A comprehensive study of incidence and clinical manifestations among Iraqi patients with newly diagnosed AML in 2022

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Abstract

Background: Leukemias are the primary cause of cancer-related mortality, AML has the lowest survival rate being one of the more prevalent leukemias in adults worldwide as well as in Iraq.

Materials and methods: The descriptive, epidemiological study was conducted on 412 newly diagnosed AML patients as a sample of the Iraqi population enrolled in the Oncology Center in the Medical City of Baghdad province and the Basrah Oncology Center in Basrah province during 2022. Their mean age was 42.09 ± 22.32 years.

Results: Among 412 patients, a median age of 40.05 was the predominant Iraqi AML which was lower than that of other developed countries. The disease was more predominant in age categories ($\geq$70) years and (60-69) years with 18.52 % and 16.26% respectively. The majority of the patients were suffering from pallor (65.29%), fever (49.76%), leukocytosis (43.20%) or cytopenia (27.18%) at the time of presentation.

Conclusion: The study indicates that the disease is highly prevalent, with a younger median age than in other nations, and the most prevalent subtype of AML was APL. The clinical and epidemiological features have effects on comprehending incidence and disease development.

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Introduction

Acute myeloid leukemia (AML), is a disease with great diversity with numerous genetic abnormalities which affect the disease outcomes. A very high number of new cases of cancer and deaths from the disease occurred globally during 2020 (1). Leukemia causes many incidences, accounting for an estimated 474,519 cases annually (2). According to the American Cancer Society (3), there will be over 24,000 leukemia-related fatalities in the US in 2022 including AML, ALL, CML, CLL3, and Other leukemias. AML offers a serious hazard since it has the lowest survival rate of any leukemia, while being one of the more prevalent leukemias in adults. Leukemias are the primary cause of cancer-related mortality among people under the age of 39 and in children while having a lower incidence than other types of cancer. Older individuals have the highest frequency of leukemia cases, with age beyond 60, the risk of incidence, particularly of AML, continually increases. Males are more likely than Females as AML patients, but the mean lifetime risk for both sexes is around 0.5%. The genetic composition profile confirms that the frequency of aberrant genes, which may be linked to leukemia cases, varies with age (4). In old age, leukemia patients have been found to have unfavourable cytogenetics, which is related to poor prognosis (5). Leukemia is one cancer type that is expected to appear in an increasing number of reports annually (2). The current study aimed to clarify the incidence of acute myeloid

leukemia among Iraqis within one year, provide statistical information on the incidence rates and their distribution among different FAB subtypes and age groups of AML patients and highlight the increase in incidence rates compared to previous decades.

Materials and methods

The descriptive, epidemiological study was conducted on newly diagnosed AML patients of the Iraqi population for both genders in 2022, (i.e., one-year duration) from two different geographical sites, at the Oncology Center in the Medical City of Baghdad province and the Basra Oncology Center in Basrah province. Patients in this study were examined clinically in addition to a questionnaire form including age, sex, address, CBC results, blast count of peripheral blood or bone marrow, and FAB subtype of AML. Diagnosis has been done also based on the morphological findings from stained smears from bone marrow samples in addition to immune phenotyping for diagnosis confirmation.

Results

1. Results of Demographic analysis

Four hundred and twelve AML patients were included in the study during 2022 from different residences of Iraq provinces with a mean age was 42.09 ± 22.32 years, and range from two months to 90 years, with a ratio of males to females about 1.4:1, (Table 1). The disease was more predominant in age categories ($\geq$70) years and (60-69) years with 18.52 % and 16.26% respectively (Figure 1).

Table 1: Results of Demographic analysis of AML patients

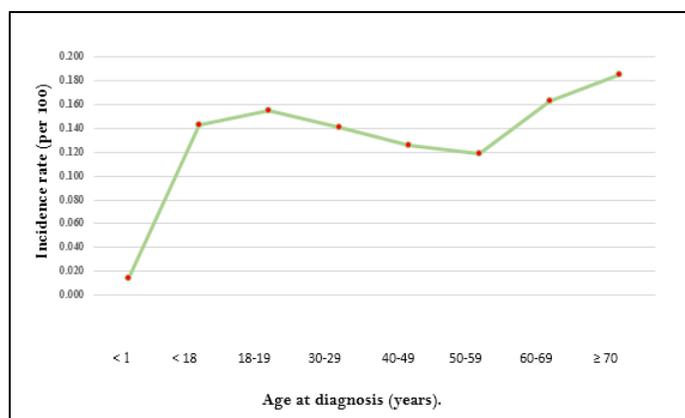| Variables	Description	No.	%
Sex	Males	241	58%
	Females	171	41.5%
Age at diagnosis	Mean ±SD	42.09±22.32	
	Median (Range)	40.5± (0.2-90)	

Figure 1: The incidence of AML patients in Iraq based on age, in 2022

Most of the patients, 124 (30.1%), were from Baghdad, 48 (11.65%) from Diyala, and 43 (10.43%) from Dhi-Qar. Number of patients from other provinces varied from (2-9 %). The newly diagnostic AML patients were classified as primary 379(91.9%) and secondary AML 33(8.1%) according to patient status, if they had any bone marrow disorder (post-AHD AML) or previous cancer and chemotherapy received for the treatment of preceding leukemia (not AML) or cancer (t-AML), so when the diagnosis was done to the first time, considered as (newly diagnosis) and who have AML considered as secondary AML. In contrast, patients who did not have any disorder or previous cancer and did not receive any chemotherapy were classified as De Novo AML or primary AML (Table 2). The primary AML patients group is moreover divided into subgroups according to FAB classification. Immunophenotyping results in seven

groups were started from M1 to M7, results show high percent (24.8%) of De novo AML patients with M3 type (promyelocytic leukemia) in classical 59 (15.57%) and variant form 35 (9.23%). Patients with M2 (18.73%), M0 (14.25%) and M5 (13.13%) type more than patients with M1 (7.92%) and M4 (8.44%) (Table 2). Secondary AML patient groups have been sub-classified into two groups according to WHO. Classification; Post-Antecedent Hematologic Disease (Post-AHD) AML group 16 (48.48%) and prior chemo-radiation exposure (therapy-related, t-AML) AML group 17(51.52%). The post-AHD AML group included patients with MPN (myeloproliferative neoplasms) 9(27.27%) more than patients with MDS (myelodysplastic syndromes) 7(21.21%), (Table 2).

Table 2: FAB classification of AML patients

FAB subtype of AML patients			No.	%
Primary AML (DE Novo AML)	**M0**		54	14.25%
	M1		30	7.92%
	M2		71	18.73%
	M3	M3-classical	59	15.57%
		M3-variant	35	9.23%
	M4		32	8.44%
	M5	M5a	19	5.01%
		M5b	27	7.12%
	M6		0	0.00%
	M7		18	4.75%
	Other		35	9.23%
Total			379	100%
Secondary AML	**Post-AHD AML**	MDS	7	21.21%
		MPN	9	27.27%
Total	**t-AML**		17	51.52%
			33	100%

2. Clinical presentations:

Majority of the patients were suffering from pallor (65.29%), fever (49.76%), leukocytosis (43.20%) or cytopenia (27.18%) at the time of presentations, so apart from patients were suffered from thrombocytopenia (29.37 %), bleeding (37.38%) and anemia (29.85%). Organomegaly, including hepatosplenomegaly, was seen in 28.88% of patients. Some patients had lymphadenopathy (20.39%) or ecchymosis (10.19%) and other clinical manifestations such as bone pain, Gum hypertrophy, weight loss, Down syndrome (in one patient), paraspinal mass with extramedullary disease (myeloid sarcoma) (so, in one patient; Figure 2).
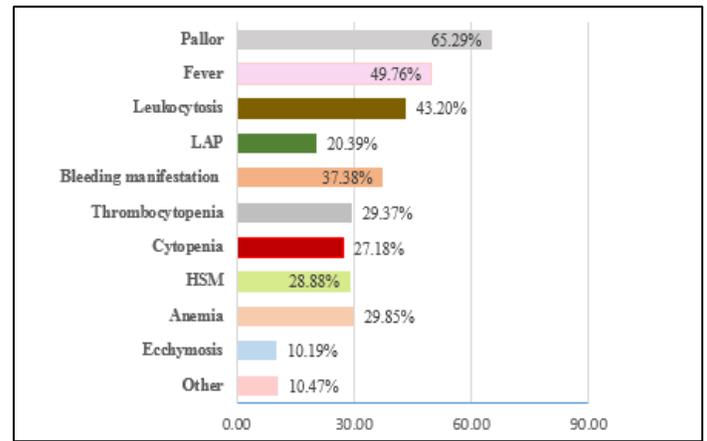

Figure 2: Clinical presentations in AML patient

Discussion

The results of the current study demonstrated 412 diagnosed AML patients within a one-year collection period, from two different geographical locations in Iraq: Baghdad (central Iraq) and Basrah (southern Iraq), and these cases were collected during the study regardless of the other AML cases that maybe we were not able to include it in our study, and perhaps much higher numbers of this disease were recorded in the statistical centers of those Oncology Centers. The presence of this incidence and for one type of leukemia requires multiple discussions and extensive research on the reasons behind the prevalence of such serious hazardous diseases in Iraqi society and the search for solutions that could contribute to the reduction of the incidence and prevalence of such diseases. A study conducted on leukemia patients who were registered and managed at the Iraqi Center for Hematology at Medical City in Baghdad (disease diagnosis and registration across all of Iraq, excluding Basrah and the Kurdistan areas), showed that there

were ٥٣٣ and 655 AML cases for the years 2018 and 2019, respectively (6). The present study indicates the occurrence of disease with a male-to-female ratio of 1.4:1, which is similar to other Iraqi studies; (7, 8). In the US, the occurrence of AML in males is 1.6 times more than in females as well (9). Chien *et al*. (2023) performed a study in 2001-2015 and their findings confirmed the result of the current study (10). Many studies have suggested that a history of MDS, and occupational and environmental exposures may be connected to the increased incidence of AML in men (11). Although AML can affect people of any age, its frequency increases with age. In the current study, this phenomenon showed up with the incidence of the 60–69 age group. The diagnosis age of patients in this study was 40.5 which is approximately similar to results from other studies on the Iraqi population (12,7). Iraqi's AML diagnosis age was lower than that of other developed countries. When AML was diagnosed, the median age in the UK, Canada, Australia, and Sweden was between 63 and 71 years old (13,14,15). Although the exact reason for these differences is uncertain, it may be related to variations in genetic origins, disease subtypes, environmental exposures, and the accessibility of medical facilities. Most of the patients who were included in the study were (30.1%), from Baghdad Province, (11.65%) from Diyala Province, and (10.43%) from Dhi-Qar Province. As for the AML cases collected from Basrah Oncology Center, there were only 11 cases, and the reason behind this is according to what was mentioned by the specialists in the center itself, the frequency of AML cases to Basrah Oncology Center is very slight compared to other types of leukemia, in addition, no information about the number of patients this year from the center's registration units, but rather this collection was through personal efforts. A total of 401 cases that collected from Baghdad Hematology Center, they included all the governorates of Iraq except the Kurdistan Region, but we did not notice a frequency of leukemia cases from Basrah Province during the year 2022 forwarded to Baghdad Hematology Center. Furthermore, we also demonstrated the incidence of primary AML more than secondary, whereby 33 cases were secondary to prior chemo-radiation exposure (therapy-related, t-

AML) AML group (51.52) and Post-Antecedent Hematologic Disease (Post-AHD) AML group (48.48%). The post-AHD AML group included patients with MPN (myeloproliferative neoplasms) (27.27%) more than patients with MDS (myelodysplastic syndromes) (21.21%), (Table 2). The occurrence of AML based on FAB subtypes, de novo -M3 AML (APL) more prevalent in the Iraqi population and this is like the result found in studies (7,16). Many of the patients were suffering from pallor (65.29%), fever (49.76%), leukocytosis (43.20%) or cytopenia (27.18%) at the time of presentations, so apart of the patients were suffering from thrombocytopenia (29.37%), bleeding (37.38%) and anemia (29.85%), it is similar to studies that conducted locally (17, 18, 7). The presence of elevated numbers of poorly differentiated myeloid cells in bone marrow, peripheral blood, and occasionally in other organs is responsible for most of AML's clinical symptoms. Most cases are presented with a combination of indicators of bone marrow failure, such as anemia and thrombocytopenia (19). Anorexia, exhaustion, pallor, fever and weight loss are typical complaints (20)

Conclusion

The findings of this descriptive study showed that the disease is highly prevalent, with a younger median age than in other nations, and that males were more likely to contract it than females. The most prevalent subtype of AML was APL. The clinical and epidemiological features differed from previously published research in certain respects but were similar in other ways as well. Studying epidemiology can aid in comprehending the incidence and progression of the disease.

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دراسة شاملة لحالات الاصابة و المظاهر السريرية بين المرضى العراقيين المصابين بابيضاض الدم النقوي الحاد المشخصين حديثا للعام (٢٠٢٢)

الخلفية: سرطان الدم هو السبب الرئيسي للوفيات المرتبطة بالسرطان، و ابيضاض الدم النقوي الحاد لديه ادنى معدل للبقاءعلى قيد الحياة كونه واحدالامن اكثر انواع سرطان الدم انتشارا بين البالغين في جميع انحاء الهالم و كذلك في العراق.

المواد و طرق العمل: اجريت الدراسة الوصفية الوبائية على ٤١٢ مريض تم تشخيصهم حديثا بابيضاض الدم النقوي الحاد كعينة من السكان العراقيين المسجلين في مركز الاورام في مدينة الطب في محافظة بغداد و مركز الاورام في محافظة البصرة خلال العام ٢٠٢٢. متوسط اعمارهم كان 42.09 ± 22.32 **سنة.**

النتائج: من بين ٤١٢ مريضا، كان متوسط العمر ٤٠,٠٥ هو سرطان الدم النقوي الحاد السائد في العراق والذي كان اقل من نظيره في البلدان المتقدمة الاخرى. كان المرض اكثر انتشارا في الفئات العمرية (≥ ٧٠) سنة و (٦٩-٦٠) سنة بنسبة ١٨,٥٢٪ و ١٦,٢٦٪ على التوالي. كان غالبية المرضى يعانون من الشحوب (٦٥,٢٩٪)، الحمى (٤٩,٧٦٪)، و زيادة عدد كريات الدم البيضاء (٤٣,٢٠٪) او قلة الكريات البيضاء (٢٧,١٨٪) في وقت المرض.

الاستنتاجات: تشير الدراسة الى ان المرض منتشر بشكل كبير، مع متوسط عمر اصغر من الدول الاخرى، و كان النوع الفرعي الاكثر انتشارا من AML هو APL. تؤثر المظاهر السريرية و الوبائية على فهم حدوث المرض و تطوره.

الكلمات المفتاحية: سرطان الدم النخاعي الحاد, سرطان الدم , الوبائي , المرضى العراقيين , المظاهر السريرية.