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Investigation and Assessment of Hepatic dysfunction and Lipid Profile in Patients with Acute Lymphocytic Leukemia in Basrah Governorate – Iraq

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الخلاصة

مرض سرطان الدم اللمفاوي الحاد (ALL) هو احد الاضطرابات الكيموحيوية المعقدة والذي يمتلك التهابات مختلفة في جسم الانسان وخاصة الاطفال. طبق وصمم العمل الحالي لتقصي وتقدير مستويات انزيمات الكبد ونمط الدهون في مرضى سرطان الدم اللمفاوي الحاد الذين خضعوا للعلاج الكيميائي اعتماداً على عوامل العمر وفصيلة الدم. سجلت زيادة معنوية بصورة عالية ($P < 0.0001$) في مستويات انزيمات كلوتامات – اوكلز الواسيتات ترانسأمينيز (GOT) وكلوتامات – بايروفات ترانسأمينيز (GPT) والفوسفاتيز القاعدي (ALP) والكليسيريدات الثلاثية (TG) والكوليسترول الكلي (TC) والدهون البروتينية عالية الكثافة (HDL) والدهون البروتينية غير مرتفعة الكثافة (Non-HDL) والدهون البروتينية ذات الكثافة الواطئة (LDL) والدهون البروتينية ذات الكثافة الواطئة جداً (VLDL) في المرضى مقارنة بمجموعة السيطرة طبقاً لعوامل العمر وفصيلة الدم. لذلك هذه المتغيرات الكيموحيوية تعد كمؤشرات لمتابعة شدة مرض سرطان الدم اللمفاوي الحاد.

Abstract

Acute lymphocytic leukemia (ALL) disease is one of complex biochemical disorders which has various inflammatory in human being especially children. The recent work was carried out and designed to investigate and assess the levels of liver enzymes and lipid profile in ALL patients which underwent chemotherapy according to blood group and age factors. Highly significant increasing ($P < 0.0001$) was recorded in the levels of glutamate–oxaloacetate transaminase (GOT), glutamate pyruvate transaminase (GPT), alkaline phosphatase (ALP), triglycerides (TG), total cholesterol (TC), high density lipoproteins (HDL), non-high-density lipoproteins (Non-HDL), low density lipoproteins (LDL) and very low density lipoproteins (VLDL) in ALL patients compared with control group according to blood group and age factors. So these biochemical parameters are considered as markers for following the severity of ALL disease.

Keywords: Acute Lymphocytic Leukemia, GOT, GPT, triglycerides, total cholesterol, high density lipoproteins

1.Introduction

Recently many individuals have different medicinal problems resulting from various diseases take place as a result of physiological and chemical disorders in the biochemical action of human cell. The disease represented by acute lymphocytic leukemia (ALL) is a risk healthy problem and it is a class of cancer disease (leukemia) which infect different persons have various blood groups and they also have family history belongs to this acute lymphocytic leukemia (1). The reasons of ALL disease are biochemical malignant disorder in bone marrow, pre-lymphoid precursors proliferate, and change of blood components of normal living cells existing in the marrow structure. Cancer is one of disease which require various therapies have different medicinal roles affect on the overall chemical and biochemical systems. Also the chemical roles lead to produce some alterations in multi-genes then the healthy disorders in the human cell lead to form several genetic mutations (2).

The reform this complex case will finally biosynthesize abnormal proteins in blood change in livers enzymes actions, difference in classes of lipids (TG, TC, HDL, LDL, and VLDL) vitamins, uric acid, malondialdehyde and some trace elements. So various problems will occur in presence of acute lymphocytic leukemia represented by the chemical disorder and genetic mutations in the living cell leading to change in levels of several biochemical parameters (3).

Many researches were established concerning the levels of antioxidant enzymes like glutamate – oxaloacetate transaminase (GOT), glutamate pyruvate transaminase (GPT), alkaline phosphatase (ALP), glutathione peroxidase (GPx), superoxide dismutase (SOD), and glutathione-S-transferase (GST) in many patients ALL in the worldwide corresponding to several factors like family history, sex and blood groups (4). The enzymes of liver functions are correlated biochemically with development of ALL disease therefore one the infection by injury of liver produces clinical forms such as hepatocellular and this case lead to alternate the primary level of GOT, GPT and ALP enzymes (5). Albumin and bilirubin levels will differ than healthy normal status of human because of ALL disease severity. Acute lymphocytic leukemia has various risk factors so this disease requires chemotherapy in order to reduce the problems belonging to this disease (6). So it was focused in the current research on the liver enzymes (GOT, GPT and ALP) levels and also levels of lipid profile (TG, TC, HDL, Non-HDL, LDL and VLDL) in sera of children patients infected by acute lymphocytic leukemia and they are treated chemotherapy in Basrah Governorate-Iraq.

2.Materials and Methods

2.1. Collection of Blood samples

The blood samples were collected by clinical procedure from various children patients infected with acute lymphocytic leukemia (ALL) present in Basrah Teaching Specialist Children Hospital-Basrah Governorate – Iraq. All the patients were treated with chemotherapy where the total number of them was 100 and they have various blood groups (A=30, B=23, AB=10, and O =37). The characteristic clinical features of ALL patients are divided into three groups according to age factor. Also, healthy individual with total number equal to 80 with blood groups are (A=20, B=25, AB=15, and O=20) control groups are recorded represented by age and blood group.

2.2. preparation of clinical samples

The sample volume is two millileters was got from venous blood belonging to children patients infected by acute lymphocytic leukemia also from healthy children. After that the blood samples were treated by clotting and they were centrifuged for 10 minutes by using centrifuge apparatus has speed equal to 4000 rpm then the total sera separated from blood samples were kept at 20°C to assess the biochemical markers whereas the remaining blood was put in test tubes in reached with heparin (7) centrifugation process was carried out for various samples for 8 minutes by using a speed equal to 3000 rpm to separate blood plasma. After that, the red blood cells were washed gently by using sodium chloride (9.0% W/V) and lyasated by using deionized water by using ratio equal to 1:1 V/V (8).

2.3. Assessment of Liver Enzymes and Lipid Profile Levels

The levels of liver enzymes represented by glutamate – oxaloacetate transaminase (GOT), glutamate pyruvate transaminase (GPT), alkalaine phosphatase (ALP) were estimated in all samples of blood belonging to children patients infected by ALL disease by cobas c111 analyzer automatically calculates the analyte activity of each sample. Also, the lipid profile represented by triglycerides (TG), total cholesterol (TC), high density lipoproteins (HDL), non-high-density lipoproteins (Non-HDL), low density lipoproteins (LDL) and very low density lipoproteins (VLDL) were assessed in samples belonging to children patients with ALL disease by measuring The ARCHITECT PLUS instrument c 4000 analyzer automatically calculates the analyte activity of each sample.

2.4. Statistical Analysis

All results obtained from the current work were indicated and expressed as mean \pm standard deviation for all children patients infected by ALL disease. All data of results were recorded and illustrated by statistical method corresponding to programmer analysis for variance univariate at the same time, the significant variation between all ALL patients and healthy individuals groups, was carried out according to statistical programmer of social science (SPSS) version 23. The regression coefficient (r) was calculated to distinguish among total means of ALL patients and control groups. The P value was corresponded for less than 0.05 for the smallest significance limit.

3.Results

Cancer diseases are considered as very risk healthy problems infect human especially children then they lead to occurrence various dangerous changes and physiological and chemical disorders in the biological system of blood. The biochemical markers such as enzymes, lipids, blood proteins, antioxidants vitamins, urea, uric acid, creatine, malondialdehyde, creatinine and trace elements will be affected clinically in presence of cancer diseases such as acute lymphocytic leukemia (ALL). Therefore, the levels of different biochemical parameters increase or decrease according to severity of this disease (9). The results in table (1) show liver enzymes activity represented by (GOT), (GPT), (ALP) in sera of children patients infected by ALL depending on blood group factor.

Table (1): Levels of the enzymes (GPT, GOT and ALP) in children patients with acute lymphocytic leukemia depending on blood group factor

| <i>Blood Group</i> | <i>Groups</i> | <i>GPT(U/L)</i> | <i>GOT(U/L)</i> | <i>ALP(U/L)</i> |
|--------------------|---------------------|----------------------|----------------------|-----------------------|
| A | Control (No.=20) | 27.75 \pm 4.37 | 28.95 \pm 4.86 | 256.20 \pm 38.48 |
| | Patients (No. =30) | 55.43 \pm 29.35*** | 65.97 \pm 31.37*** | 407.53 \pm 88.65*** |
| B | Control (No.= 25) | 27.92 \pm 4.46 | 29.12 \pm 5.24 | 278.08 \pm 45.06 |
| | Patients (No.=23) | 58.39 \pm 28.38*** | 60.22 \pm 28.01*** | 408.43 \pm 73.29*** |
| AB | Control (No. =15) | 26.60 \pm 4.99 | 27.93 \pm 5.43 | 274.73 \pm 45.76 |
| | Patients (No.= 10) | 54.78 \pm 27.90*** | 59.78 \pm 29.87*** | 394.44 \pm 84.73** |
| O | Control (No. = 20) | 28.25 \pm 5.66 | 29.45 \pm 5.92 | 283.10 \pm 49.32 |
| | Patients (No. = 37) | 56.47 \pm 28.75*** | 64.42 \pm 30.27*** | 379.92 \pm 99.81*** |

* P < 0.05, ** P < 0.001, *** P < 0.0001

The results of (GPT) enzyme recorded various levels in ALL patients represented by 55.43 ± 29.35 , 58.39 ± 28.38 , 54.78 ± 27.90 and 56.47 ± 28.75 U/L according to blood group (A, B, O and AB) respectively whereas (GOT) results showed different levels equal to 65.97 ± 31.37 , 60.22 ± 28.01 , 59.78 ± 29.87 and 64.42 ± 30.27 U/L for the same children patients having the same blood group. Concerning (ALP) there were various values of levels represented by 407.53 ± 88.65 , 408.43 ± 73.29 , 394.44 ± 84.73 and 379.92 ± 99.81 U/L were measured in blood samples belonging to ALL patients in the blood groups (A, B, O and AB) respectively. Lipid profile is considered as biochemical parameter for determination of the severity of any cancer disease including acute lymphocytic leukemia according to sex, age, blood group and family history. The levels values belonging to TC, TG, VLDL, LDL, HDL and Non-HDL are illustrated in table (2) depending on blood group factor for ALL patients and healthy individuals.

Table (2): Levels of lipid profile (TC, TG, VLDL, LDL, HDL and Non-HDL) in children patients infected by ALL disease according to blood group factor.

| Blood Group | Groups | TC (mg/dl) | TG (mg/dl) | VLDL (mg/dl) | LDL (mg/dl) | HDL (mg/dl) | Non-HDL (mg/dl) |
|-------------|--------------------|-----------------------------------|----------------------------------|---------------------------------|----------------------------------|---------------------------------|----------------------------------|
| A | Control (No.=20) | 159.01 \pm 9.56 | 127.17 \pm 17.69 | 23.21 \pm 1.70 | 89.00 \pm 8.11 | 56.60 \pm 4.23 | 55.65 \pm 3.34 |
| | Patients (No.=30) | 122.10 \pm 26.28 ^{***} | 96.22 \pm 23.91 ^{***} | 18.69 \pm 5.55 ^{**} | 58.00 \pm 21.49 ^{***} | 39.40 \pm 6.30 ^{***} | 85.23 \pm 17.52 ^{***} |
| B | Control (No.= 25) | 159.65 \pm 8.55 | 123.10 \pm 6.42 | 22.96 \pm 1.87 | 88.36 \pm 9.63 | 57.36 \pm 4.99 | 55.48 \pm 3.49 |
| | Patients (No.=23) | 120.65 \pm 21.32 ^{***} | 93.39 \pm 21.42 ^{***} | 17.17 \pm 5.41 ^{***} | 54.65 \pm 18.18 ^{***} | 39.57 \pm 8.98 ^{***} | 85.13 \pm 17.18 ^{***} |
| AB | Control (No.=15) | 159.32 \pm 8.67 | 122.14 \pm 7.33 | 23.06 \pm 1.61 | 87.60 \pm 5.81 | 56.47 \pm 5.61 | 54.80 \pm 4.17 |
| | Patients (No.= 10) | 108.85 \pm 29.29 ^{***} | 93.85 \pm 15.02 ^{***} | 15.71 \pm 3.09 ^{**} | 51.67 \pm 14.92 ^{***} | 43.00 \pm 5.85 ^{***} | 79.11 \pm 16.56 ^{**} |
| O | Control (No.=20) | 161.27 \pm 7.06 | 122.87 \pm 7.17 | 23.33 \pm 1.48 | 88.35 \pm 9.30 | 56.90 \pm 5.38 | 55.45 \pm 3.99 |
| | Patients (No.= 37) | 113.89 \pm 24.34 ^{***} | 95.08 \pm 25.29 ^{***} | 18.92 \pm 5.76 ^{**} | 54.68 \pm 18.88 ^{***} | 41.82 \pm 8.61 ^{***} | 85.58 \pm 18.46 ^{***} |

* P < 0.05, ** P < 0.001, *** P < 0.0001

From table (2), it was found that the levels of TC were recorded to be in the values equal to 122.10 ± 26.28 , 120.65 ± 21.32 , 108.85 ± 29.29 and 113.89 ± 24.34 mg/dl in children patients having blood group (A, B, O and AB) respectively

whereas TG showed various values of levels were 96.22 ± 23.91 , 93.39 ± 21.42 , 93.85 ± 15.02 and 95.08 ± 25.29 mg/dl in the same blood group belonging to ALL patients. In regard to VLDL the levels which were measured, they gave various values equal to 18.69 ± 5.55 , 17.17 ± 5.41 , 15.71 ± 3.09 and 18.92 ± 5.76 mg/dl depending to A, B, O and AB group while different levels were assessed for LDL represented by 58.00 ± 21.49 , 54.65 ± 18.18 , 51.67 ± 14.92 and 54.68 ± 18.88 mg/dl for the same blood group belonging to children patients infected by acute lymphocytic leukemia. Concerning HDL, it was noticed that the levels values were found to be equal to 39.40 ± 6.30 , 39.57 ± 8.98 , 43.00 ± 5.85 and 41.82 ± 8.61 mg/dl for the same blood group of ALL patients. Non-HDL showed various values of levels were 85.23 ± 17.52 , 85.13 ± 17.18 , 79.11 ± 16.56 and 85.58 ± 18.46 mg/dl in the same blood group belonging to ALL patients.

Table (3) indicates the values levels belonging to GPT, GOT and ALP enzymes in blood serum of children patients with ALL disease and healthy subjects according to age factor.

Table (3): levels of enzymes (GOT, GPT and ALP) in children patients with acute lymphocytic leukemia depending on age factor.

| <i>Age Trimester (Years)</i> | <i>Groups</i> | <i>GOT (U/L)</i> | <i>GPT (U/L)</i> | <i>ALP (U/L)</i> |
|------------------------------|-----------------------|-------------------------|-------------------------|--------------------------|
| First (1-6) | Control (No. =35) | 29.51 ± 4.84 | 28.60 ± 4.57 | 233.89 ± 24.83 |
| | ALL patient (No.=57) | $63.33 \pm 29.33^{***}$ | $54.32 \pm 27.99^{***}$ | $402.35 \pm 78.64^{***}$ |
| Second (7-12) | Control (No. =25) | 28.96 ± 5.99 | 27.96 ± 5.29 | 301.68 ± 29.60 |
| | ALL patient (No.=22) | $57.55 \pm 27.44^{***}$ | $49.82 \pm 25.55^{**}$ | $390.73 \pm 95.21^{***}$ |
| Third (13-17) | Control (No. = 20) | 27.90 ± 5.22 | 25.85 ± 4.27 | 306.55 ± 34.17 |
| | ALL patients (No.=21) | $69.33 \pm 34.77^{***}$ | $66.62 \pm 31.33^{***}$ | $384.62 \pm 111.19^{**}$ |

* $P < 0.05$, ** $P < 0.001$, *** $P < 0.0001$

Various levels belonging to GOT enzyme were assessed with values equal 63.33 ± 29.33 , 57.55 ± 27.44 and 69.33 ± 34.77 U/L in the first, second and third age trimesters respectively in ALL children patients and control groups (healthy individuals) whereas levels GPT were estimated to be in the values 54.32 ± 27.99 , 49.82 ± 25.55 and 66.62 ± 31.33 U/L for the same age trimesters but the levels of ALP enzyme were recorded to be 402.35 ± 78.64 , 390.73 ± 95.21 and $384.62 \pm$

111.19 U/L for the same age trimesters belonging to ALL patients

Table (4) indicates various levels belonging to TC, TG, VLDL, LDL, HDL and Non-HDL were assessed in children patients infected by ALL disease represented by 114.59 ± 24.80 , 93.17 ± 24.26 , 17.44 ± 5.17 , 55.04 ± 19.05 , 41.00 ± 8.06 and 82.32 ± 17.61 in the first age trimesters while the same lipid profile showed different values of levels equal to 118.20 ± 25.32 , 95.41 ± 21.31 , 18.37 ± 5.43 , 59.64 ± 22.77 , 39.86 ± 8.37 and 87.05 ± 18.07 in the second age trimesters. Also, Various levels equal to 120.61 ± 26.75 , 99.17 ± 21.46 , 17.95 ± 5.41 , 49.81 ± 14.24 , 40.67 ± 8.65 and 87.86 ± 17.30 were noticed for the same lipid profile in the third age trimester.

Table (4): Levels of lipid profile (TC, TG, VLDL, LDL, HDL and Non-HDL) in children patients with acute lymphocytic leukemia according to age factor.

| Age Trimester (Years) | Groups | TC (mg/dl) | TG (mg/dl) | VLDL (mg/dl) | LDL (mg/dl) | HDL (mg/dl) | Non-HDL (mg/dl) |
|-----------------------|-----------------------|--------------------------|-------------------------|------------------------|-------------------------|------------------------|-------------------------|
| First (1-6) | Control (No. =35) | 158.79 ± 9.16 | 125.86 ± 13.67 | 22.92 ± 1.71 | 89.23 ± 8.02 | 56.40 ± 4.36 | 55.54 ± 2.99 |
| | ALL patients (No.=57) | $114.59 \pm 24.80^{***}$ | $93.17 \pm 24.26^{***}$ | $17.44 \pm 5.17^{***}$ | $55.04 \pm 19.05^{***}$ | $41.00 \pm 8.06^{***}$ | $82.32 \pm 17.61^{***}$ |
| Second (7-12) | Control (No. =25) | 159.98 ± 6.83 | 121.03 ± 7.22 | 23.00 ± 1.70 | 86.40 ± 8.91 | 56.96 ± 5.18 | 55.20 ± 4.19 |
| | ALL patients (No.=22) | $118.20 \pm 25.32^{***}$ | $95.41 \pm 21.31^{***}$ | $18.37 \pm 5.43^{***}$ | $59.64 \pm 22.77^{***}$ | $39.86 \pm 8.37^{***}$ | $87.05 \pm 18.07^{***}$ |
| Third (13-17) | Control (No. = 20) | 161.48 ± 8.84 | 123.25 ± 7.42 | 23.69 ± 1.48 | 89.35 ± 8.51 | 57.65 ± 5.76 | 55.35 ± 4.17 |
| | ALL patients (No.=21) | $120.61 \pm 26.75^{***}$ | $99.17 \pm 21.46^{**}$ | $17.95 \pm 5.41^{***}$ | $49.81 \pm 14.24^{***}$ | $40.67 \pm 8.65^{***}$ | $87.86 \pm 17.30^{***}$ |

* $P < 0.05$, ** $P < 0.001$, *** $P < 0.0001$

The children patients infected by acute lymphocytic leukemia diseases were suffering from an increase in Non-HDL but decrease in TC, TG, VLDL, LDL and HDL.

4. Discussion

The infection by acute lymphocytic leukemia (ALL) disease leads to happen different biological and biochemical problems in human especially children which have weak immunity and deficiency in the enzymatic and non-enzymatic antioxidants. Also, the effects of age and blood groups are important to follow the severity of this dangerous disease. The biochemical parameters which represented by liver enzymes (GPT, GOT and ALP) and lipid profile such as (TG), (TC), (HDL), (Non-HDL), (LDL) and (VLDL) are very necessary chemical markers for investigation and evaluation of progress in ALL disease (10,11). The factors of age and blood groups are correlated biochemically with liver enzymes and lipid profile where various studies were established in the many countries in the world belonging to children with different age and blood groups infected by acute lymphocytic leukemia. From these pre- studies, it was found that age and blood groups had a biochemical correlation with the increase or decrease of levels of liver enzymes and lipid profile (12). The enzymes (GOT, GPT and ALP) recorded highly significant difference ($P < 0.0001$) in their levels in blood serum of children patients with ALL disease compared with healthy subjects depending on blood group factor especially in A and B group and also a high significant increasing was noticed in the levels of GOT enzyme. The liver enzymes of the current study showed a highly significant increasing ($P < 0.0001$) in their levels values especially for GOT and GPT when they compared with the same values of these enzymes which were recorded in healthy children (control group) according to age factor especially in the first and third age trimesters. The biochemical explanation of these statements are illustrated by depletion process of GPT, GOT and ALP enzymes which were assessed in pre - time compared with other kinds of cancer that represent the abundance of these enzymes will decreases the probability of infection by ALL disease (13). Several sings belonging to ALL symptoms include infection by neutropenia, bruising, fever and fatigue are correlated with acute lymphocytic leukemia therefore study of levels of liver enzymes such as GPT, GOT and ALP is very important to know the severity of this dangerous disease (14). There is a medicinal and biochemical relationship between lipid profile with the occurrence of acute lymphocytic leukemia and this case can be explained by existence of several disorders in blood components which lead to presence of the blood in abnormal status. Many researchers established clinical studies on the classes of lipid such as triglycerides, total cholesterol, phospholipids, glycolipids and lipoproteins in blood serum of patients especially children infected by ALL disease (15,16). Lipid profile showed a high significant decrease ($P < 0.0001$) in their levels except Non-HDL showed a highly significant increase ($P < 0.0001$) in

their levels compared with healthy children according to blood group factor especially in the (A, B, AB and O) group. Concerning age factor of ALL children patients a highly significant difference ($P < 0.0001$) in the levels of TG, TC, HDL, Non-HDL, LDL and VLDL when they compared with control group especially in the second and third age trimesters. Various studies indicated the biochemical role of lipid profile in presence of acute lymphocytic leukemia and the alteration in the levels of TG, TC, HDL, Non-HDL, LDL and VLDL were explained statistically. So, the assessment of these biochemical parameters can be caused by malignant cells reliance on abundance or deficiency in these classes of lipid (17,18).

Conclusions

The liver enzymes (GPT, GOT and ALP) showed clear increase in their levels in sera of ALL patients compared with healthy children according to age and blood group factors. Also, the lipid profile (TC, TG, VLDL, LDL, HDL and Non-HDL) recorded a high significant difference in regard to their levels in acute lymphocytic leukemia in patients children compared with control groups depending on alteration of age and blood group. Therefore, clinical biochemical correlation between the both (liver enzymes and lipid profile) and age belonging to ALL patients and their blood groups. Finally liver enzymes and lipid profile can be carried out as useful prognostic biochemical markers in ALL disease.

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