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# Trace Elements in Serum of Thi-Qar Leukemia Patients

[1]Afrah A. Maktoof , Nabeel M. Abed[2] , Rsha S. Nuhair[3]

[1,3] Department of biology , College of Science, University of Thi-Qar ,

[2]Veternary Medicine Collage, University of Thi-Qar,

Email: afrah.m_bio@sci.utq.edu.iq , nabeel.mahdi.abed@utq.edu.iq dr.rasha_bio@sci.utq.edu.iq

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## Abstract

In the present study, the concentrations of ALT,AST,ALP total protein , urea and creatinine and some trace elements Cooper (Cu),Iron (Fe) and Zinc (Zn) in the serum of 40 adult patients with diagnosed of leukemia (after treatment) were studied.

Samples were collected from oncology center/AL-Habboubi Teaching Hospital in Thi-Qar province, Serum levels of liver enzyme and trace elements were compared with(25) healthy group samples. It was found that a significant increase ($P<0.05$) in liver enzyme ALT, AST, ALP concentrations in blood serum of control and patients with leukemia . Also there is significant increase in urea serum level in patients at ($p<0.05$) and increase in creatinine but non significant . As regards the results of trace elements Serum levels of Cu and Fe elements were significantly higher in with leukemia patients than in the controls ($p\leq 0.05$). Also the level of Zinc was higher but statistically not significant ($p>0.05$).

**Key words**: leukemia .Liver Enzymes, urea and creatinine

## Introduction

Leukemia ( liquid cancer ) which was occur due to developing of bone marrow , cells in the blood, , and lymphatic system. In leukemia, the abnormal white blood cells flood the marrow, providing no room for red blood cells and platelets. This can affect a patient in several ways i.e. anemia, drop in platelet count and lack the ability to fight infections due to abnormal nature of white blood cells, ( 1). Leukemia is the 12th most Common cancer in the world. (2) In the part of the world where Iraq is located, cancer seems a growing health problem in terms of incidence and mortality, it has become increasingly important as concern with development and progress that has been achieved in Iraq (3,4).

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Ahmed (5) notice that leukemia was the third most common cancer in Thi-Qar in 2000 – 2005 ,(3) recorded 3523 cancer patients , 336 of them with various types of leukemia in Cancer Control Unite in Thi-Qar Governorate and During a five year period (2005-2009).There are four major types of leukemia: Acute Lymphoid Leukemia (ALL) , Chronic Myeloid Leukemia (CML) , Acute Myeloid Leukemia (AML), Chronic Lymphoid Leukemia (CLL) ,The latter two types are the most common among adults. (6). There are many risk factors of developing leukemia among both children and adults such as High-dose radiation exposure ,exposure to certain chemotherapy drugs, long-term occupational exposure to benzene , long-term exposure to herbicides and or pesticides ,Although viruses have been implicated in the etiology of other leukemia‘ cigarette smoking and genetic disorders(7, 8) Trace elements are classified as essential trace elements like Cu, Fe, Zn, K, Mg, Mn, … or non-essential trace elements like cadmium , mercury ,As… according to whether an organism can grow and complete its life cycle in their absence.(9). Blood consider the transport medium for the nutrients and trace elements to and from the tissues and,, therefore, provides rapid and reliable information about the trace elements .metabolism in human body (10). These elements are combined into the structures of proteins, Enzymes, and complex carbohydrates. They take part in biochemical reactions together with enzymes (11). Transaminase enzymes have a role in metabolism of amino acid in living cells, important examples are aspartate aminotransferase (AST), alanine amino transferase (ALT) and Alkaline Phosphatase (ALP)(12) .Urea is the detoxification product of the ammonia derived from deamination of amino acids. Urea is considered to be the end product of protein catabolism. Creatinine is a catabolic end product, an anhydride of creatine (or phosphocreatinine) .produced by loss of water (or phosphoric acid) from the molecule in an irreversible reaction. Creatinine is excreted from the body via the urine (13).Therefore, the aim of this study was to investigate the distribution of some liver enzymes and trace Eelements in serum of Thi-Qar leukemia patients.

## Material and methods

### Sampling

### Patients Characteristics

This study comprised 40 adult patients with leukemia their ages ranges between 16 to 65 years. The group consisted of males and females, referred to the oncology center/AL-Habboubi Teaching Hospital in Thi-Qar province. All patients receiving courses of chemotherapy or radiotherapy; the control subjects were 25 healthy volunteers who live in these province.

### Sample Preparation

Venous blood sample (5 ml) was collected from the antecubital vein of each of leukemia patients and healthy group in sterile tube without any additives .The blood was

then allowed to clot and centrifuged for 15 minutes at 3000 rpm to extract the serum. The Serum samples were stored aliquots at -20 °C until used for biochemical analysis.

## Studied parameters:

**Measurements of Aspartate Aminotransferase (AST) (U/I):**

Aspartate aminotransferase is measured by monitoring the concentration of oxaloacetate hydrazone formed with 2,4-dinitrophenyl-hydrazine (14).Alanine aminotransferase is measured by monitoring the concentration of pyruvate hydrazone formed with 2,4-dinitrophenyl-hydrazine(14).

**Measurements Alkaline Phosphatase (ALP) (U/I):**

This measurement was done by using the colorimetric determination of alkaline phosphatase activity (Biolabo-France) (15).

**Measurements of Total Protein (g/L) :**

The total protein was estimated by using a special chemical kit prepared by BIOLABO, SA, Maizy/ France).Colorimetric method is described by (16)**.**

**Measurements of Urea( mg/dl) :**

Urea concentration was determined by using a special urea Kit (bioSystems, Spain) (17)

**Measurements of Creatinine( mg/dl) :**

Creatinine concentration was determined by using a special creatinine Kit (BIO-LABO. SA, Maizy , France). (18).

**Measurements Of Serum Trace Element (µg/ml) :**

All standard elements and chemicals used were supplied by Sigma-Aldrich, Germany. Serum elements Cu,Fe and Zn of all samples were measured using flame atomic absorption spectrophotometer (FAAS, Model AA646, Shimadzu Corporation, Kyoto, Japan) (19).

## Statistical Analysis:

Standard analysis of the data was performed using the computerized statistical program: The SPSS program.The results were expressed as mean± standard division (M ± S.D). Analysis of variance (ANOVA) was used to compare the results. The differences are considered to be significant at ($P \leq 0.05$).

## Results and discussion

leukemia is heterogeneous aggressive disease in which different clinical manifestation are show (20). In this study, the results in table (1) showed a significant increase ($P<0.05$) in liver enzyme ALT,AST,ALP concentrations in blood serum of control and patients with leukemia .our results are in agreement with (21) were record significantly increased in three liver enzymes in patients with leukemia . Another research study done by (21) and (22) showed a significant increase in both enzymes ALT,AST in serum of

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patients with leukemia. The hepatic infiltration is one of the main reason to raise the level of these enzymes among leukemia patients. The known defect in the membranes of mitochondira and cytoplasm would lead to evaluate AST level in the blood.( 21).

High level of ALT and AST enzyme are commonly detectable at initial stage in leukemia and that direct to hepatic injury( 23). The elevated of leukemic cell may lead to increase of transaminase enzyme concentration due to the toxicity of chemotherapy treatment (21). Gao (24) attributed the high level of AST and ALT enzymes in people with leukemia to chemotherapy that adversely affects liver function. These results are in agreement with other studies done on serum AST activity in patients with ALL, AML and Lymphoma (25, 26) .Several studies reported elevation of ALP activity in early stages of patients serum of breast cancer, ovarian cancer, esophageal cancer, prostate cancer, brain cancer, colorectal cancer and lung cancer when compared with normal controls (27) , acute lymphoblastic leukemia(28 ) . Saif *et al* .,(29) refer to the elevation in ALP activity occurs because of the accelerated denovo synthesis of the enzyme . While Charnow (30) mention because the increase of tumor necrosis factor-α and its direct effect on the expression of alkaline phosphatase in vascular smooth muscle cells .

**Table 1: The mean and standard deviation of ALT, AST,ALP Total protein , urea and creatinine in leukemia patients group and control group.**

| Characteristic | Control group mean ± SD N=25 | Patients group mean ± SD N=40 | P Values |
|---|---|---|---|
| **ALT (U/I)** | 24.95 ± 1.6 | 53.78 ± 6.8 | <0.05 |
| **AST (U/I)** | 65.83 ± 3.97 | 95.87 ± 4.21 | <0.05 |
| **ALP (U/I)** | 26.58 ± 2.2 | 60.65 ± 5.71 | <0.05 |
| **Total protein (g/L)** | 6.87 ± 1.89 | 7.18 ± 1.2 | N.S |
| **Urea( mg/dl)** | 51.00 ± 4.56 | 60.12 ± 7.8 | <0.05 |
| **Creatinine ( mg/dl)** | 3.83 ± 1.5 | 4.78 ± 1.96 | N.S |

Also there is significant increase in urea serum level in patients at ($p<0.05$) and increase in creatinine but non significant . These results are in agreement with other studies done on serum urea and creatinine level in patients with different type of leukemia (31) and agreement with study of (32) after treatment the value urea and creatinine elevated in some patients and these are shown in the tables (1) these elevation values are due to the complication in kidney because of the nephrotoxic drugs taken the patients such as cytotoxic drugs ( anthracycline derivatives ).

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**Table 2: The mean and standard deviation of Cooper (Cu),Iron (Fe) and Zinc (Zn) in leukemia patients group and control group**

| Trace element | Control group mean ± SD N=25 | Patients group mean ± SD N=40 | P Values |
|---|---|---|---|
| **Cu (µg/ml)** | 1052 ± 206.555 | 1238.4± 214.195 | <0.05 |
| **Fe (µg/ml)** | 1009.5 ± 313.8 | 1260.885± 612.8 | <0.05 |
| **Zn (µg/ml)** | 56.715 ± 8.825 | 68.215 ± 7.5 | N.S |

Serum levels of Cu, Fe and Zn of the leukemia cases and healthy human were shown in (Table 2). Serum levels of Cu and Fe elements were significantly higher in with leukemia patients than in the controls ($p \leq 0.05$).

Copper is a vital dietary element that is a component of many metalloenzymes that are needed for oxidative metabolism process (33). This results of Cu levels are in agreement with study conducted by (34) and (35). The researcher on (36) pointed to a positive relationship between the level of copper and pathologic conditions which accompanied by increased rate of tissues destruction and / or proliferation.

Some investigators combined between copper deficiency and haematological and neurological abnormalities. They consider copper deficiency as an established cause of haematological abnormalities but is frequently misdiagnosed (37).Our results are in agreement with (38 ) studies in leukemic patients in which serum Cu levels have been found to be higher than those of controls. iron(Fe) is an essential element for sustaining life and a fundamental component of many enzymes and proteins that are essential for cell growth and replication.(39).

The results obtained in this study showed significant increase in the concentration of Fe in the serum of patients with leukemia as compared with the control group.these results go in accordance with the finding of other study by (40).

Fe values reported in this work agree with the values reported by (41) who found high level of Fe in children with ALL but different from those obtained by (42).Fe can induce free radicals which lead to genetic material DNA breaks and oncogenes activation. .This was suggested by four epidemiological studies, showing a higher cancer risk in patients with larger iron stores than in those with small iron stores. In addition to its effect on carcinogenesis, iron also maintains the growth of malignant cells as well as growth of pathogens (43).

Increased levels of iron in the blood of patients may also be associated with increased risk of cancer by inducing the mutations of cells( 44 , 45).

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Zinc is known as an essential component of more than 300 metalloenzymes that are necessary for human health (46).Zinc values reported in the present study agree with the values reported by (42 and 40) whose found that no significant differences for the concentration of Zn was found between the patients and control groups.In countries in which diet naturally rich in zinc are consumed, the mortalities from cancers at major sites are also higher than in countries where the national diets provide less zinc; the major source of dietary zinc is beef (47).

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