1.7:1. The FAB-M2 was followed by FAB-M1 (26.58%), M5 (17.2%), M3 (7.59%), M4 (5.06%), M0 (3.8%) and M7 (1.26%). FAB-M6 was not seen in our study. This finding in our study was in accordance with a recent study done by Al-Nuzaili et al. (2022) at NOC in Sana'a city [2] and other studies that reported M2 to be the most common subtype in their studies [1,6,23,24] and in contrast to other studies that showed a predominance of M1 in her study [13]. It is reported that different AML subtypes have different prognostic values [25]. FAB subtypes M0, M5, M6, and M7 were associated with the worst prognosis, while M2 and M4 have a good prognosis. AML-M3 has the best prognosis of all subtypes of AML [25]. Similar previous studies suggest male predominance in AML [1,2,6,19]. In a recent study done by Al-Nuzaili et al. in 2022, there was male predominance in AML, shown by a male to female ratio of 1.3:1 [2]. In other 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 the pattern of changes in basic hematological parameters in AML patients (n=79), we found high prevalence of anemia (97.5%), leukocytosis (82.3%), and thrombocytopenia (96.2%) in AML patients. The mean hemoglobin was decreased (mean of 7.9 g/dL), the total leukocyte count was increased (mean of 89.8 × 10^9/L), and the platelet count was decreased (mean of 48.6 × 10^9/L). Similar patterns of changes in hematological parameters were reported in other studies [1,2,6,13,25,26]. In a recent study done by Al-Nuzaili et al. in 2022, where total leukocyte count was increased (mean 97.6 ± 89.4 × 10^9/L) while hemoglobin and platelet count were decreased (mean 8.0 ± 1.6 g/dl and 41.7 ± 21.2 × 10^9/L, respectively [2]. Other 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) [25]. In our study, we found that Hb was significantly negatively correlated with WBC (p=0.034) and positively with platelets (p=0.006).

Abbreviations

PB: Peripheral blood; CBC: Complete Blood Count; BM: Bone marrow; FAB: French-American-British; WHO: World Health Organization; EDTA: Ethylene Diamine Tetra acetic Acid; RBC: Red Blood Cell; WBC: White Blood Cell; HMs: Hematological Malignancies; NOC: National Oncology Center; ACR: Aden Cancer Registry; AML: Acute Myeloid Leukemia; ALL: Acute Lymphoblastic Leukemia; CML: Chronic Myeloid Leukemia; CLL: Chronic Lymphocytic Leukemia; HCL: Hairy cell leukemia; MDS: Myelodysplastic syndromes; MF: Myelofibrosis; PCN: Plasma cell neoplasms; MPN: Myeloproliferative neoplasm; HL: Hodgkin lymphoma; NHL: non-Hodgkin lymphoma; MM: Multiple myeloma;

MCL: Mantle cell lymphoma; FL: Follicular lymphoma; BL: Burkitt lymphoma;

Ethics approval and consent to participate

Ethical approval was obtained from Authority Al-Gomhori Hospital, National Oncology Center (NOC), University of Science & Technology Hospital and Al-Mamoon Diagnostic Medical Center. No need for informed consent because the used data were registered and anonymous just with coded number and without any link to patient's identity. All data were kept confidential.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interest

The authors declare that they have no competing interests.

Conflict of interest

There is no conflict of interest.

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Authors' contributions

MAA developed the idea, wrote, drafted and edited the manuscript. KAA, KSA, AMA and SHAH has edited the manuscript. YHA has worked practically and analyzed the data. All authors read and approved the final manuscript.

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