

**The Role of Plasma Homocysteine Level in Leukemia Disease and its Relationship with the Blood Component The White Blood Cell and Hemoglobin in Patients Tikrit-Iraq**

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**Abstract**

Overall this paper to investigate the relation Homocysteine (Hcy), WBC, and Hemoglobin with Leukemia (Blood cancer) disease. Studies of Iraqi men in Tikrit Hospital. Leukemia and is characterized by an abnormal proliferation of blood cells, white blood cells (leukocytes). **Objectives:** To investigate homocysteine levels in Leukemia disease and its relationship with White blood cells (WBC) and Hemoglobin (Hb) (repeated). **Methods:** This investigation performed as a case control study for two groups as 40 Leukemia patients and 25 as a control. Patients for two group in Tikrit-Iraq. Leukemia patients were selected based on the criteria of the American Psychological Association. plasma homocysteine level were measured by HPLC method at UV detector 338nm WBC and Hb were measured by method Manual blood count Hemacytometer is a counting chamber according to WHO. **Results:** 40 Patients in group 1 plasma Homocysteine was  $21.15 \pm 8.9 \mu\text{mol/L}$ , but in control group plasma Homocysteine was  $12.00 \pm 4.33$  ( $p=0.83$ ). The average plasma homocysteine level in the group 2 of patients was  $10.56 \pm 3.99 \mu\text{mol/L}$ , Homocysteine in the control group 2 was  $28.11 \pm 9.75 \mu\text{mol/l}$ , ( $p=0.78$ ). **Conclusion:** The average plasma homocysteine level in Leukemia patients was higher than in the control group; however, it shows a significant relationship with the WBC and Hb.

**Keywords:** Homocysteine, Leukemia disease, WBC, Hb, Iraq

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دور مستوى الهوموسستين في امراض اللوكيميا وعلاقتها مع مكونات الدم كريات الدم البيضاء والهيموغلوبين في مرضى تكريت -العراق

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### الخلاصة

ان البحث تحقق عن العلاقة بين بلازما الهوموسستين وكريات الدم البيض والهيموغلوبين مع مرض اللوكيميا(سرطان الدم). درست لمرضى سرطان الدم الرجال في مستشفى تكريت وخصصت كحالة الشاهد لكريات الدم من(الكريات البيض). **هدف البحث:** التحقق من العلاقة بين مستويات الهوموسستين في مرضى اللوكيميا وعلاقته مع كريات الدم البيض. **والهيموغلوبين. الطريقة:** البحث انجز على مجموعتي سيطرة 25 شخص كمجموعتي سيطرة غير مريضة ومجموعتين مرضى عدد 40 مريض. مجموعتي المرضى في مدينة تكريت تم اختيارها تبعا لمعايير منظمة الفسلجة الامريكية. ان مستويات الهوموسستين تم قياسها بواسطة تقنية (HPLC) كروماتوغرافيا الضغط العالي. وكانت ضمن طول موجي 338 نانوميتر. وكريات الدم البيضاء والهيموغلوبين تم قياسها بطريقة يدوية في عداد كريات الدم الهوموسايتوميتر طبقا لمواصفات WHO منظمة الصحة العالمية. **النتائج:** 40 مريض في مجموعتين، المجموعة الاولى كان مستوى الهوموسستين  $8.9 \pm 21.15$  مايكرومول/لتر. وفي مجموعة السيطره الاولى كان تركيزه  $4.33 \pm 12.00$  مايكرومول/لتر في ( $p=0.83$ ). وكان معدل مستوى الهوموسستين في مجموعة المرضى الثانية  $3.99 \pm 10.56$  مايكرومول/لتر وفي مجموعة السيطرة الثانية  $9.75 \pm 28.11$  مايكرومول/لتر في ( $p=0.78$ ). **الاستنتاج:** معدل مستوى البلازما هوموسستين ارتفع في مجموعتي مرضى لوكيميا الدم بالمقارنة مع مجموعتي السيطرة ولوحظ اهمية كريات الدم البيض ومستوى الهيموغلوبين مع الهوموسستين في مرض اللوكيميا.

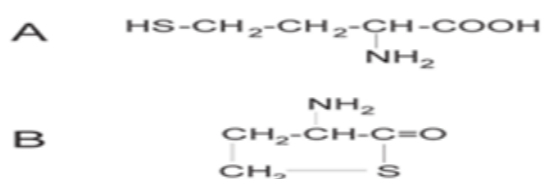
**الكلمات المفتاحية:** هوموسستين. مرض اللوكيميا. كريات الدم البيضاء. الهيموغلوبين. العراق

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### Introduction

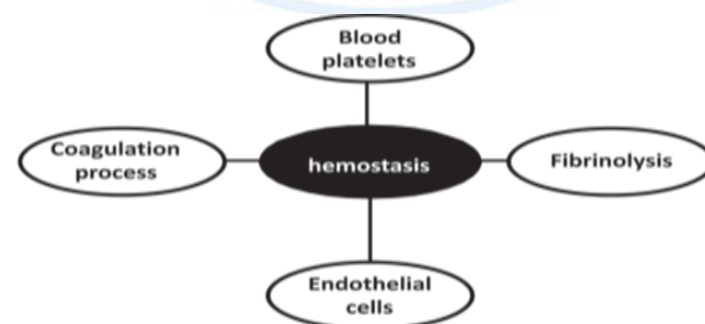
Homocysteine is a sulfur amino acid and an intermediate in methionine metabolism (1). The chemical structure and its thiolactone is presented Fig.1



**Figure 1.** The chemical structure of Homocysteine (A) and its thiolactone(B).

Increase homocysteine levels in cells defined as hyperhomocysteinemia while decrease of homocysteine levels in cells defined hypohomocysteinemia has been correlated with many diseases, as cardiovascular and atherosclerosis (2), hyperhomocysteinemia result from various factors, as lifestyle diseases, sex, diet, drugs, and age. Unbalanced in diet, leading deficiency of vitamins B2, B12, B6 and folic acid and relations with an increase in Homocystein conc. As well as alcohol, smoking and coffee also lead to increased Homocysteine range, Increase of Homocystien found in human pathologies, involve neurodegenerative diseases, (3). The authors review describes the effect of hyperhomocysteine on different components of blood platelets, endothelial cells, plasmatic fibrinogen and plasminogen, Fig.2

Hemostatic abnormalities. The normal hemostatic mechanisms prevent the hemorrhage(4).



**Fig 2.** Metabolism of homocysteine.

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Regulates the properties of blood, are described by interactions of homocysteine and its different derivatives, including homocysteine thiolactone, and major components of hemostasis as endothelial cells, , plasmatic fibrinogen and plasminogen, and blood platelets, are also discussed. The blood vessel wall, blood platelets, fibrinolytic proteins and coagulation factors.

A vascular endothelium maintains the balance between stimulation of platelet and activation prevention, and between coagulation and fibrinolysis as well as between vasoconstriction and vasodilation(50). In hemodialysis patients, plasma range of total homocysteine are influenced by nutritional case. To investigate the association between homocysteine serum ranges as a marker and WBC counts marker for inflammation,(6). White blood cells as important marker for disease processes. Increase levels WBC also be considered a risk factor for infarction, and decreases during hemodialysis is investigated as a function of different dialysis membranes (7,8). Homocysteine metabolism is consists two pathways: Remethylation to methionine, which requires vitamins B-complex as coenzymes; and transsulfuration of cysteine, which requires the B6 coenzyme.(9). Hyperhomocysteinemia is correlated with many diseases as disorders, autoimmune, congenital anomalies, kidney diabetes, dysfunction, and malignant diseases,(10,11). Many mechanisms are supposed for infarction in patients, as leukemic infiltration effects of the antileukemic therapy and chemot-therapy, as leukostasis syndrome(12). Leukocytosis is elevate WBC count as the leukocyte count as mention above in normal range and Leucocytosis is Increase in the account circulating leucocytes more  $11 \times 10^3$  account. Elevated leukocytes lead to increases due to monocyte precursors in the bone marrow that is stimulated by products for inflammation.(13), and intravascular coagulation deficiency of coagulation factors(8). WBC count was  $11,000/\text{mm}^3$ , which made leukostasis less likely, The white blood cell count was  $900/\text{mm}^3$  it will made less than leukostasis[14], WBCs including neutrophils, lymphocytes, monocytes, eosinophils, and basophils [15]. White blood cells (WBC) considered as an important Biomarker for several disease and processes so elevated White blood considered a risk factor for acute infarction, disease and stroke(16). indicating further that leukostasis was unlikely thrombosis.

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Homocysteine is found to be elevated in rapidly growing tumors even though not treated with drugs. It was also proposed that homocysteine as a potential tumor marker(17).

### **Aim of study:**

To investigate homocysteine levels in Leukemia disease and its relationship with White blood cells(WBC) and Hemoglobin.

### **Materials and Methods**

Eighty Leukemia patient and 50 control healthy human categories for two groups depended to period age (19-25) year and (25-55) year, Forty patients with leukemia and 25 healthy people. First the patients groups as were studied in Tikrit hospital/Iraq, from May 2014 to June 2015. This study was performed with patients consent and approved by the Ethics Committee all patients and control samples carried out in Erbil-Iraq. The diagnosis of Leukemia disease was based on the diagnostic criteria of American Psychological Association(18). Measurements of plasma homocysteine, have been described (19). Briefly, Homocysteine was determined by High performance liquid Chromatography technique (HPLC); with UV detector at 338nm; WBC were measured by Hemacytometer is a counting chamber according to WHO method and Hb blood by Manual method (20).

### **Results**

Mean age patients and control groups was  $20.1 \pm 2.1$  and  $40.2 \pm 3.2$  ; previously. Gender in both groups is male. Both group patient and control regarding age and gender, number of patients according to deterioration scale was shown in Figure 1. The mean levels of homocysteine in patients  $21.15 \pm 8.9 \mu\text{mol/l}$ , while in control group 1 is  $12.0 \pm 4.33 \mu\text{mol/l}$ . Non-significant differences in homocysteine level in patients and control groups ( $p=0.83$ ). The mean homocysteine of patient group 2  $28.11 \pm 9.75 \mu\text{mol/l}$  and in the control group 2 was  $10.56 \pm 3.99 \mu\text{mol/l}$ . difference of homocysteine mean range in patients and control group 2 was significant ( $p=0.78$ ). There was a significant For estimating the homocysteine cut point. average levels WBC account for patients was  $22.5 \pm 9.92 (10^6 \text{cell/l})$ , and in the control group 1

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was  $7.62 \pm 2.11 (10^6 \text{ cell/l})$ . difference of WBC in patients and control in group 1, was high significant ( $p=0.65$ ). average of WBC of patients group2 is  $30.89 \pm 11.5 (10^6 \text{ cell/l})$  while in control group 2 is  $6.53 \pm 2.01 (10^6 \text{ cell/liter})$ . difference range for patients group and control group 2 is clear significant ( $p=0.92$ ). There was a significant For estimating the WBC. The average level of Hb in patients was  $5.84 \pm 1.46 \text{ g/dl}$ , and in the control group 1 was  $10.91 \pm 3.38 \text{ g/dl}$ . The difference of level in patients and control group1 was no significant ( $p < 0.001$ ). average Hb in a patient group 2 was  $5.34 \pm 2.33 \text{ g/dl}$  in the control group 2 was  $11.35 \pm 4.58 \text{ g/dl}$  and difference Hb level in patients and control groups 2 was no significant ( $p < 0.001$ ). There was a significant For estimating the All results showed in Table 1, Fig 3 and Table 2, Fig 4.

**Table 1- Comparison of all measured parameters between control and Leukemia Patient group1(Data presented as Mean  $\pm$  SD).Based on age(19-25)year.**

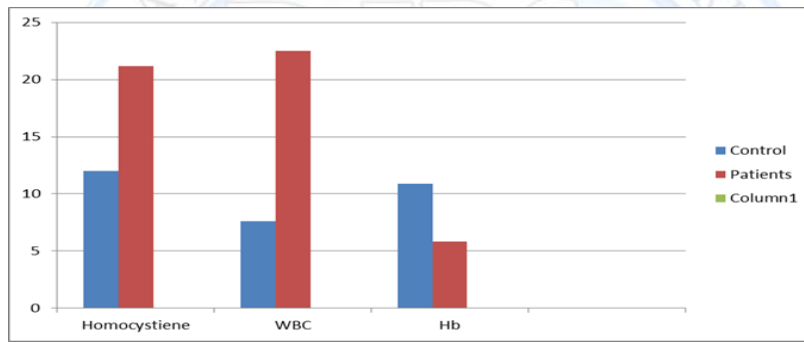
Parameters	Controls Mean $\pm$ SD N=25	Patient Mean $\pm$ SD N=40	P value
Homocystiene $\mu\text{mol/L}$	12.0 $\pm$ 4.33	21.15 $\pm$ 8.9	0.83
WBC X $10^6 \text{ Cell/L}$	7.62 $\pm$ 2.11	22.5 $\pm$ 9.92	0.65
Hb g/dl	10.91 $\pm$ 3.83	5.84 $\pm$ 1.46	<0.001

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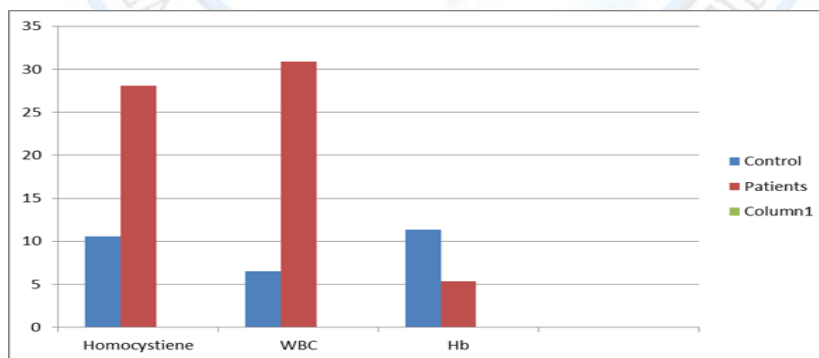
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**Table 2-Comparison of all measured parameters between control and Leukemia Patient group 1(Data presented as Mean ± SD).Based on age (25-55)year**

Parameters	Controls Mean±SD N=25	Patient Mean±SD N=40	P value
Homocystiene μmol/L	10.56±3.99	28.11±9.75	0.78
WBC X 10 <sup>6</sup> Cell/L	6.53±2.0	30.89±11.50	0.92
Hb g/dl	11.35±4.58	5.43±2.33	<0.001



**Figure-3.parameters in control and Leukemia Patient in group1**



**Figure-4.parameters in control and Leukemia Patient in group1**

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**Discussion**

Concentration of homocystein in blood is influenced in a genetic factors and by interaction between other factors (21), homocysteine levels depends on sex, smoke ,age , function of e liver ,kidneys, physical activity and diet.[22], also various compounds is lead reduction of Hemocystien as Folic acid and B6,vitamins should be mentioned [23,24]. In the results of study showed, increased Hcy concentration in blood of patients and comparison with control groups and increase WBC in patients comparison with control while decrease Hb in two groups patients rather than high in control groups.Other experiments indicate that elevated homocysteine and vitamins deficiency are direct associated with oxidative stress (25). Anothers indicate that regular of antioxidants, and correlated with metabolites, and correlations with a decline risk cancer(26). All mechanisms protection Hemocystien act are unknown still now (27),another study point flammatory cytokines as well as the range of lectin-oxidized low-density of lipoprotein reduced in homocystien fed wide range of biological effects, involve antiplatelet, and anti-inflammatory,anticancer (28).

In conclusions, homocysteinemia to hemostatic abnormalities is complex and still this study showed that the homocysteine range in Leukemia patients group higher significantly in comparison with the control group, However, there is relationship homocysteine We recommend that in future studies to carried out on a large number of samples taken from patients.



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