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EVALUATION OF SOME BLOOD PARAMETERS IN PATIENTS WITH ACUTE MYELOID LEUKEMIA PATIENTS IN IRAQ

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Abstract
Acute myeloid leukemia (AML) is a type of leukemias that begins in the bone marrow and has the potential to metastasize to several organs. The study aimed to assess the changes in some serum biomarkers in Iraqi individuals with AML and explore their role in disease progression. The current investigation comprised 100 individuals (males and females): 50 diagnosed with AML and a control group of 50 healthy participants. Blood samples were taken from AML patients and healthy individuals to evaluate the serum levels of certain biomarkers. The following parameters have been studied: estimation the indicators of liver [alanine aminotransferase (ALT), aspartate aminotransferase (AST)], and kidney functions (urea and creatinine); assessment of lipid profile [total cholesterol (TC) and triglycerides (TG)]; evaluation of some hematological parameters such as erythrocytes (RBCs), hemoglobin (Hb), hematocrit (HCT), leukocytes (WBCs), and thrombocytes (platelets). This study emphasizes the role biomarkers play in AML prediction and suggests that early detection is essential to improving patient survival rates and developing successful treatment plans.
Keywords: Blood parameters, Lipid profile, AML, Iraqi patients.

INTRODUCTION

Leukemia is a cancer of the bone marrow. The United States recorded approximately 59,610 newly diagnosed cases of leukemia in 2023, with an anticipated 23,710 fatalities resulting from the disease (ACS, 2023). According to Iraqi Cancer Registry annual report, leukemia ranked fifth (5.34%, 4.22/100,000 P) in the list of cancerous diseases for both sexes in Iraq for the year 2020 (ICB, 2020).

Adults most commonly develop AML, with a specific genetic subtype classifying AML cases. Gaining a more comprehensive comprehension of the genetic alterations that commonly take place in AML is offering valuable information into the underlying causes of the abnormality in these cells (ACS, 2018). Lipids have a crucial role in the composition of cell membranes and have been linked to cancer progression's underlying mechanisms. Furthermore, lipid metabolism is crucial for providing cellular energy and communication, as well as facilitating other vital components of tumor cell growth. Hence, the assessment of serum lipid profile, which includes measurements of TC and TG, holds significant value in predicting malignant prognosis (Bai *et al.,* 2023).

Researchers are learning more about how the liver and kidneys work by looking at the levels of ALT, AST, urea, and creatinine in the blood serum of people with acute leukemia. Moreover, numerous studies have observed the impact of myeloid leukemia, particularly AML, on the parameters of liver and kidney functions (Alwan *et al.,* 2009; Jumaah *et al.,* 2021).

Automated hematology analyzers produce precise full blood count (CBC) outcomes for almost all samples. The CBC is a common medical test that may recommend to monitor the health. In cancer case, This blood test is utilized for the purpose of aiding in the diagnosis of some types of blood malignancies, including leukemia and lymphoma (Milcic, 2009; Gulati *et al.,* 2022).

This study aims to assesses the changes in some blood biomarkers of Iraqi individuals diagnosed with AML in Dhi Qar Governorate and investigates their role in AML initiation as well as and explores the possibility of using them as prognostic factors to detect the disease.

MATERIALS AND METHODS

Experimental design

Patients who visited the AL-Nasiriyah Teaching Hospital in AL-Nasiriyah City for the examination and treatment of AML from September 2023 to February 2024 provided all the samples for this study.

Only Iraqi patients, both males and females, who were diagnosed with AML and had their diagnosis confirmed by pathology reports, participated in this study. This research investigated fifty (50) AML patients and fifty (50) healthy participants. We informed the participants about the study and obtained their consent. The scientific ethical committee approved the project.

The specimens were obtained from asymptomatic individuals who had no prior medical conditions or ongoing illnesses. The ages of the healthy individuals chosen for this investigation were the same as those of the sick.

Diagnosis of AML

A specialized hematologist examined and diagnosed all patients. In order to diagnose AML, doctors use various tests during a physical examination to confirm the presence of the disease. Therefore, this study approves medical reports based on various techniques such as CBC, bone marrow examination, flow cytometry, and positron emission tomography (PET) scan.

Collection of blood samples

To conduct hematological and biochemical evaluations, both AML patients and normal controls had a total of five milliliters of venous blood drawn from their cubital vein. The blood was

obtained using a disposable syringe. For the analysis of certain hematological parameters, a volume of 1 ml from each blood sample was transferred into a tube containing ethylenediaminetetraacetic acid (EDTA).

To quantify the concentrations of several biochemical indicators in blood serum, a volume of four milliliters of blood was placed in glass tubes with no any substance that prevents clotting, and left at a room temperature for a duration of one hour. Following coagulation, the serum specimens were separated using centrifugation, transferred into Eppendorf tubes using a micropipette, and then stored under freezing circumstances at -20°C till they were analyzed (Themel *et al.,* 2004).

Estimation of liver function indicators

The serum ALT and AST levels was determined automated using Cobas c111 device with a kit provided by Switzerland/ Roche . This kit enables the quantitative detection of human ALT and AST. The test was carried out according to the manufacturer's instructions.

Estimation of kidney function indicators

This test used to determine serum creatinine and urea levels .It was measured automated by using cobas c111 device with a kit given by Switzerland/Roche. The test was conducted in accordance with the manufacturer's instructions.

Estimation of lipid profile indicators

Cobas c111 device with kit provided by Switzerland/Roche. A method was employed to measure the amounts of total cholesterol and triglycerides in the serum of humans. The test was conducted in accordance with the instructions provided by the manufacturer.

Hematological parameter estimation

The hematological parameters were determined using the usual automated method for a complete blood count. A hematology analyzer (Siemens) measured the blood indices in this study, including the erythrocyte (RBCs), leukocyte (WBCs), and thrombocyte (platelets) counts, along with the values of hemoglobin (Hb) and hematocrit (HCT).

Statistical analysis

In order to know the significant differences in the results obtained from this study, the statistical analyses were performed utilizing the MedCalc Statistical Software Package (Version 20.215). The independent t-test was used to compare many groups. The statistical study utilized the measures of central tendency, specifically the mean, as well as the measure of dispersion, namely the standard deviation. A significance level of <0.05 was deemed appropriate for all tests. Biochemical markers in serum of AML patients and control groups.

RESULTS

The results of this study demonstrate a statistically significant increase ($p<0.05$) in the levels of ALT, AST, urea, creatinine and TG in the serum of individuals diagnosed with AML as compared to healthy individuals. On the other hand, the results showed a significant decrease ($p<0.05$) in the concentration of TC in the serum of individuals diagnosed with AL as compared to control group. Table (1). and

Table 1: Biochemical markers in serum of AML patients and control groups.

Parameter	AML patients	Healthy group
ALT (U/L)	86.54±4.43*	21.39±3.09
AST (U/L)	51.24±11.15*	25.79±6.46
Urea(mg/dl)	34.63±8.70*	21.25±3.49
Creatinine (mg/dl)	1.72±0.41*	0.61±0.26
TG (mg/dl)	179.16±41.78*	114.92±34.58
TC (mg/dl)	119.80±40.74*	161.79±26.88

- Values are means ± SD. Independent t-test.
- (*) =Significant differences exist at the $p<0.05$.

With regard to hematological parameters, the findings indicate significant decreases ($p<0.05$) in the overall count of RBCs, WBCs, and platelets, in addition to significant decreases ($p<0.05$) in the levels of Hb and HCT. Table (2). In terms of hematological criteria, the results show that the total number of RBCs, WBCs, and platelets, as well as the levels of Hb and HCT, have decreased significantly ($p<0.05$). Table (2).

Table 2: Hematological criteria in serum of AML patients and control groups.

Parameter	AML patients	Healthy group
RBCs (10^6/µl)	2.93±0.94*	4.83±0.58
Hb (g/dl)	7.25±1.53*	13.39±1.74
HCT (%)	20.89±5.29*	38.16±5.39
WBCs (10^3/µl)	22.32±5.19*	7.85±1.65
PLT (10^3/µl)	57.66±32.79*	282.02±60.49

- Values are means ± SD. Independent t-test.
- (*) =Significant differences exist at the $p<0.05$.

DISCUSSION

Liver function

The results of this study revealed a significant elevation in levels of ALT and AST in the serum of individuals diagnosed with AML. Our findings corroborate the results of previous studies that demonstrated a significant elevation in blood concentrations of both enzymes among leukemia patients (Islam *et al.,* 2020; Jumaah *et al.,* 2021; Al-mansouri *et al.,* 2023).

The elevated enzymatic activity observed in leukemia patients may be attributed to hepatic infiltration. High levels of AST are linked to an infiltrative disorder that happens when the membranes of mitochondria and cytoplasm are damaged (Kumar and Keerthana, 2016).

Hepatic damage results in elevated levels of ALT and AST in people with leukemia (Carvalhana *et al.,* 2016). Thus, as the number of leukemic cells increases, the concentration of transaminase enzymes in the serum increases (Verma *et al.,* 2014).

5.4. Kidney function

This study found that AML patients had higher levels of urea and creatinine in their blood, which is in line with previous clinical findings that showed a link between higher levels of these hydrogen products and a higher disease prevalence (Mohammed, 2007; Jumaah *et al.,* 2021; Al-mansouri *et al.,* 2023).

Urea and creatinine are indicators that measure the kidneys' efficiency in performing their functions of filtering waste from the blood. Several disease states have shown high serum uric acid levels to play an important role (Maiuolo *et al.,* 2016). A

current study's findings suggest that measuring these indicators may be useful for predicting renal outcomes (Seki *et al.,* 2019).
A lot of research says that the high level of uric acid in the serum is caused by the breakdown of nucleic acids in leukemic cells. This could mean that there is pathological hostility present (Alvarez-Lario, and Macarron-Vicente, 2010; Yamauchi *et al.,* 2013; Seki *et al.,* 2019).
Leukemia patients may experience clinically progressed hyperuricemia due to several problems such as tumour lysis syndrome, severe medication responses, and renal failure. Additional investigation reveals that the rise in blood uric acid levels in certain patients is a result of underexcretion induced by renal failure (Yamauchi *et al.,* 2013).
Moreover, due to the fact that creatinine is a naturally occurring molecule within the body, its breakdown and processing might vary between individuals according to a range of circumstances (Beddhu *et al.,* 2003). Creatinine remains the universally accepted standard for diagnosing renal failure. However, it is important to note that its significance lies in assessing kidney function rather than confirming the presence of actual damage (Seller-Perez *et al.,* 2013).
According to a previous study by Drent *et al.* (1996), leukemia cells entering the kidneys or leukemia cell byproducts like uric acid and phosphate can cause kidney problems in AML.
Previous studies have demonstrated the presence of renal disorders in AML patients, both before and after chemotherapy. Renal problems can arise from the use of nephrotoxic medications, and the risk of renal disorders is heightened during chemotherapy due to the toxic nature of the agents administered (Toblem *et al.,* 1980; Keeting *et al.,* 1982).

5.5. Lipid profile

The present study analyzed the serum lipid profile of patients newly diagnosed with AML. We found significantly lower total cholesterol levels and higher triglyceride concentrations compared to healthy individuals. Our results were in agreement with most studies in this area (Einollahi *et al.,* 2013; Usman *et al.,* 2015; Ozturk, 2021).
Leukemia patients frequently exhibit dyslipidemia, which refers to atypical blood lipid patterns. The anomalies in blood lipid levels of leukaemia patients have been extensively observed in an effort to delineate the distinctive characteristics of these profiles in such patients (Usman *et al.,* 2015).
In their study, Casalou *et al.* (2011) discovered that primary leukemia cells had a higher accumulation of cholesterol in bone marrow areas that are rich in leukemia. This accumulation is connected with the aggressiveness of the disease and also affects the functioning of a receptor-tyrosine in cancerous leukemia cells.
According to a report by Liang *et al.* (2022), the patients with advanced myeloid leukemia had lower serum levels of total cholesterol, HDL, and LDL compared to control subjects, indicating lipid metabolism disorders in the bone marrow microenvironment,
In one experimental study, it was proven that leukemic cells secrete a leukemia inhibitory factor (LIF), which reduces the plasma cholesterol level through up-regulation of the LDL receptors on liver cells (Cebi *et al.,* 2015).
On the other hand, it is believed that cancer cells use de novo-produced fatty acids for membrane production, energy supply, and proliferation Menendez and Lupu, 2007; Kuemmerle *et al.,* 2011). In neoplasms that do not proliferate rapidly, the need for lipids to fight apoptosis increases (Rysman *et al.,* 2010).
Researchers have shown that plasma lipid concentrations significantly predict the prognosis of leukemia patients undergoing chemotherapy. Therefore, researchers consider the lipid profile of leukemia patients as a potential prognostic or diagnostic factor, which could potentially serve as a simple test to monitor the patients' response to chemotherapy, a promising therapeutic target (Usman *et al.,* 2015; Bai *et al.,* 2023).

5.6. Hematological parameters

The results of the current investigation have confirmed a notable decrease in some hematological parameters among individuals diagnosed with AML, specifically RBC count, Hb, HCT, and platelet count in comparison to the control group.
Nevertheless, a recent study has demonstrated that AML cells secrete interleukin-6 (IL-6), which hinders the development of erythroid cells at the pro-erythroblast stage (Zhang *et al.,* 2020). Blocking IL-6 has demonstrated efficacy in improving anemia caused by AML and extending overall life, indicating that targeting this route could be a promising therapeutic strategy (Sariani *et al.,* 2021).
Also, the results showed a significantly higher leucocyte (WBC) count (leukocytosis) in patients with AML. These findings were in accordance with those reported by other Iraqi and worldwide studies (Alizadeh *et al.,* 2011; Hasan *et al.,* 2017; Ayub and Ibraheem, 2020; Shah and Rivero, 2020).
Leukemia is distinguished by the abnormal growth of malignant cells in bone marrow, which can occur at any stage of development (Wang *et al.,* 2011). AML is a cancerous disease that affects the generation of blood cells in the bone marrow. It is caused by the abnormal growth and buildup of leukemic blast cells, which restrict the normal growth and development of blood cells (Al-Husseiny, 2008; Lichtman *et al.,* 2010).
In all acute myeloid leukemia cases, leukocytosis was the most common. A higher WBC count means that these cells are multiplying too quickly, which is a sign of leukemia. Patients with leukemia may link the growth of blast cells to thrombocytopenia and a drop in Hb and HCT, which are signs of anemia (Ayub and Ibraheem, 2020).

CONCLUSION

Subjects with AML have altered serum levels of biochemical markers and hematological criteria used in this study compared to healthy individuals. These results may support the evidence about the potential role of these markers in AML disease. Studying AML with a large cohort is necessary to gain further insights and validate the usefulness of these criteria in combination with other cancer markers. These markers may be of interest as independent prognostic factors for the malignant progression of this disease. Therefore, the research and follow-up on the use of standard, inexpensive, and easy-to-measure tests for predicting the evolution of AML is warranted.

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