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Transaminases Enzymes and Renal Function in Leukemia

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Abstract:-

Atotal of 67 patients with acute myeloblastic leukemia (AML) , acute Iymphoblastic leukemia (ALL) ,chronic myeloblastic leukemia (CML) were included in this study.

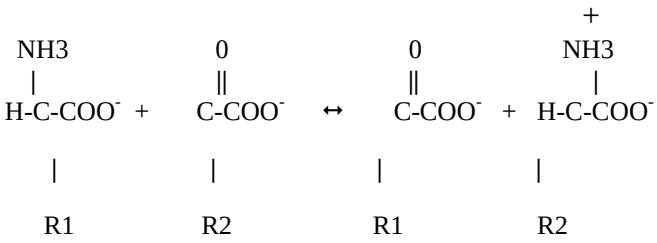
conducted during the period form 16th of February to 19th of October 2004 . 34 patients with AML , 20 patients with ALL and 7 patients with CML , 6 patients were dead during the first course of chemotherapy treatment. 67 a house hold relatives were taken as a control preferred age and sex match. sampling was conducting in (national center of hematology - Baghdad). Samples were collected before and after the first course of chemotherapy treatment which was about 6 weeks . the major site of amino acid degradation in mammals is the liver .So the following tests were performed in serum (GOT,GPT,and Caeruloplasmin) activities and (urea , creatinine and uric acid) concentration.

Serum GOT , GPT activities were estimated in (AML , CML) before chemotherapy treatment and they were found insignificantly higher than control groups , in all patients after chemotherapy treatment were found significantly higher than control groups . Serum uric acid concentrations in (AML , ALL, CML) before / after chemotherapy treatment were significantly higher than control groups . serum uric acid concentration in (AML , ALL, CML) before chemotherapy treatment were significantly higher than after treatment. serum urea and creatinine concentrations in (AML , ALL, CML)before / after chemotherapy treatment were higher than control groups . serum urea and creatinine concentrations in (AML , ALL, CML) before chemotherapy treatment were lower than after' treatment.

There is a different change in the level of trace elements in serum of leukemia patients before and after chemotherapy treatment as compared with control . further investigation needed to estimate the accurate cases of these changes.

Introduction :-

Transamination is the term given to the process in which the amino group is transferred from an amino acid to an a-keto acid. As result a different amino acid and a-keto acid are formed. This process is catalyzed by enzymes referred to transaminase or aminotransferase.

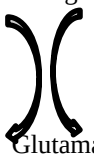


The major site of amino acid degradation in mammals is the jver. The a - amino group of many amino acids is transferred to a -ketoglutarate to form glutamate , which is then oxidatively deaminated to yield NH4 . This reaction is catalyzed by glutamate dehydrogcnase[I].

$(CH2)2 + NAD + H_2O \leftrightarrow NH4 + (CH2)2 + NADH + H$
| or NADPH | or NADPH
COO^- COO^-
Glutamate a – Ketoglutarate

The sum of the reactions catalyzed by aminotransferases and glutamate dehydrogenase.

O
+ ||
a-Amino acid a – Ketoglutarate $NADH+NH4 \rightarrow NH2\text{-}C\text{-}NH2$




a-Keto acid Glutamate NAD+H20 Urca

In terrestrial vertebrates, NH4 is converted into urea , which is excreted as feaces.
Transaminase enzymes have a role in metabolism of amino acid in living cells, two clinically important examples are GOT and GPT. [2-3]
It's called also aspartate aminotransferase (AST), is one of the most important of transaminases enzymes, catalyzes the transfer of the amino group of aspartate to a ketoglutarate [4].

COOH COOH COOH COOH
| | | |
CH-NH2 C=O GOT CH-NH2 C=O
| + | ↔ | + |
CH2 (CH2)2 (CH2)2 CH2
| | | |
COOH COOH COOH COOH
a- L-
L-Aspartic Ketoglutaric Glutaric Oxalo acetic
Acid acid acid acid

GOT activity is widely distributed in human tissues: heart, liver, skeletal musele and kidney. The optimum conditions of maximum enzyme activity are pH=7.4 and temp.=37C^o.The enzyme stability 3 days in 25C,I week in 5Coand 1 month in -25C^o. The clinical usefulness of the enzyme is largely restricted to the diagnosis of heart and liver diseases. Large amount of GOT may be released into the blood. Very high levels are observed in acute liver disease while lesser elevation is seen in chronic liver disease [1,2,5] . It is also called alanine amino transferase (ALT) which is prevalent in mammalian tissue catalyzes the transfer of the amino group of alanine to a –ketoglutarate.

COOH COOH
| |
H-C-
COOH C=O COOH NH2
| | GPT | |
H-C-
NH2 + (CH2)2 ↔ C=O (CH2)2
| | | |
CH3 COOH CH3 COOH
L- a-
Alanine Ketoglutaric Pyruvic L-Glutamic
acid acid acid

GPT found in a highest concentration in livers in spite of its active occurrence in skeletal museles, heart and kidneys. The GPT activity in tissues is generally less than GOT.

Significant elevation of S.GOT occurs in sever acute hepatitis where the enzyme is released in to the circulation. GPT level found to increased in the following diseases :- Infection hepatitis ,liver cirrhosis and biliary cirrhosis, Ostructivejaundice, liver cancer [4,5,6,7].

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.

In terrestrial vertebrates, urea is synthesized through the urea cycle, High levels of NH4 are toxic to humans. The synthesis of urea in the liver is the mqjor route removal of NH4.

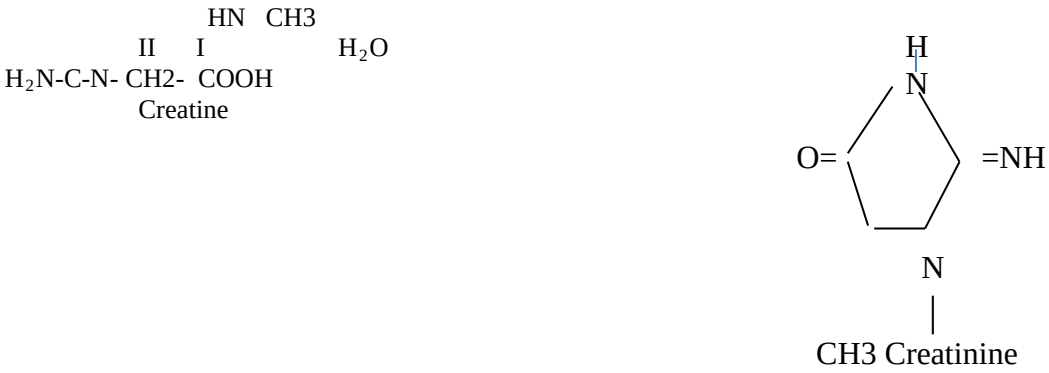
A deficiency of any enzymes of the urea cycle results in coma and death shortly after birth Partial deficiencies of these enzymes cause mental retardation, lethargy, and episodic vomiting.

A low protein diet leads to lowering of the ammonium level in the blood. A high concentration of ammonium ions shifts the equilibrium of the reaction catalyzed by glutamate dehydrogenase. [5] towards the formation of glutamate. NH4 then reacts with glutamate to form glutamine. Elevated levels of glutamine are found in the cerebrospinal fluid of patients with hyperammonemia and may lead directly to brain damage [8].

The kidneys excrete urea. Urea is free to pass through all membranes of the body and equally distributed in the body water. The concentration of urea in the body water depends upon the rate of production by the live I' and the rate of removal by the kidneys.

In most patients the rate of production is a reflection of the protein intake. In sever liver disease, the ability of liver cells to form urea is impaired, ammonia accumulate and urea level fall. The rate of removal depends upon urea concentration . In the plasma and capacity of the kidney to remove urea from the plasma (kidney function) .In most clinical situation, changes in urea levels are more dependent upon kidney function then upon liver function. The normal value is (15 - 45) mg /dI [1,4,7].

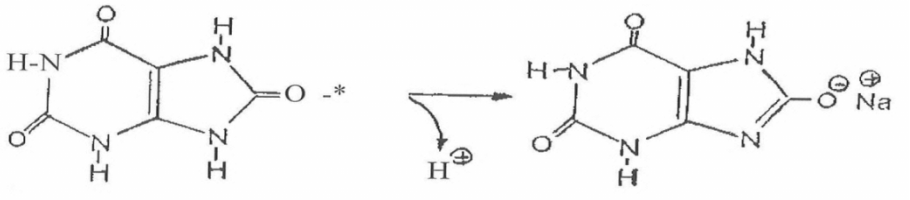
Creatinine is a catabolic end product ,an anhydride of creatine (or phosphocreatinine) produced by loss of water (or phosphoric acid) from the molecule in an irreversible reaction. Creatinine is excreted from the body via the urine [7].



These reactions occur in kidney and liver .the norma] value of S. creatinine (0.1-1.4) mg/dl depending on age ,sex and muscle mass [3,7,8].

Nucleic acids contain bases of two different types, pyrimidines and purins. The catabolism of the purines (adenine and guanine) product uric acid by xanthine oxidase.

Increased level of s.uric acid is found in acute and chronic nephritis ,urinary obstruction, high purine diet, diabetic keto acidosis, malignant tumors especial]y with extensive neucrosis. Decreased level of s. uric acid is found in proximal renal damage where urate reabsorption will reduced, xanthineoxidase deficiency ,salicylate and cinchophen therapy. Uric acid is present in plasma as sodium urate [1,7].



Urate is formed by three ways. Denovo synthesis, metabolism of endogenous DNA,RNA and other purine containing molecules such as A TP, breakdown of dietary nucleic acids. Uric acid seems to be a major protective antioxidant against NCh and HOCI. The normal values of s.uric acid varies from adults to children: men (2.7-7.5)mg/dl, women: (2.5-6) mg/dl, children: (2.5) mg/dl[1.8].

Aims of this study incIude :-

Evaluation of S.GOT , S.GPT , S. Urea , S. Creatinine and S.Uric acid in patients with ALL, AML and CML before and after the first course of chemotherapy and with the controls .

Subjects and methods :-

Patients:-

Sampling was conducted in (National center of hematology -Baghdad during the period from 16th of February to 19th of October 2004.

Sixty seven blood cancer patients 36 males and 31 females were included in this study and classified as follows:-

(7) Patients with CM L (4 males and 3 females) with age range (27-59) years.
(20) Patients with ALL (12 males and 8 females) with age range (6-55) years.
(34)Patients with AML (14 males and 20 females) with age range (14-56).
(6)Patients who were dead before end of the first course of chemotherapy (6 males) with age range(6-55) years.(5) Patients AML and one was ALL.

1. All patients were newly diagnosed.
2. The samples were collected before any chemotherapy treatment, and after the first course of chemotherapy, it was about 6 weeks.
3. Sixty seven a house-hold relatives were taken as a control preferred age and sex match and were examined their WBC, RBC, platelete.
4. Chemotherapy treatment for CML was (hydroxyurea, alphainterferon and glivec), AML (daunorubicin or doxorubicin and T' cytosine arabinoside), ALL (daunorubicin or doxorubicin and vincristine).

Venous blood samples (6 ml) from each patient before and after icmotherapy and control were transferred into plain tube without iticoagulant. The blood was left to clot and serum was obtained by centrifugation at 3000 rpm for 10 min by centrifuge then serum were removed , the serum was estimated of (GOT , GPT , U , Cr, and U.A).

Assay:-

a-oxaloglutarate + L-aspartate GOT » L-glutamate + oxaloacetate GOT was measured by monitoring the concentration of oxaloacetata hydrazine formed with 2,4- dinitropheny lhydrazine.

Rl	GOT Buffer	phosphate buffer L-aspartate a -oxaloglutarate	L00mmol/L PH7.4
R2		2,4dinitrophenyl hydrazine	2mmol/L
R3		Sodium hydroxide	4 mol/L
R4	Standard	pyruvate	2 mmoI/L

Pipette into test tubes:-

		Sample
Serum	Sample blank	0.1 ml
GOT Buffer	0.5ml	0.5ml

Mixed ,and was incubated for exactly 30 min at 37 C^o .

2,4 dinitropheny lhydrazine	0.5ml	0.5ml
Sample	0.1 ml	

Mixed ,was allowed to stand for exactly 20 min .at (20- 25) C^o .

Sodium hydroxide	0.5ml	0.5ml

Mixed ,then read the absorbance of the sample A sample against the sample blank after 5 min. at 546 nm.
The activity of GOT in the serum was obtained from the table .

Absorbance	U/L	Absorbance	U/L
0.02	7	0.100	36
0.030	10	0.110	41
0.040	13	0.120	47
0.050	16	0.130	52
0.060	19	0.140	59
0.070	23	0.150	67
0.080	27	0.160	76
0.090	31	0.117	89

a-oxaloglutarate + L-alanine GOT » L-glutamate + pyruvate

GPT was measured by monitoring the concentration of pyruvate hydrazine formed with 2,4- dinitrophenylh ydrazine.

Rl	GOT Buffer	phosphate buffer L-aspartate a -oxaloglutarate	L00mmol/L,PH7.4 200 mmol/L 2 mmol/L
R2		2,4dinitrophenyl hydrazine	2mmol/L
R3		Sodium hydroxide	4 mol/L
R4	Standard	pyruvate	2 mmoI/L

Pipette into test tubes:-

		Sample
Serum	Sample blank	0.1 ml
GOT Buffer	0.5ml	0.5ml

Mixed ,and was incubated for exactly 30 min at 37 C^o .

2,4 dinitropheny lhydrazine	0.5ml	0.5ml
Sample	0.1 ml	

Mixed ,was allowed to stand for exactly 20 min .at (20- 25) C^o .

Sodium hydroxide	0.5ml	0.5ml

Mixed ,then read the absorbance of the sample (A sample) against the sample blank after 5 min. at 546.

The activity of GPT in the serum was obtained from the table [9]:-
Absorbance U / L Absorbance U / L

Absorbance	U/L	Absorbance	U/L
0.025	4	0.275	48
0.050	8	0.300	52
0.075	12	0.325	57
0.0100	17	0.350	62
0.0125	21	0.375	67
0.0150	25	0.400	72
0.0175	29	0.425	77

Enzymatic determination of urea according to the following reaction:
Urea+ H_2O urease » 2NH3 + CO2

In an alkaline medium, the ammonium ions react with the salicylate and hypochlorite to from a green colored indophenol (2.2 diearboxyl indophenol).

Rl	standard	urea	8.33mmoJ/L or 0.52/L
R2	enzyme	urease	>5.000 U/L
R3	color	phosphate buffer PH 8 sodium salieylate sodium nitroprusside EDTA	40 mmol/L 52 mmol/L 2.83 mmol/L 1 mmol/L
R4 alkaline reagent		sodium carbonate sodium hypochlorite	83 mmol/L 3.75 mmol/L

R2 was added to a bottle of R3 (working solution).

	Blank	Standard	Sample
Standard		10 u/L	
- Sample			10 u/L
R2+R3	1ml	1ml	1ml

Shaked ,then was ineubated for at least 5 min. at 37 C^o or 10min. at (20-25) C^o ,the absorbance was read at 580 nm [10.11].

Serum Cr. (mmolIL) = $\frac{\text{A-samnle}}{\text{A -standard}}$

A sample :- Absorbance of sample

Astandard' Absorbance of standard

Kinetic determination without deproteinization ,the complex fonned by creatine and picric acid in an alkaline medium was measured .The speed of absorbanee change was proportional to the creatinine concentration.

Rl	picric aeid solution	pierie aeid	35 mmol/L
R2	NaOH solution	sodium hydroxide	0.32 mol/L
R3	standard	ereatinine	>mg/dL(l76.8 umol/L)

R I was diluted with R2 (working solution):-

	standard	sample
Working solution	1000 u L	1000 u L
R3	100 u L	—
sample	—	100 u L

Mixed, then poured immediately into cuvette. After exactIy 20 seconds.
Read Al of sample and standard at 492 nm . Exactly 80 seconds after the first reading ,was read A2 of sample and standard. [12,13].

$$\text{Creatinine in serum (umol/L)} = \frac{(A2\text{-}A1)\text{sample}}{(A2\text{-}A1)\text{standard}}$$

Uric acid was oxidized by uricase to allantoine and hydrogen peroxide ,according to the following equation-:

$$\text{Uric acid} + O_2 + H_2O \xrightarrow{\text{uricas}} \text{Allantonic} + Co_2 + H_2O_2$$

$$2H_2O_2 + \text{4- amimophenazone} + \text{2,4dichloro-phenol-sulfonate} \xrightarrow{\text{peroxidase}} 4H_2O + \text{quinoneimine}$$

Reagent (1) Buffersolution
a)Phosphate buffer Ph 7.4
b)2,4-DHBs 50mmol/L
Reagent (2) 4 mmol/L
Enzymes 70U/L
a)Uricase 660 U/L
b) Peroxidase I mmol/L
c) 4-aminophenazone
Reagent (3)
Standared
Uric acid 357umol/L

R(2) was dissolved with 30 ml of buffer R(I).That is called working reagent ,this working reagent is stable 3 weeks at 2-8 C^o and for 7 days at 20-25 C^o.

Reagent	Blank	Standard	Test
Working reagent	lml	Iml	Iml
Standard	—	20 µL	
Serum	—	—	30 µL

Mixed, then was incubated 5 min at 37 C^o .The colour was stabled for 30 min. The absorbance was recorded at 510 nm against blank. [14,15].

$$\text{Uricacid} = \frac{\text{Asample}}{\text{A standard}} \times N$$

N = 357 µmol/L
N = 60 mg/dL
N = 6 mg/ dL

Statistical Method's:-

The statistical package for social sciences (SPSS) program on the computer was used, results were expressed as mean ± SD.

Pearson correlation coefficient (r) was used to test the relation between two parameters, [16].

Results and Discussion :-

Table(I) and figure (I) showed the serum GOT activity of patients before and after treatment and control. It was found that serum GOT activity in (AML, response and resistant, CML) before treatment was statistically insignificant higher than of control graups (P>0.05).

Serum GOT activity in (ALL, response, resistant and patients who dead) before treatment was statistically significant higher than of contra I groups (PO.05).

Serum GOT activity in all types of leukemic patients (excepted CML) after treatment was statistically significant higher than of control groups (P<0.05), CML was statistically insignificant higher than of control graups (P>0.05).

Serum GOT activity (AML, response, resistant, CML)in patients before treatment was statistically significant lower than serum GOT activity of patients after treatment (P<0.05), serum GOT activity (ALL, response, resistant) in patients before treatment was statistically significant higher than serum GOT activity of patients after treatment (P<0.05).

Serum GOT activity of CML was lower than serum GOT activity of AML and ALL before and after treatment.

Serum GOT activity of patients who response to treatment lower than serum GOT activity of patients who resist to treatment and serum GOT activity of patients who dead was higher than serum GOT activity of AML and CML.

GOT elevations are common during chemotherapy in patients with leukemia / lymphoma. Drug induced GOT elevations are absence of other liver function abnormal, and can be hepatic infiltration [17]. These results are in agreement with other studies done on serum GOT activity in patients with ALL, AML and Iymphoma [18, I 9,20].

Liver function tests and B. U and creatinine determinations are necessary prior to the initiation of therapy because many chemotherapeutic agents may adversely affect either renal function or hepatic function. Additionally, some agents, such as methotrexate, may be contraindicated in individuals with hepatic dysfunction [21].

Table (1): -Mean of serum GOT activity U/L, standard deviation (SD), T-Test, P value for patients before and after treatment and control.

GOT activity ULL Mean ± SD

Type	No.	T-Test P value					
		C	B	A	B-C	B-A	A-C
AML	34	10.91±5.11	14.32±8.20	21.91±4.82	2. 106,0.053	4.74,0.001 *	4.07,0.001 *
Response	8	10.25±5.44	12.43±4.26	16.00±4.14	1.814,0.113	5.45,0.001	2.87,0.024
Resistant	21	10.10±4.92	14.33±7.44	21.50±15.61	2.141,0.055	2.1,0.005*	3.28,0.004*
ALL	20	12.50±3.76	34.55±14.53	1.95±12.27	6.55,0.001'	4.2,0.001 *	3.22,0.004
Response	12	12.50±3.92	34.00±16.26	19.00±1.91	4.40,0.027*	2.5,0.027*	2.30,0.042 *
Resistant	7	13.29±3.30	35.14±13.46	23.42±15.79	277,0.005*	3.493,0.013*	3.5,0.013*
CML	7	11.00±5.16	12.00±4.93	15.43±7.02	1.137,0.299	-3.154,0.02*	2.21,0.068
Death	6	11.30±5.61	25.67±12.94		95,0.0108*		

Mean of GOT activity U / L

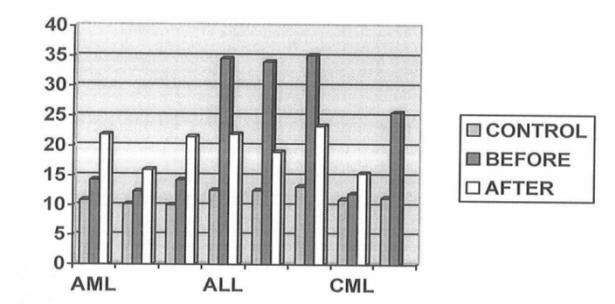


Figure (1):- Mean of serum GOT activity UIL in AML,ALL, (Response, Resistant), CML before and after treatment, death and control.

Table(2) and figure (2) showed the serum GPT activity of patients before and after treatment and control. It was found that serum GPT activity in (AML, response and resistant and CML) before treatment was statistically insignificant higher than of control groups (P>0.05).

Serum GPT activity in (ALL, response, resistant and patients who dead) before treatment was statistically significant higher than of control groups (P<0.05), serum GPT activity in all types of leukemic patients (excepted CML) after treatment was statistically significant higher than of control groups (P<0.05),CML was statistically insignificant higher than of control groups (P>0.05) .

Serum GPT activity in (AML, response, resistant) patients before treatment was statistically significant lower than serum GPT activity of patients after treatment (P<0.05).
Serum GPT activity in (ALL, response, resistant) patients before treatment was statistically significant higher than serum GPT activity of patients after treatment (P<0.05), CML before treatment was statistically insignificant lower than of patients after treatment (P>0.05).

Serum GPT activity of CML was lower than serum GPT activity of AML and ALL before and after treatment.

Serum GPT activity of patients who response to treatment lower than serum GPT activity of patients who resist to treatment and serum GPT activity of patients who dead was higher than serum GPT activity of other patients.

These results are in agreement with other studies done on serum GPT activity in patients with ALL, AML and Iymphoma [18,19,20].

Table (2): -Mean of serum GPT activity U/L, standard deviation (SD) T-Test,P value for patients before and after treatment and Control.

Type	No.	GPT activity U/L Mean +SD			T-Test, P value		
		C	B	A	B-C	B-A	A-C
AML	34	85±3.53	89.09±7	16.76±15.49	0. 178,0.860	4.04,0.001*	2.9,0.006
Response	8	9.00±3.6	9. I 3±0.35	12.75±3.15	3.60,0.09	5.35,0.001*	2.5,0.05*
Resistant	21	8.24±3.24	8.48±4.72	16.00±15.50	0. I9, 0.85	2.59, 0.018*	2.2 ,0.04*
ALL	20	8.34±2.63	21.75±12.83	12.25±8.65	2.543,002*	3.4,0.003*	2.1,0.005*
Response	12	8.50±3.15	20.25±14.82	10.71±5.35	2.67,0.022*	1.6,0.012*	2.3,0.01*
Resistant	7	8.14±2.41	23.14±10.02	12.92±10.54	3.21,0.018*	4.77,0.003*	2.9,0.03*
CML	7	7.86±3.58	8.29±4.89	10.43±6.68	1.758,0.129	-5.60,0.596	2.09,0.0*
Death	6	8.33±5.61	23.87± I 2.94		1.99,0.102		

B- Before , A-After , C-Control*
P<0.05

Mean of GPT activity U/ L

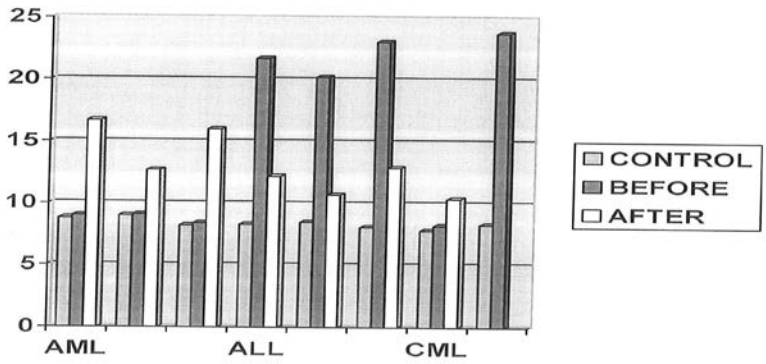


Figure (2): Mean of serum GPT activity UIL in AML,ALL, (Response, Resistant), CML, before and after treatment, death and control.

Table(3) and figure (3) showed the serum urea concentration of patients before and after treatment and control. It was found that serum urea concentration in all types of leukemie patients before treatment was statistically insignificant higher than of control groups (P>0,05).

Serum urea concentration in all types of leukemic patients(excepted CML) after treatment was statistically significant higher than of control groups (P<0.05),CML after treatment was statistically insignificant higher than of control groups (P>O.05).

Serum urea concentration in all types of leukemic patients(excepted CML) before treatment was statistically significant higher than serum urea concentration of patients after treatment (P<O.05), CML before treatment was statistically insignificant higher than serum urea concentration of patients after treatment (P>O.05).

Serum urea concentration of CML was lower than serum urea concentration of AML and ALL before and after treatment.

Serum urea level of patients who response to treatment lower than serum urea level of patients who resist to treatment and serum urea level of patients who dead was higher than serum urea level of other patients. These results are in agreement with other studies done on serum urea concentration in patients with ALL, AML [21].

Table (3): - Mean of serum urea concentration mmol/L, standard deviation (SD), T- Test, P value for patients before and after treatment and control.

Type	No.	U.concentn	ition	Mean± SD		T-Test	value
		C	B	A	B-C	B-A	A-C
AML	34	4.435±0.730	5.156±2.150	7.332±3.302	7.88,0.069	7.3,0.01	4.9,0.001*
Response	8	3.963±0.730	4.563±0.909	5.587±1.273	2.428,0.056	4.4,0.003	2.94,0.01 *
Resistant	21	4.348±0.719	5 .105±2. 123	7.270±3.390	1.6,0.13	5.0,0.00*	3.9,0.00 1 *
ALL	20	4.310±0.785	5.150±2. 1 00	5.900±2.200	6.02,0.12	6.5,0.001	3.8,0.001 *
Response	12	4.208±0.794	5.09±2.020	5.783±2.279	1.67,0.123	0.98,0.03	2.34,0.04*
Resistant	7	4.357±0.800	4.829±2.154	6.489±1.968	0.70,0.51	5.,0.002*	3.65,0.01*
CML	7	3.971 ±1.460	4.300±0.545	5.086±0.771	0.57,0.59	2.09,0.08	1.96,0.097
Death	6	4.700±0.522	6.850±2.455		1.87,0.120		

B- Before , A-After , C-Control*
P<0.05

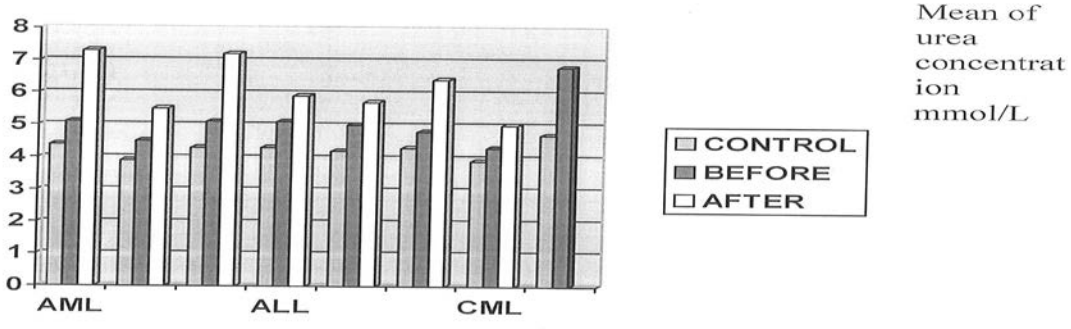


Figure (3):- Mean of serum urea concentration mmol/L in AML,ALL, (Response, Resistant), CML, before and after treatment, death and control.

Table(4) and figure (4) showed the serum creatinine concentration of patients before and after treatment and control It was found that serum creatinine concentration in all types of leukemic patients before treatment was statistically insignificant higher than of contra 1 groups (P>O.05).

Serum creatinine concentration in all types of leukemic patients after treatment was statistically insignificant higher than of control groups (P>O.05).

Serum creatinine concentration in all types of leukemic patients before treatment was statistically insignificant lower than serum creatinine concentration of patients after treatment (P>O.05).

Serum creatinine concentration of CML was lower than serum creatinine concentration of AML and ALL before and after treatment.

Serum creatinine level of patients who response to treatment lower than serum creatinine level of patients who resist to treatment and serum creatinine level of patients who dead was higher than serum creatinine level of other patients.

These results are in agreement with other studies done on serum creatinine level in patients with ALL, AML [21,22].

Table (4): -Mean ofsenul1 creatinine concentrationjlU1101/L, standard deviation (SD), T - Test, P value for patients before and after treatment and control.

Type	No.	Cr. concentration umol/L Mean ±SD			T-Test P value		
		C	B	A	B-C	B-A	A-C
AML	34	89.794±13113.7	95.362±25.540	109.421 ±29	1.14,0.26	1.4,0.1	3.58,0.1
Response	8	82.5] 3±3.789	91.813±14.844	94.175±17.805	0.9,0.39	1.79,0.12	0.51,0.63
Resistant	21	89.690±13.453	96.510±29.700	115.800±3130	0.95,0.36	0.6,0.1	3.4,0.3
ALL	20	88.000±9.150	88.8±19.210	96.330±15.880	1.32,0.34	-3.1,0.3	1.52,0.21
Response	12	85.210±18.450	89.108±11.515	96.670 ± 7.550	1.14,0.28	0.62,0.55	-1.4,0.177
Resistant	7	87.071 ±2.907	95.2U 15.18	99.500±15.63	-1.4,0.19	2.05,0.86	1.06,0.33
CML	7	87.570±13.510	88.140±14.940	92.940±15.23	1.42,0.21	-2.16,0.5	-0.69,0.52
Death	6	89.500±13.990	07.330±18.00		1.55,0.18		-0.69,0.52

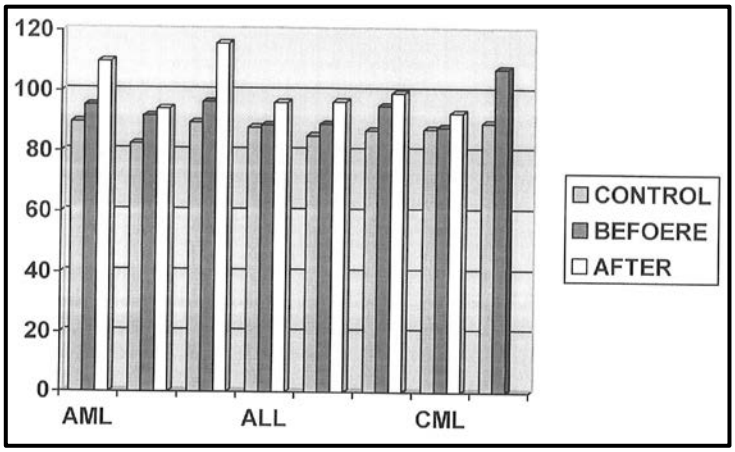


Figure (4):- Mean of serum creatinine concentration nmol/L in AML,ALL,(Response, Resistant), CML, before and after treatment, death and control.

Table(5) and figure (5) showed the serum uric acid concentration of patients before and after treatment and control It was found that serum uric acid concentration in all types of leukemic patients before treatment was statistically significant higher than of control groups (P<O.05), and serum uric acid concentration in all types of leukemic patients after treatment was statistically significant higher than of control groups (P<O.05).

Serum uric acid concentration in all types of leukemic patients before treatment was statistically significant higher than serum uric acid concentration of patients after treatment (P<O.05).

Serum uric acid concentration of CML was less than serum uric acid concentration of AML and ALL before and after treatment.

Serum uric acid level of patients who response to treatment less than serum uric acid level of patients who resist to treatment and serum uric acid level of patients who dead was more than serum uric acid level of other patients.

The increase in urate concentration, typically seen as a consequence of treatment of haematolgical malignancy, increased rate of turnover of nucleic acid, as in malignancies, tissue damage or starvation [21].

Table (5): -Mean of serum uric acid concentration jimol/L, standard deviation (SD), T - Test, P value for patients before and after treatment and control.

Type	No.	U.A concentration umoI/L Mean ±SD			T-Test P value		
		C	B	A	B-C	B-A	A-C
AML	34	245.32±41.87	597.53±51.48	309.91±48.01	33.5,0.001*	22,0.001*	6.03,0.001*
Response	8	240.63±32.03	588. 14±61.18	307.13±58.05	32.5,0.001*	12,0.001*	3.8,0.007*
Resistant	21	246.00±37.73	617.25±32.20	319.05±43.04	23.8,0.001*	15,0.001*	5.7,0.001 *
ALL	20	247.10±37.52	601.22±14.32	312.55±50.80	34.5,0.001*	25,0.001*	7.36,0.001*
Response	12	244.92±38.63	594.83±38.20	298.17±38.2	21.9,0.001*	32,0.001*	3.2,0.008*
Resistant	7	242.57±33.63	609.57±15.18	331.86±66.43	23.9,0.001*	12,0.001*	3.9,0.008*
CML	7	216.57±23.60	450.14±144.97	248.43±33.75	4.7,0.003*	3.1,0.022	1.5,0.017*
Death	6	259.17±69.89	607.5O±6.44		12.2,0.001		

B-Before, A-After, Contral *
P<O.05

Mean of U> A concentration umol/L

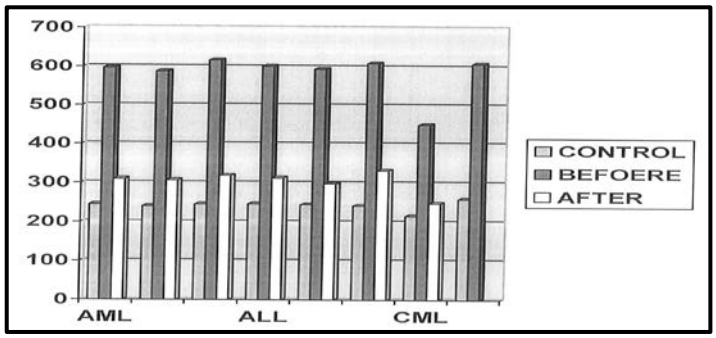


Figure (5):- Mean of serum uric acid concentration lill10VL in AML,ALL,(Response, Resistant), CML, before and after treatment, death and control.

Conclusion :-

Serum (GOT , GPT) activities and (U , Cr) concentration were elevated after chemotherapy treatment than before it . Therefore , chemotherapy treatment may be caused to impairment of liver and renal functions .

Referances :

1. L. stryer" biochemistry " 3rd edition ,W.H. freeman and company, New York , 1988 , P 596.
2. Robert L, Katherine J . , Joseph J . " Principles and Applications of Inorganic ,Organic and Biological chemistry" 2nd edition , WBC , MC , Graw HilI 1997 , P 242 .
3. Zubay ceoffery , "Biochemistry" Vol(1) , 3rd ed., WMC Brown communications , U.S.A 1993 , P 280.
4. Thommas M . , Derlin J . " text of Biochemistry with clinical correlations " A wiley Medical publication , New York, 1982 , P185.
5. Joan F. Zilva , peter R ., Pannall and Philip D. Mayne "Clinical chemistry in diagnosis and treatment" ,5th ed , 1988 , P 523.
6. Ottaway G.H. , Apps D.k. ,Bailliere T ., "Biochemistry "4th ed ,London, 1984 , P322.
7. Harry R . Mathews ,Richard A.Preed , Roger L . Miesfeld , " Biochemistry a short Course" ,Wi1ey -liss, U.S.A 1997 ,P 255.
8. Sylvia S. , Mader W. , " Biology " 6th ed ,Me. Graw - HilI, New York, 1998 , P 185.
9. Reitman .S., and Frankel,S. ,"Amer .JClin.Path. {1957}, 28{56} 983-988.
10. FawcettJK. ,Scott JE. "J Clin. Path." 1960,13,156-159.
11. Patton C. J, Crouch S.R. ,"Anal.Chem." 1977 ,49,464 ,469.
12. Bartels H., "Clin. Chemo Acta. "37,193-197 (1972).
13. Henry, R. , "Clin. Chemo Principles and Techniques"2l1d ed. ,Harper and Row , P543 (1974.(
14. Barham and Trinder, "Analyst Clin. Chemo ",97,142,(1972).
15. Fossatin ,"Princip. Clin. Chemo "28,227, (1980).
16. Bailey N. 1. "Statistical Methods in Biology ", Ltd. Press (1974).
17. Gao Y.J. , WU. Y. ,Lu. F. J ,"serum alanine aminotransferase elevation in children with leukemia or lymphoma during chemotherapy , childrins hospital , Fundan University, Shanghaig , China, 2002.
18. Yokota S. , Hayashi Y. ,Kabayashi M. , Kamashitta S. ,"Liver Function studies in children with acute lymphocytic leukemia aftel' cessation of therapy , Med pediator. Oncol. Department of pediatrics , university of Tokyo hospital , jappan , 1994 ,23 (2) , 111-5.
19. Scolyer R.A. , Brun M. , Rozario J "Acute Basophilic leukemia presenting with abnor malliver function tests and the absence of blast cells in the peripheral blood. "Pathology"department of anatomical pathology , Canberra hospital, Garran ,Australia ,Feb. ,(2000), 32(1) ,52-2.
20. Adrienne R. ,Jeyanthi R. ,Ram an arayan an M. "leukemia Cutis "Medicine ,March ,2005.
21. William J Marshall (2000) ,Clinical chemistry London ,U.K. 4th ed . ,P 543.
22. study in pations with hematologie mal ignancies and Renal or hepatic impairment , (National Cancel' Institute)2002.