Impact of Chemotherapy on the hematological parameters of Acute Myeloid Leukemia Iraqi patients

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ABSTRACT

Background: Acute myeloid leukemia (AML) is characterized as an aggressive blood cancer with rapid growth of immature leukemic cells. AML primarily impacts bone marrow and blood, resulting in alterations in every single hematological parameter that is present in the peripheral circulation. These changes are also observed in most patients following chemotherapy. **Objective:** This study aims to compare the changes in the hematological parameters of acute myeloid leukemia Iraqi patients before, during, and after chemotherapy treatment to healthy controls. **Method:** 120 AML cases were studied. Based on the chemotherapy stage, 40 patients were assigned to each group (newly diagnosed, under treatment, and relapsed). Baghdad Teaching Hospital, Iraq, provided the cases and samples from February 2022 to April 2023. This study also included 40 healthy controls. All individuals had peripheral blood drawn. An automatic hematology analyzer counted haemoglubin (HB), White blood cells (WBC), and Platelets (PLT). **Results:** Results showed that the distribution according to gender revealed that the prevalence of AML was (61.66) % for males and (38.33) %for females. Smoking was also recorded in this study, 57 (47.5%) smoker patients and 63 (52.5%) non-smoker patients, and most of the clinical cases, according to the French-American-British system (FAB), was in M3 p= (0.0001). The patients' ages ranged from 15 to 75 years old, and thirty-eight cases (31.666%) out of (120) were up to 40 years old. Results showed differences in hematological parameters between the control and AML patients group, before, under treatment, and relapsed, with lower Red blood cells (RBCs), WBCs, Hb, and platelets in the patient's group than the control, the exceptions being made for newly diagnosed and relapsed patients, whose WBC counts were elevated. After chemotherapy, most hematological parameters decreased significantly except PLT, which was higher in the treated patients. **Conclusion:** AML affects the patient's hematological parameters, making them at abnormal levels, increase or decrease, during different stages of disease and Chemotherapy. WBC, HB, and Platelet count show different levels after Chemotherapy and relapse.

Keywords: AML, Chemotherapy, Hematological parameters, WBC count, Hemoglobin levels, Platelets count, newly diagnosed, under treatment, relapsed.

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1-INTRODUCTION

Leukemia is a diverse category of hematologic malignancies caused by leukocyte malfunction. Leukemia is divided into two main categories, myeloid and lymphoid, based on the origin of the cell type affected. It is also categorized as acute or chronic based on the speed of cell proliferation (1). Acute myeloid leukemia (AML) is a severe hematological cancer where immature leukemic blasts proliferate rapidly (2). The pathophysiology of AML is identified by stopping maturation at an early stage of development in bone marrow cells. The arrest maturation may be due to the activation or inactivation of some genes, such as (FLT3, DNMT3A, and NPM1), in addition to other abnormalities in genetics and epigenetics (3). The arrest maturation of cells firstly produces decreases in normal blood cells, then various degrees of anemia, neutropenia, and thrombocytopenia, and secondly, a fast increase in several abnormal myeloblasts with a decrease in apoptosis, so they accumulate in the

bone marrow, blood, and then spleen and liver (4). The most prevalent acute leukemia is AML, which includes a mutation in hematopoietic stem cells that causes uncontrolled proliferation, self-renewal, and differentiation (5). Thus, accumulating numbers of immature hemopoietic progenitors replace the normal Red blood cells (RBCs), white blood cells (WBCs), and platelets (PLT)(6). Most patients after chemotherapy have elevated WBCs, decreased Hb, and PLT because AML mainly affects bone marrow and blood (7). AML occurs when hematopoietic stem cells (HSCs) are altered into leukemic stem cells (LSCs) by mutation, which multiply rapidly and produce blast cells rather than mature blood cells. This imbalance causes extra blasts and a deficiency of regular blood cells (8). The aim of the study is to compare the hematological parameters of the three groups of acute myeloid leukemia Iraqi patients (before chemotherapy, under chemotherapy, and relapsed) and then compare them with healthy control.

2-Material and Method

The research was conducted from January 2022 until April 2023. 160 people participated in the study. One hundred and twenty Iraqi male and female acute myeloid leukemia patients from Baghdad Teaching Hospital, Baghdad/Iraq, were included in this study, forty of them were newly diagnosed, forty were on treatment, and forty were relapsed, their ages between (15-75) years and the clinical information were obtained from their hospital files and case-sheet records, comparing with forty healthy people as control. The research protocol was granted approval by the Ethics Committee of the Iraqi Ministry of Health/Al-Nahrain University, and prior to their inclusion in the study; all patients provided written informed consent. AML is morphologically classified depending on the FAB classification system. RBC, WBC, Hb, and platelet were determined by Haemato-analyzer 5- Parts. The sample was taken from a vein and collected by drawing blood into a tube containing an anticoagulant, EDTA, to stop its natural clotting. On board the analyzer, the sample is agitated to distribute the cells evenly, then diluted and partitioned into at least two channels, one of which is used to count red blood cells and platelets, the other to count white blood cells and determine the hemoglobin concentration.

Statistical analysis

Statistical analysis SPSS 23 was used for data. Mean and standard error were used to express results. Mean differences were tested using the independent samples T-test. The significant probability was 0.05 or less. This study used Chi-square test to compare 0.05 likelihood percentages.

3-Results

The AML patients' age range was between (15-75) years old. Thirty-eight cases (31.666%), out of (120) were up to forty years old, and only two patients (1.666 %) were up to seventy years old, and the other patients ranged in between, as shown in Table (1), and the overall mean age was 43.2 years. The distribution of patients according to gender revealed that the prevalence of AML was (61.666%) for males and (38.333%) for females, as shown in Table (2). Results demonstrated that (47.5) % of AML patients were smokers and (52.5) % were nonsmokers, as shown in Table (3). Approximately the patients were grouped according to the FAB classification system; out of 120 AML patients, the M3 subtype had a percentage of (47.5 %) followed by M2 (24.375%), whereas the lowest one was in M6 and M7, as shown in Table (4).

Table (1): Distribution of age groups in AML patients

Age groups (year)	No. of patients	Percentage (%)
15-20	9 (9/120)	7.5 (7.5/100)
21-30	26 (26/120)	21.666 (21.666/100)
31-40	13 (13/120)	10.833 (10.833/100)
41-50	38 (38/120)	31.666 (31.666/100)
51-60	19 (19/120)	15.833 (15.833/100)
61-70	13 (13/120)	10.833 (10.833/100)
Over 70	2 (2/120)	1.666 (1.666/100)
Total	120	100
Chi-Square (χ^2) (P-value)	---	12.382 ** (0.0001)
*** (P≤0.05).**		

Table (2): Distribution of AML patients according to Gender

Gender	No of patients	%
Male	74 (74/120)	61.666 (61.666/100)
Female	46 (46/120)	38.333 (38.333/100)
Total	120	100
Chi-Square (χ^2) (P-value)	---	8.100 ** (0.0044)
*** (P≤0.05).**		

Table (3): Distribution of AML patients according to Smoking

Smoking	No of patients	%
Smokers	57 (57/120)	47.5 (47.5/100)
Non-smokers	63 (63/120)	52.5 (52.5/100)
Total	120	100
Chi-Square (χ^2) (P-value)	---	0.40 NS (0.527)
NS: Non-Significant.		

Table (4): Distribution of AML patients according to the French-American-British system (FAB)

Subtype	No of patients	%
M0	4 (4/120)	3.333 (3.333/100)
M1	11 (11/120)	9.166 (9.166/100)
M2	29 (29/120)	24.166 (24.166/100)
M3	57 (57/120)	47.5 (47.5/100)
M4	1 (1/120)	0.833 (0.833/100)
M5	18 (18/120)	15 (15/100)
M6	0 (0/120)	0 (0/100)
M7	0 (0/120)	0 (0/100)
Total	120	100
Chi-Square (χ^2) (P-value)	---	21.367 ** (0.0001)
*** (P≤0.05)**		

Results showed differences in hematological parameters between the control and AML patients group with lower RBCs, WBCs, Hb, and platelets in the patients compared to the control, with exceptions being made for newly diagnosed and relapsed patients, whose WBC counts were elevated and PLT higher in treated patients as shown in table (5). Results explained that a significantly increased level of WBCs (P≤0.05) in newly diagnosed patients (30.49±1.7) and relapsed patients (38.98±3) compared with the healthy control group (7.14±2.3), but the WBC level decreased in under treatment patients (12.53±1.1) so no significant differences between control and under treatment group. Hb level in this study primarily showed low mean concentration (7.63±0.878) in newly diagnosed patients compared with control (13.09±0.952), then (8.8±1.697) and (8.45±1.341) for under treatment and relapsed patients *respectively,* before chemotherapy the Hb concentrations was statically decreased (P≤0.05) in the newly diagnosed group compared to healthy control. This study showed that there are no significant differences in the platelet count between the control (193.13±3.244), newly diagnosed (78.98±8.132), under treatment (201.99±11.49), and relapsed (100.39±12.198) group, with significantly decreased (P≤0.05) in the platelets count in the newly diagnosed patients compared to the under-treatment patients. Other hematological parameters studied were RBC, monocytes, and Lymphocytes, there were no significant differences between the patients and healthy control for RBC and Monocytes with the following values (5.38±0.9 control, 3.09±0.8 newly diagnosed, 4.17±0.2 under treatment and 3.52±0.3 relapsed) for RBC and (6.25±1.963 control, 9.61±2.087 newly diagnosed, 7.5±1.586 under treatment and 6.14±2.95 relapsed) for monocytes. On the other hand, Lymphocytes significantly lower (P≤0.05) in AML patients of all groups than in controls (41.04±1.975 control, 13.02±2.286 newly diagnosed, 22.59±3.016 under treatment and 26.5±2.506 relapsed).

Table (5): Comparison between different groups of AML patients in RBC, WBC, Hb, Lymphocytes, Monocytes, and PLT

Groups		10^9/L	% (Mean±SE)				
		WBC	RBC	HB (g/dl)	Lymphocytes	Monocytes	PLT 10^9/L
Controls		A 7.14±2.3	A 5.38±0.9	A 13.09±0.952	A 41.04±1.975	A 6.25±1.963	A 193.13±3.244
AML Cases	Newly Diagnosed	B 30.49±1.7	A 3.09±0.8	A 7.63±0.878	B 13.02±2.286	A 9.61±2.087	B 78.98±8.132
	Treated	A 12.53±1.1	A 4.17±0.2	A 8.8±1.697	B 22.59±3.016	A 7.5±1.586	A 201.99±11.49
	Relapse	B 38.98±3.2	A 3.52±0.3	A 8.45±1.341	B 26.5±2.506	A 6.14±2.95	B 100.39±12.19
	Total	B 27.33±1.3	A 3.59±0.9	A 8.29±0.952	B 20.7±1.975	A 7.75±1.963	A 127.12±3.244

The different letter means significant differences (P≤0.05), and values are given by mean±SE. The first letter compared to controls, and the 2nd letter is multiple ANOVA Test analysis within the studied group variables.

4-Discussion

In acute myeloid leukemia (AML), aberrant cells proliferate rapidly in the bone marrow, disrupting blood cell synthesis (9). The most prevalent kind of acute leukemia in adults is called AML, which has a high mortality rate (10,11). The disease is defined by the uncontrolled growth of abnormal clones of myeloid progenitor cells into malignant myeloblasts, which cannot carry out normal blood cell functions (12). AML includes many clinical and hematological changes (13,8). The age range of samples was between (15-75) years old. Thirty-eight cases (31.666%) out of (120) were up to forty years old, only two patients (1.666 %) were up to seventy years old, and the other patients ranged between the patient's mean age was (43.2) years. These results were comparable to other Iraqi studies (14,15,16,17). Other local studies showed that 38.17 years was the mean age of AML patients (18), but (19) mentions that 35.27 years was the mean age. Results of the current study showed that the distribution of patients according to gender revealed that the prevalence of AML was (61.666) % for males and (38.333) for females. The high incidence of leukemia in males compared to females could be because of the difference in the nature of the business, the influence of hormones, genetic factors associated with sex, and

environmental exposures (20,21,22). These results are compatible with (23,24,17), which shows that males are more infected with AML than females. Results demonstrated that (47.5) % of AML patients were smokers and (52.5) % were nonsmokers. This result was similar to (25), who found that AML incidence was associated with cigarette smoking. Smoking leads to an increased risk of acute myeloid leukemia in adults. According to the FAB classification system, results showed that cases out of 120 AML patients were M3 subtype with a percentage of (47.5 %) followed by M2 (24.375%), whereas the lowest one was in M6 and M7. These results agreed with other local studies (26,27,16) in which M3 was the most frequent subtype. In this study, results explain the differences in hematological parameters between the AML patients and control group before, under treatment, and relapsed, with lower RBCs, WBCs, Hb, and platelets in the patients than the control group, the exception being made for newly diagnosed and relapsed patients, whose WBC counts were elevated and PLT higher in treated patients. These results are similar to those in (17), which found that AML patients had higher total leukocytes, lower Hb, and lower platelets than healthy controls. (28) also have similar results, as they stated, Platelets, Hb, and WBCs were all reduced in the patient group relative to the control group, except for the newly diagnosed patients, whose WBCs were elevated. Also, the same changes in AML patients were reported by (29,11,30,31) in their studies, where total leukocyte count was increased while hemoglobin and platelet count was decreased. Results explained a significant increase in the level of WBCs in newly diagnosed patients ($30.49\pm1.7\times 10^9$ /L) and relapsed patients ($38.98\pm3\times 10^9$ /L) compared with the healthy control group (7.14±2.3), another study showed that the mean WBC count was $35.9 \pm 23.2 \times 10^9$/L (16) and ($38.6 \times 10^9$/L) (32). Then the level decreased in under-treatment patients (12.53±1.1). These results are comparable to the result reported by (33), which stated that WBC count decreased in under-treatment patients compared to newly diagnosed patients, and another study by (18) showed that the means of bone marrow blasts and WBC count were significantly reduced after treatment compared to that before treatment. And (17) revealed that white blood cell and hemoglobin counts decreased significantly after chemotherapy and no significant differences between the under-treatment and the control group. Another researcher stated that compared to the control group, AML patients had substantially higher white blood cell and neutrophil counts (34,35). This could be because leukemia involves the clonal proliferation of cancer cells, which can manifest in the bone marrow at any stage of development, including the lymphoid, myeloid, or pluripotent stages. (36). Hb level in this study primarily showed a low mean concentration of 7.63±0.878g/dL in newly diagnosed patients compared with control (13.09±0.952); this closely resembles the results of (33) that showed (8.90±1.34, 13.20±0.99) for newly diagnosed and control *respectively,* then 8.8±1.697 and 8.45±1.341 for under treatment and relapsed patients respectively, this similar to (16) study that showed low mean hemoglobin concentration (7.2 ± 1.7 g/dL). Also, similar other Iraqi studies were reported by (37,38).Before chemotherapy, hemoglobin concentrations in newly diagnosed patients were significantly lower than in the healthy control group. The platelet count in the current study revealed that there are no significant differences between the control (193.13±3.244), newly diagnosed (78.98±8.132), under treatment (201.99±11.49), and relapsed (100.39±12.198) group, with significantly decreased in the platelets count in the newly diagnosed patients compared to the under-treatment patients, and this resembles to (17) study which stated that platelets in under treatment patients were higher than in the newly diagnosed. The results shown by (18) explain that there were no significant differences in means of platelet count and hemoglobin (Hb) level after treatment compared to that before treatment. Another study by (16,38,39) showed that platelet count was ($53.1 \pm 27.6 \times 10^9$/L, 51×10^9/L, and 60×10^9/L) respectively. In this study, PLT, except for under-treatment patients, and Hb count were significantly lower in AML patients than in the control group, which is comparable with the results of (35). Another hematological parameter studied was monocytes and Lymphocytes. The number of Monocytes showed no significant differences between the patient's groups and the healthy control with the following values (6.25±1.963 control, 9.61±2.087 newly diagnosed, 7.5±1.586 under treatment and 6.14±2.95 relapsed). On the other hand, Lymphocytes were significantly lower in AML patients of all groups than in controls (41.04±1.975 control, 13.02±2.286 newly diagnosed, 22.59±3.016 under treatment, and 26.5±2.506 relapsed). This finding was comparable with the results of (35). ,It is higher in under-treatment and relapsed patients than newly diagnosed patients before chemotherapy; these results are consistent with the results of (17).

It demonstrated that lymphocyte numbers significantly rise after chemotherapy compared to levels before treatment. As a result of leukemic cell-induced alterations in the bone marrow, hematological parameters measured by a complete blood count (CBC) test, which is firstly done on individuals suspected of having leukemia, change (40). One of the most notable features of acute myeloid leukemia (AML) is an increase in white blood cell (WBC) counts in the blood, a condition known as leukocytosis. This is due to the bone marrow producing excessive immature white blood cells called blasts (41). There are many mechanisms that explain leukocytosis in AML; one of them is that the bone marrow's megakaryocytes and elytroid precursor cells are replaced by leukemic cells, which causes changes in hematological parameters (31). The second one discovered that there were defective in the pathways induction that controls the development and division of hematopoietic stem cells. Of hematopoietic stem cells is the source of the increase in white blood cells in AML (42). Thirdly, leukocytosis is frequently observed in AML patients with gene mutations that control cell proliferation and division, including FLT3, NPM1, and CEBPA (43).In patients with acute myeloid leukemia, the levels of hemoglobin and platelets in the bloodstream drop before chemotherapy. This is because cancer cells take over the bone marrow cells that normally make these substances and consume the nutrients that the cells need to make them (44). Anemia sets in after chemotherapy because an overabundance of white blood cells (WBCs) occurs due to blast overpopulation in the bone marrow, reducing platelet production and, ultimately, hemoglobin levels (45). Because chemotherapy destroys quickly dividing cells, including white blood cells, these cells dropped dramatically in AML patients undergoing treatment (46).

5-Conclusion

The study sheds light on the changes in the hematological parameters related to AML and the effect of chemotherapy on it. The results conclude that AML affects the patient's hematological parameters, making them abnormal, increasing or decreasing them during different stages of disease and chemotherapy. WBC, HB, and Platelet count show different levels after Chemotherapy and relapse.

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Noorhan S. Al-Maliki

Conflict of interest:

The authors affirm that they are free from any ties or financial conflicts of interest that may have seemed to impact their work.

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تأثير العلاج الكيميائي على مؤشرات الدم لدى مرضى سرطان الدم النخاعي الحاد في العراق

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[1,2] كلية التقنيات الاحيائية ، جامعة النهرين، بغداد، العراق

الخلاصة

خلفية البحث: سرطان الدم النخاعي الحاد (AML) هو ورم خبيث مكون للدم يتميز بالانتشار المفرط لخلايا سرطان الدم غير الناضجة. يؤثر سرطان الدم النخاعي الحاد بشكل رئيسي على الدم ونخاع العظام،مما يسبب تغيرات في جميع المؤشرات الدموية في الدم المحيطي، وهذه التغييرات موجودة أيضًا في معظم المرضى بعد العلاج الكيميائي. **الهدف من البحث:** الهدف من هذه الدراسة هو مقارنة التغيرات في المعايير الدموية للمرضى العراقيين المصابين بسرطان الدم النخاعي الحاد قبل العلاج الكيميائي، وتحت العلاج الكيميائي وفي مرحلة الانتكاس مع معامل السيطرة. **الطريقة ومواد العمل:** أجريت دراسة على 120 مريضا بابيضاض الدم النخاعي الحاد. والتي تم تقسيمها إلى 40 مريضاً لكل مجموعة (المشخصون حديثاً، تحت العلاج، والانتكاس)، وذلك حسب مراحل المرضى الذين يخضعون للعلاج الكيميائي. تم الحصول على الحالات والعينات من فبراير 2022 إلى أبريل 2023 من مستشفى بغداد التعليمي، بغداد، العراق. وبالإضافة إلى ذلك، تم تسجيل 40 شخصا أصحاء في هذه الدراسة كمعامل سيطرة. تم أخذ عينات الدم المحيطية من جميع المشاركين. باستخدام محلل أمراض الدم الآلي تم تحديد عدد عدد كريات الدم البيضاء و مستويات الهيموجلوبين والصفائح الدموية. **النتائج:** أظهرت النتائج أن التوزيع حسب الجنس أظهر أن نسبة انتشار المرض كانت (61.66)% للذكور و(38.33) للإناث. سجل التدخين أيضًا في هذه الدراسة، 57 (47.5٪) مريضًا مدخنًا، و63 (52.5٪) مريضًا غير مدخن، وكانت معظم الحالات السريرية وفقًا لـ FAB، في M3. الفئة العمرية لمرضى سرطان الدم النخاعي المزمن كانت بين (15-75) سنة، ثمانية وثلاثون حالة (31.666%)، من أصل (120) كانت أعمارهم تصل إلى أربعين سنة. أظهرت النتائج اختلافات في مؤشرات الدم بين مجموعة السيطرة ومرضى سرطان الدم النخاعي المزمن قبل وتحت العلاج والانتكاس، مع وجود اختلاف كبير بين المجموعتين فيما يتعلق بكرات الدم الحمراء وكريات الدم البيضاء والهيموجلوبين والصفائح الدموية، حيث كانت أقل في المرضى من مجموعة السيطرة باستثناء كريات الدم البيضاء التي كانت أعلى في المرضى الذين تم تشخيصهم حديثاً والانتكاس من مجموعة السيطرة، ثم لوحظ انخفاض كبير في معظم مؤشرات الدم بعد العلاج الكيميائي باستثناء مستوى الصفائح الدموية الذي كان أعلى في المرضى المعالجين. **الاستنتاج:** يؤثر سرطان الدم النخاعي المزمن على المؤشرات الدموية للمرضى مما يجعلهم في مستويات غير طبيعية، زيادة أو نقصان، خلال مراحل مختلفة من المرض والعلاج الكيميائي. يظهر عدد عدد كريات الدم البيضاءو مستويات الهيموجلوبين والصفائح الدموية مستويات مختلفة بعد العلاج الكيميائي والانتكاس.

الكلمات المفتاحية: سرطان الدم النخاعي الحاد، العلاج الكيميائي، مؤشرات الدم، عدد كريات الدم البيضاء، مستويات الهيموجلوبين، عدد الصفائح الدموية، تشخيص حديث، تحت العلاج، الانتكاس.