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Study of the hematological parameter changes of Iraqi Acute Myeloid Leukemia patients before and after Chemotherapy

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ABSTRACT

Objective: To assess the alterations in hematological indicators of Iraqi patients with acute myeloid leukemia before and post-chemotherapy.

Material and method: This is a case-control study of newly diagnosed acute myeloid leukemia (AML) cases in the Iraqi population diagnosed between February 2022 and November 2022 at the Iraqi Center for Hematology in the Medical City in Baghdad teaching hospital. Peripheral blood samples were taken from all participants. An automated hematology analyzer determined WBC, HB, and Platelet count. Blast cell% in the peripheral blood was estimated on Giemsa-stained blood smears. The blood film examination was done for WBC differential count. Mean and standard deviation was used for quantitative, while frequency and percentages were used for qualitative data.

Results: A total of 40 patients were newly diagnosed with AML, the majority of the patients were male, and the most common subtype of AML was Acute myeloblastic leukemia-M2. Most of the patients are between 51-61 (35%) years old. Most patients had leukocytosis, anemia, and thrombocytopenia, and blast cells were present in the peripheral blood of 90% of the AML patients. The results also showed a significant increase in WBC count and a significant decrease in platelet count and hemoglobin concentrations in AML patients compared to healthy controls. A significant decrease was observed in most of the hematological parameters after Chemotherapy.

Conclusion: In this study, all patients with AML have abnormal levels of all hematological parameters. The patients who received Chemotherapy show different levels of these parameters, such as WBC, HB, Platelet count and Blast cells. It is obvious that AML has a strong impact on the hematological parameters.

Keywords: *Acute myeloid leukemia, Hematological parameters, WBC count, Platelets count, Hemoglobin levels, Chemotherapy*

INTRODUCTION

The generation of abnormal leukocytes characterizes leukemia and can occur as a primary or secondary process. Depending on the speed of cell proliferation, leukemia can be categorized as acute or chronic and can involve either the myeloid or lymphoid cell lineages. The major subtypes of leukemia include acute myeloid leukemia (AML) and chronic myeloid leukemia (CML), which affect the myeloid lineage, and acute lymphoblastic leukemia (ALL) and chronic lymphocytic leukemia (CLL), which affect the lymphoid lineage (1).

Acute Myeloid Leukemia (AML) is a collection of neoplastic blood disorders categorized by the proliferation and growth of immature hematopoietic cells in the bone marrow and peripheral blood resulting in ineffective erythropoiesis and bone marrow failure. Acute myeloid leukemia (AML) is more commonly observed in adults, with nearly 80% of acute leukemia cases in adults being AML, while it accounts for only 20% of acute leukemia in children (2).

The subtypes of AML are classified based on the maturity level of white blood cell precursors and the nature of their malignant transformation at the time of diagnosis. Developing countries bear a heavier burden of cancer, including hematological malignancies, due to factors such as population growth, aging and urbanization, changes in diet, improved infection control, and increased tobacco consumption (3).

Acute myeloid leukemia mainly affects the blood and bone marrow, causing changes in all the hematological parameters in the peripheral blood, such as raised white blood cells, decreased hemoglobin levels and decreased platelet count and this pattern of changes present in the vast majority of patients after chemotherapy treatment (4). In AML, the hematopoietic stem cells (HSCs) are mutated and transformed into leukemic stem cells (LSCs) that proliferate rapidly, producing blasts instead of mature blood cells. This leads to an imbalance in the blood cell populations, with excess blasts and a shortage of normal blood cells (5). For patients after Chemotherapy, the increase in WBCs is due to the overproduction of blasts, the decrease in platelet count is due to the overcrowding of the bone marrow with blasts, which leads to a decrease in the production of platelets and the decrease in hemoglobin is due to the reduced production of red blood cells in the bone marrow, which results in anemia (6).

Before Chemotherapy, WBCs significantly decreased in AML patients because chemotherapy targets rapidly dividing cells, including WBCs, and lead to their destruction (7).

The objective of the present study was to assess the hematological profile of acute myeloid leukemia (AML) in Iraqi patients and to compare their results with healthy subjects.

MATERIALS AND METHODS

We conducted a case-control study of acute myeloid leukemia cases for both adult genders in the Iraqi population diagnosed between February 2022 and November 2022 at the Iraqi Center for Hematology, a clinical center in the Medical City in Baghdad teaching hospital IRAQ.

This study involved a cohort of forty (40) patients who were newly diagnosed with AML, consisting of 25 (62.5%) males and 15 (37.5%) females. All participants were adults. Thirteen (13) patients, consisting of 7 females and six males, were monitored following the completion of a single course of standard induction chemotherapy. The study excluded the relapsed cases of AML and patients on Chemotherapy and radiotherapy for AML. Thirty-seven (37) healthy volunteers, comprising 22 (59.5%) male and 15 (40.5%) female individuals, were recruited for this study. The healthy volunteers had no previous history of leukemia.

Relevant history was recorded on a proforma. Hb, WBC, RBC, and platelet count were determined on Hematology Sysmex XS-500i and XT-1800 CBC analyzers. Blast cell % was estimated on Giemsa-stained blood smears. Blood film examination (peripheral blood smear) for WBC differential count. Morphological classification of AML was done depending on FAB criteria.

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Data was entered and analyzed on SPSS version 27. Quantitative variables like Hb, TLC, platelet count, and blast cell percentage were analyzed by mean ± standard deviation. Qualitative variables, i.e., gender and AML subtypes, were presented as frequencies and percentages. Descriptive statistical analysis was made, including sums, proportions, percentages, mean, median, and standard deviations. Multinomial logistic regression analysis was executed to assess the association between variables. Data outputs were also presented with charts, tables, and figures accordingly. P-value ≤ 0.05 was taken as significant.

The Ethical approval committee (EAC) approved the study in the Ministry of higher education and scientific research - University of Anbar/IRAQ.

RESULTS

In this study, 40 patients newly diagnosed with AML were included. Among these patients, 25 (62.5%) were male, and 15 (37.5) were female. Most of the study participants, 15 (35%), were 51–61 years old with a mean age of 49.6±9.8 years, as shown in Figure (1).

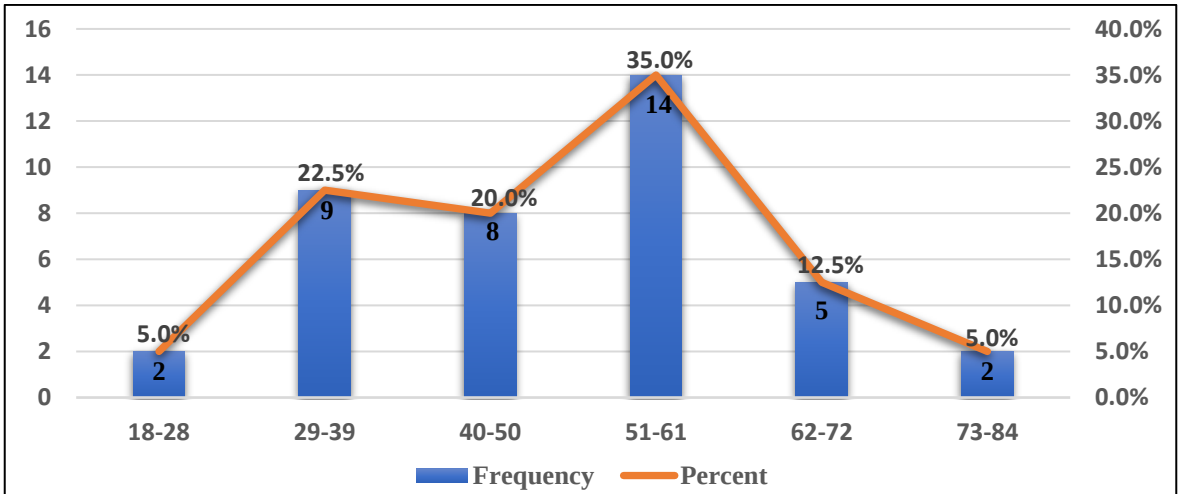

Figure 1 :Distribution of patients according to age groups

By AML subtype, Acute myeloblastic leukemia-M2 was the predominant (FAB) subtype (11 patients – 27.5%), followed by Acute promyelocytic leukemia (AML-M3) in 10 patients (25%). Concerning the distribution of AML FAB subtypes according to gender, acute myeloblastic leukemia (M2) was the highest among males, followed by acute promyelocytic leukemia (M3) and AML-M4, while among the females, its equal distribution to some extent as shown in the Table (1).

TABLE 1: Pattern of FAB subtypes in different sex groups in 40 cases of AML

AML Subtype	Males	Females	Total	Percentage
AML-M0	1	1	2	5%
AML-M1	2	3	5	12.5%
AML-M2	7	4	11	27.5%
AML-M3	6	4	10	25%
AML-M4	5	4	9	22.5%
AML-M5	1	2	3	7.5%
Total	25	15	40	100%

This study measured hematological parameters in newly diagnosed AML patients. As Shawn in Table (2), most patients had leukocytosis (95%), anemia (100%), and thrombocytopenia (95%). The mean WBC count was 59.76 × 109/l, ranging from 11.3 to 248.4 × 109/l. The Hb level varied between 3.8 and 13.7 g/dL, and the platelet count decreased (Thrombocytopenia) in 38 patients (95%) and is normal in the rest (5%). Blast cells ≥ 20% in the peripheral blood were present in most AML patients 36(90%).

TABLE 2: Pattern of change in the hematological parameters in study patients (N=40)

Parameters		Frequency (%)	Mean ± SD	Range
WBC count (x109/L)	Leukopenia	0	59.76 ± 55.91	11.3- 248.4
	Normal	2(5%)		
	Leukocytosis	38(95%)		
Haemoglobin (g/dL)	Low	40(100%)	8.55 ± 2.07	3.8 - 13.6
	Normal	0		
Platelet count (x109/L)	Thrombocytopenia	38(95%)	62.23 ± 35.45	11 - 165
	Normal	2(5%)		
	Thrombocytosis	0		
Peripheral Blood (WBC) Differential	Blast cells < 20%	4(10%)	49.58 ± 22.05	15 - 93
	Blast cells ≥ 20%	36(90%)		
	Neutrophils %		21.50 ± 5.02	9 - 32
	Lymphocyte %		30.26 ± 12.9	11 - 57
	Monocytes %		1.94 ± 0.62	2 - 3
	EO %		1.17 ± 0.51	1 - 2

Total WBC count significantly increased in the patients with AML compared to their count in healthy control (P value <0.001). The platelets count was significantly decreased in the newly diagnosed patients compared to their count in healthy control (P value <0.001). There was a significant decrease in hemoglobin concentrations in the patients (before Chemotherapy) compared to healthy control (P value = 0.003) Table (3).

TABLE 3: Basic hematological parameters in patients compared to Healthy control.

Parameters	Groups	Mean ± SD	Range	p-value
WBCs (x109/L)	Patients	59.76 ± 55.91	11.3 - 248.4	<0.001*
	Healthy	7.26 ± 1.74	4.49 – 11.89	
Platelet count (x109/L)	Patients	62.23 ± 35.45	11 - 165	<0.001*
	Healthy	234.32 ± 64.45	131 - 380	
RBC count (x1012/L)	Patients	2.74 ± 0.92	1.15 – 4.50	<0.001*
	Healthy	4.80 ± 0.69	2.60 – 6.63	
HGB (g/dL)	Patients	8.55 ± 2.07	3.8 - 13.6	0.003*
	Healthy	11.93 ± 1.78	8.4 – 15.8	

A subset of 13 patients out of the initial cohort of 40 was subjected to a post-chemotherapy follow-up after four weeks. Their blood samples were collected once again and subsequently analyzed during this follow-up. The results were then compared to their respective pre-chemotherapy values, and the resultant data was presented in Table (4). Following Chemotherapy, the study revealed a marked decline in both white blood cell and hemoglobin counts (P<0.001 and

P=0.042, respectively), while platelet count did not exhibit a significant reduction (P=0.0361). Furthermore, blast cell percentage witnessed a significant decrease after Chemotherapy compared to before (P=0.001). The neutrophil percentage displayed a considerable decrease after Chemotherapy (P=0.031) compared to the baseline levels, whereas lymphocyte levels showcased a remarkable increase post-chemotherapy (P<0.001) in comparison to the pre-treatment levels. Additionally, the study found a significant increase in monocyte percentage after chemotherapy (P<0.001), while eosinophil percentage exhibited a significant reduction after Chemotherapy (P=0.001) compared to before Chemotherapy.

TABLE 4: Hematological parameters for AML patients before and after Chemotherapy for the follow-up group.

Parameters	Chemotherapy	Mean ± SD	Range	p-value
WBCs (x109/L)	Before	47.12 ± 30.50	24.50 – 119.90	<0.001
	After	2.42 ± 1.06	0.71 – 4.90	
Platelet count (x109/L)	Before	65.92 ± 19.37	39 - 113	0.361
	After	47.35 ± 19.28	19 - 74	
HGB (g/dL)	Before	9.21 ± 2.41	5.1 – 12.9	0.042
	After	7.39 ± 2.01	2.4 – 11.3	
Blast Cells%	Before	31.37 ± 12.27	18 – 55 %	<0.001
	After	3.00 ± 1.26	1 – 5 %	
Neutrophils%	Before	26.93 ± 5.02	20 - 36	0.031
	After	20.79 ±5.39	13 - 42	
Lymphocytes%	Before	34.01 ± 12.94	16 - 54	<0.001
	After	63.52 ± 6.22	43 - 73	
Monocytes%	Before	2.09 ± 0.50	1 - 3	<0.001
	After	4.29 ± 2.10	1 - 7	
Eosinophils%	Before	1.49 ± 0.45	0.7 - 2	0.001
	After	2.79 ± 0.76	1 - 4	

DISCUSSION

Acute leukemia is defined as any cancer that manifests as an increase in immature hematopoietic elements (blasts) that have not completed their maturation and have not differentiated into fully differentiated hemopoietic cells. AML has a wide spectrum of clinical features and hematological changes (8). It is the commonest leukemia in adults, with the lowest survival rate of all other leukemias (9). In developing countries, the incidence of AML is increasing due to lifestyle changes, the inadequacy of health facilities, and increased exposure to carcinogens (10). Ionizing radiations, exposure to chemicals like benzene and pesticides, and other risk factors cause genetic mutations in myeloid series cells and transform them into leukemic clones (10, 11).

The present study showed that the frequency of AML among males (62.5%) was significantly higher than the females (37.5%). The overall ratio of males/females was (2:1.2). Several studies have investigated the higher incidence of AML in men compared to women, as well as sex differences in the treatment and outcomes of other types of cancer. The findings suggest that various factors, including genetic factors, hormonal differences, and environmental exposures, may contribute to these disparities (12-14).

The results of the studied groups have shown that the minimum age of onset in this study was 19 years old, while the maximum age registered was 82 years, the mean age of patients with AML included in this study was 49.6 ± 14.5 years. Among Forty patients with acute myeloid

leukemia, most of the patients were between 51-61 (35%) years old, 29-39 (25%) years old, and 40-50 (20%), while only (5%) were 73 years or older. Those results were comparable to other Iraqi studies in 2009, 2017, and 2020 and an Egyptian study in 2016 (15-18). AML is the most frequent type of leukemia in adults, constituting nearly 80% of all cases. The reason for its high incidence is the asymptomatic nature of the disease in its early stages and its slow progression. The accumulation of cancerous cells is a gradual process that occurs over time, and as a result, individuals are generally diagnosed at an older age. The prevalence of AML is more common in the adult population due to the absence of symptoms and its slow-growing nature (19). Generally, This high preponderance of older adults for acute myeloid leukemia may be mainly due to the advancement of age where many environmental exposures to carcinogens, irradiations, and malignant mutations due to clonal expansion occur more frequently. (20, 21). The incidence of leukemias is influenced by age and race, with a higher frequency observed in certain age groups and ethnicities. In the United Kingdom, more than 40% of all cases of leukemia are diagnosed in individuals over 65 years of age. (22).

The commonest AML subtype in this study was AML-M2, which accounted for 11 cases (27.5% of all subtypes) that are comparable with local data, and the international studies where M2 or M4 subtypes were the most common (23-25).

Complete blood count (CBC) is the first test done in patients suspected of having leukemia; CBC reflects the changes in the bone marrow caused by the leukemic cells (26). One of the most important characteristics of AML is the increase in the number of white blood cells in the bloodstream, known as leukocytosis. This increase is caused by the overproduction of immature white blood cells, known as blasts, in the bone marrow (27). Several studies have investigated the underlying mechanisms of leukocytosis in AML. One study by the American Society of Hematology (2013) found that the increase in white blood cells in AML is caused by abnormal activation of signaling pathways that regulate the proliferation and differentiation of hematopoietic stem cells (28). Another study by Dohner et al. (2000) found that genetic mutations in genes involved in regulating cell growth and division, such as FLT3, NPM1, and CEBPA, are common in AML patients with leukocytosis (29).

The changes in hematological parameters are due to leukemic cells replacing the megakaryocytes and erythroid precursor cells in the bone marrow (30). In the present study, the basic hematological parameters in cases of newly diagnosed AML patients were as raised total leukocyte count, low Hb, and low platelet compared to healthy control. The decrease in the level of hemoglobin and platelets in the bloodstream of acute myeloid leukemia patients before Chemotherapy is mainly due to the replacement of normal bone marrow cells by cancer cells which consume the nutrients needed to produce platelets and hemoglobin (31). Thrombocytopenia is a well-documented finding in AML, and so is the association of bleeding with falling platelet count. Gaydos was the first to document that bleeding in leukemias is attributed to a low platelet count (32).

Almost Similar patterns of changes in hematological parameters were reported by Sultan S in his study, where total leukocyte count was increased (mean 43 ± 6.8x109/L), while hemoglobin and platelet count was decreased (mean 8.2± 2 g/dl and 62±7.8x109/L respectively) (33). Similar patterns of changes in hematological parameters were shown by Naeem, Preethi, Chang and Asif in their studies (8, 9, 30, 34). platelets and hemoglobin. In addition, the cancer cells may produce substances that inhibit the production of platelets and hemoglobin (31).

CONCLUSION

After Chemotherapy, AML patients typically show improvements in their hematological parameters compared with before. This improvement is represented by a significant decrease in the Blast cell percentage in the peripheral blood, which are immature blood cells that can be indicative of leukemia. Other improvements may include an increase in

hemoglobin levels and platelet counts. The study highlights the hematological changes associated with AML and emphasizes the need for better healthcare facilities and the management of carcinogenic exposure.

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