

## **Evaluation of G-ST, GOT and GPT activities in Sera of leukemic patients before and after treatment.**

**تقدير فعالية أنزيمات الـ G-ST , GOT , والـ GPT في أمصال مرضى إبيضاض الدم قبل وبعد العلاج.**

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### **Abstract**

The activities of G-ST, GOT and GPT were measured in 50 patients with Chronic Myeloid Leukemia, CML of males and females before and after treatment with Glevic and compared to 50 healthy controls were included in this study.

Serum G-ST activity was found in leukemic patients (males and females) before and after treatment were significantly higher than control groups. Serum G-ST activity before treatment was significantly higher than that of after treatment.

Serum (GOT and GPT) activities in males and females before treatment were found significantly higher than that in control groups, but has no significant difference as compared to that found in control groups after treatment.

### **الخلاصة**

تم قياس مستويات نشاط انزيمات الـ G-ST و GOT و الـ GPT في امصال دم 50 مصاباً بمرض ابيضاض الدم النقائي المزمن من الذكور والاناث قبل وبعد العلاج بمركز الـ (Glevic) وتمت مقارنتهم مع 50 شخصاً طبيعياً من الذكور والاناث بأعمار مقاربة لأعمار هؤلاء المصابين.

وجد ان النشاط الانزيمي للـ G-ST لكلا الجنسين قبل وبعد العلاج له قيمة معنوية احصائية اعلى من المجموعة الضابطة وان النشاط الانزيمي للـ G-ST قبل العلاج كان ذو قيمة معنوية اعلى من القيمة المعنوية بعد العلاج.

كما وجد ان النشاط الانزيمي للـ GOT و الـ GPT لكلا الجنسين قبل العلاج لهما قيم معنوية احصائية اعلى من المجموعة الضابطة بينما ليست لهما أي قيمة معنوية بعد العلاج.

### **Introduction**

The transaminases are enzymes involved in the transfer of an amino group from  $\alpha$ -amino acids to 2-keto acids, they need pyridoxal -5'- phosphate as a cofactor for optimal activity. They are widely distributed in human body<sup>(1),(2)</sup>. Elevation of liver transaminases reflect damage of the liver plasma membrane<sup>(3)</sup>.

Transaminases are released from the liver when hepatocytes are injured. Measurement of these enzyme activities in serum is one of the standard laboratory test for liver damage caused by a variety of conditions<sup>(4),(5)</sup>.

Glutathione -S- transferase (G-ST, EC. 2.5.1.18) is present in high amount in liver and in lower amount in other tissues. A variety of G-ST are present in human tissues. The exhibit different substrates specificities and can be separated by electrophoretic and other techniques. If the

potentially toxic xenobiotics were not conjugated with Glutathione, GSH, they would be free to combine covalently with DNA, RNA or cell protein and thus lead to serious cell damage<sup>(6)</sup>.

G-ST play an important role in the detoxification of both endogenous and exogenous compound by catalyzing the conjugation of reduced GSH with a wide range of electrophils to form thioester<sup>(7),(8)</sup>.

Glutamate oxaloacetate Transaminase (GOT, EC.2.6.1.1) is present in high concentration in cell of cardiac and skeletal muscles, liver, kidney and erythrocytes. Damage to any of these tissues may increase GOT level<sup>(9),(10)</sup>.

#### **Causes of raised GOT activities:**

Artefactual, during the neonatal period, circulatory failure with shock and hypoxia, myocardial infarction, acute viral or toxic hepatitis, cirrhosis, infectious mononucleosis (due to liver involvement), cholestatic jaundice, malignant infiltration of the liver, skeletal muscle disease, after trauma or surgery (especially after cardiac surgery), sever haemolytic episodes<sup>(1)</sup>.

Glutamat pyruvate Transaminase (GPT, EC.2.6.1.2) is present in high concentration in liver and to a lesser extent in skeletal muscle kidney and heart. Measurement of GPT activity in serum used an indicatory of hepatocellular damage<sup>(11),(12)</sup>.

#### **Causes of raised GPT activities:**

Circulatory failure with shock and hypoxia, acute viral or toxic hepatitis, cirrhosis, infectious mononucleosis, cholestatic jaundice, surgery or extensive trauma and skeletal muscle disease (much less affected than GOT), congestion secondary to congestive cardiac failure<sup>(1),(13)</sup>.

Leukemia arise when a differentiating hematopoietic cell does not complete its development program but remains in an immature, proliferative state. Leukemia have been found in every hematopoietic lineage. Leukemia is a group of malignant disorder of the haemopoietic tissue characterized by accumulation of abnormal white cells in bone marrow. These abnormal cell may cause bone marrow failure, a raised circulating white cell count and infiltrate other organs. Thus common but not essential features include abnormal white cell in the peripheral blood, a raised total white cells, evidnce of bone marrow failure live, anemia, neutropenia, thrombocytopenia, and involvement of other organs (e.g. liver, spleen, brain, skin, lymph nods)<sup>(14-16)</sup>.

A drug called imatinib (Gleevec or Glivec), has been designed specifically to block abnormal protein produced by BCR-ABL gene and can reduce the number of leukemia cells much greater extent than any drugs<sup>(14)</sup>.

The aim of this study include determination of serum G-ST, GOT and GPT activities in patients with leukemia, CML before and after the first course of treatment with Glevic and to compare with that found in control group.

## **Material and Methods**

### **Blood Samples:**

(5ml.) from each of 50 leukemic patients (25 males and 25 females) with age ranged between (20-60) years before and after treatment, and 50 house-hold relatives were taken as control (25 male and 25 females) with age ranged between (20-60) years, were transferred into plain tube without anticoagulant and left at room temperature for 20 minutes for clotting, and then centrifuged at 3000 rpm for 10 minutes, serum was then taken and used for measuring G-ST, GOT and GPT activities.

Glevic had been administreted orally at a dose of 400 mg daily through out the course of chemotherapy treatment (one month).

**Estimation of Serum G-ST activity:**

G-ST activity was determined according to the spectrophotometric method with some modification, using kit supplied by (Bio labo/France)<sup>(10,17)</sup>.

**Estimation of Serum GOT activity:**

GOT activity was measured by monitoring the concentration of oxaloacetate hydrazone formed with 2,4-Dinitrophenyl hydrazine, using kit supplied by (Bio labo/France)<sup>(18)</sup>.

**Estimation of Serum GPT activity:**

GPT activity was measured by monitoring the concentration of pyruvate hydrazone formed with 2,4-Dinitrophenyl hydrazine, using kit supplied by (Bio labo/France)<sup>(18)</sup>.

**Results and Discussion**

**Serum G-ST Activity**

Table(1) and Fig.(1) represent the results of serum G-ST activity in males and females before treatment was significantly higher than control groups, serum G-ST activity in males and females after treatment was significantly higher than control groups. These data showed a decrease in G-ST activities in males and females groups after treatment.

G-ST catalyzes conjugation reaction of a wide variety of electrophiles with glutathione, since most of the chemical carcinogens are electrophiles, G-ST take on considerable importance in carcinogen inactivation<sup>(19,20)</sup>.

G-ST elevated in blood patients with chronic liver disease and all types of leukemia cause of the peroxidative damage of cells<sup>(21)</sup>. It was confirmed that detoxifying enzyme G-ST play an important role in glutathione dependent protection against lipid peroxidation<sup>(22)</sup>. These results are in agreement with other studies done on G-ST activity in patients with leukemia<sup>(23,24)</sup>.

**Serum GOT Activity**

Table(2) and Fig.(2) represent serum GOT activity in patients of males and females before and after treatment and control. It was found that serum GOT activity in males and females patients before treatment was significantly higher than of control groups.

Serum GOT activity in males and females patients after treatment was non significantly difference than of control groups. Serum GOT activity in males was significantly higher than GOT activity of females before treatment.

These results are in agreement with other studies done on serum GOT activity in patient with leukemia and lymphoma<sup>(25),(26)</sup>.

GOT elevation are common during chemotherapy in patients with leukemia, lymphoma, drugs induced GOT elevation are not associated absence of other liver function abnormal, and can be hepatic infiltration<sup>(27)</sup>.

In infiltrative disorder in which there is damage to both mitochondrial and cytoplasmic membrane, there is a proportionally greater elevation in GOT activity<sup>(28)</sup>.

GOT exist as two isoenzyme fractions located in the cell cytoplasm and mitochondria. The interacellular concentration of GOT may be 70 times higher than the extracellular concentration. The cytoplasmic isoenzyme is the predominant form occurring in serum<sup>(29)</sup>.

**Serum GPT Activity**

Table(3) and Fig.(3) represent that serum GPT activity in males and females patients before treatment was significantly higher than of control groups.

Serum GPT activity in females was statistically significant higher than serum activity of males before treatment. Serum GPT activity in males and females after treatment has non significantly difference as compared to the control groups. These results are in agreement with other studies done on serum GPT activity in patients with several types of leukemia<sup>(25)(26)</sup>.

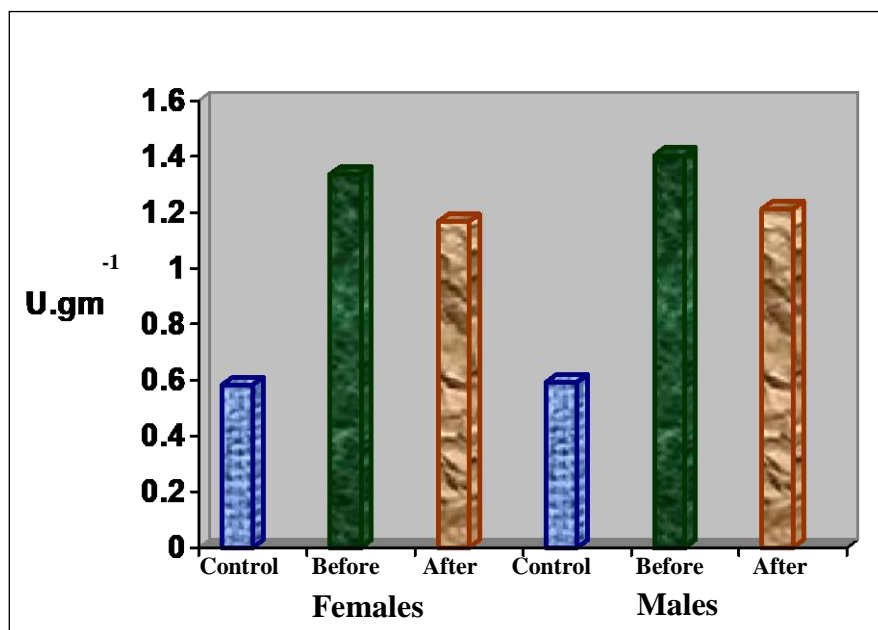
Clinical application of GPT assays are confined mainly to evaluation of hepatic disorders, leukemia and lymphoma. Higher elevations are found in hepatocellular disorder than in extrahepatic or intrahepatic obstructive disorder. GPT elevations are frequently higher than those of GOT and tend to remain elevated longer as result of the longer half-life of GPT in serum (16 hours and 24 hours) respectively<sup>(30)</sup>.

GPT levels have historically been compared with levels of GOT to help determine the source of an elevated GOT level and to detect liver involvement concurrent with myocardial injury<sup>(31)</sup>.

Note that GPT is more specific for hepatic disease than GOT<sup>(32)</sup>.

**Table(1): serum G-ST activity for patients before and after treatment with control groups.**

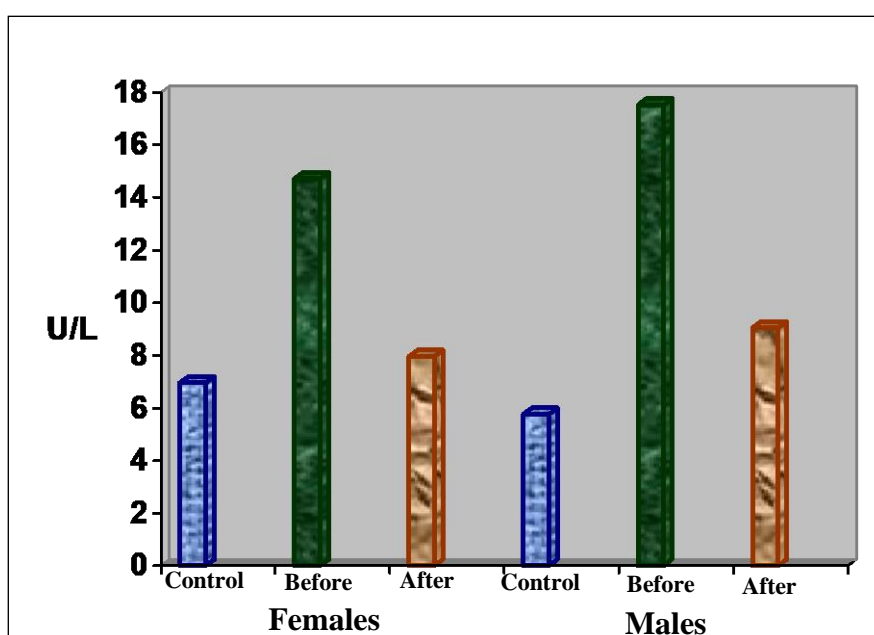
Groups		Control	G-ST activity before treatment U.gm <sup>-1</sup>	G-ST activity after treatment U.gm <sup>-1</sup>
Females	Number	25	25	25
	Mean ±SD	0.582 ± 0.038	1.336 ± 0.067	1.166 ± 0.136
Males	Number	25	25	25
	Mean ±SD	0.592 ± 0.071	1.404 ± 0.165	1.212 ± 0.114



**Fig.(1): G-ST activity for patients before and after treatment with control.**

**Table(2): serum GOT activity for patients before and after treatment with control groups.**

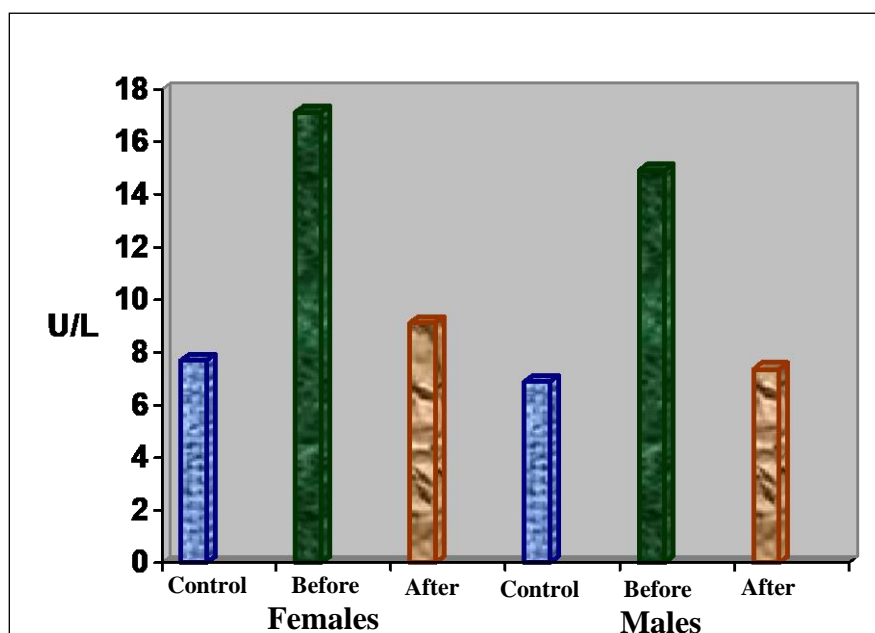
Groups		Control	GOT activity before treatment U/L	GOT activity after treatment U/L
Females	Number	25	25	25
	Mean $\pm$ SD	6.960 $\pm$ 2.850	14.720 $\pm$ 8.448	7.960 $\pm$ 5.388
Males	Number	25	25	25
	Mean $\pm$ SD	5.760 $\pm$ 3.766	17.520 $\pm$ 6.758	9.040 $\pm$ 3.88



**Fig.(2): GOT activity for patients before and after treatment with control.**

**Table(3): serum GPT activity for patients before and after treatment with control groups.**

Groups		Control	GOT activity before treatment U/L	GOT activity after treatment U/L
Females	Number	25	25	25
	Mean $\pm$ SD	7.680 $\pm$ 3.508	17.120 $\pm$ 7.902	9.120 $\pm$ 6.495
Males	Number	25	25	25
	Mean $\pm$ SD	6.880 $\pm$ 3.597	14.920 $\pm$ 7.554	7.360 $\pm$ 4.319



**Fig.(3): GPT activity for patients before and after treatment with control.**

## Conclusion

Serum G-ST activity was found in leukemia, CML. Patients (males and females) before and after chemotherapy treatment were found significantly higher than control groups. G-ST activity before treatment was significantly higher than after treatment.

Serum GOT and GPT activities in leukemia, CML patients (males and females) before treatment were found significantly higher than control groups, but no significant difference than control groups after treatment.

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