A COMPARATIVE STUDY OF CERULEOPLASMIN OXIDASE WITH COPPER AND RENAL FUNCTION TESTS IN SERA OF LEUKEMIA AND MULTIPLE MYELOMA PATIENTS DURING THE TREATMENT

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Abstract

Ceruloplasmin oxidase (CP) activity, Copper concentration (Cu) and renal function was measured in sera of 87 patients with blood cancer (leukemia and multiple myeloma) ,34 patients with acute myeloblastic leukemia (AML),20 patients with acute lympholastic leukemia(ALL),13 patients with chronic myeloblastic leukemia (CML), 20 patients with multiple myeloma aged (5-62) years. In addition to 87 healthy individuals of match age and sex were utilized as control throughout this study.

The first part of this study was devoted to measure of CP activities in sera of control and patients group before and after the first course of chemotherapy treatment (about 6 weeks). It was found that CP activities significantly higher than control groups ($P<0.05$) while the levels before chemotherapy were significantly higher than that after chemotherapy ($P<0.05$).Mean of sera CP levels of patients who passed away were higher than other patients.

The second part of this study dealt with follow the changes in some biochemical parameters including blood creatinine (Cr), blood urea (U), uric acid (U.A) and copper (Cu) concentrations to evaluate the renal function as a complication in the studied patients.The results indicated the following:-

-The levels of U.A and Cu in sera of patients pre and post chemotherapy were significant more ($P<0.05$) than that of control group, while their levels before chemotherapy were significantly higher ($P<0.05$) than that after chemotherapy.

-Blood urea U and Cr levels in sera of patients pre and post chemotherapy were insignificant more ($P>0.05$) than that of control group, the levels of both parameters before chemotherapy were significantly higher ($P<0.05$) than that after chemotherapy.

To check if there is a relationship between CP activity with all of the above parameters before taking any dose of chemotherapy A-significant-positive-correlation was found between CP and U.A ($r>0.5$) while a non-significant positive correlation between CP and Cr, U ($r<0.35$).

Conclusion of over all results in the present study enable the one to use serum CP, Cu and U.A rather than U and Cr as a biochemical marker to aid in the prognosis the blood cancer throughout treatment. Another conclusion is patients with blood cancer should evaluate their renal function through out taking their chemotherapy (especially first does) by measuring CP, Cu and U.A in their sera.

دراسة مقارنة للسيروبلازمين اوكسيديز مع النحاس واختبارات وظائف الكلى فى امصال المرضى باللوكيميا والمايلوما المتعددة خلال العلاج

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الخلاصة

تم قياس فعالية انزيم السيروبلازمين اوكسيديز CP وتركيز النحاس Cu وفحص وظيفة الكلى في امصال ٨٧ مرضى بسرطان الدم (اللوكيميا والمايلوما المتعددة)، حيث اشتملت ٣٤ مريض مصاب باللوكيميا المايلوبلاستك الحادة، ٢٠ مريض مصاب باللوكيميا اللمف الحادة، ١٣ مريض المايلو بلاستك المزمنة، ٢٠ مريض مصاب بالمايلوما المتعددة تراوحت مدى اعمارهم (٥-٦٢) سنة بالاضافة الى ٨٧ شخصا من الاصحاء بنفس االعمر والجنس استخدموا كمجموعة سيطرة خلال هذه الدراسة.

هدف الجزء الاول من هذه الدراسة الى قياس فعالية CP في امصال مجموعة المرضى والسيطرة قبل وبعد الكورس الاول للعلاج الكيميائي (الذي استغرق حوالي ٦ اسابيع) لقد وجد ان فعالية CP للمرضى ازدادت بصورة ملحوظة عن مجاميع السيطرة ($p<0.05$) بينما كانت المستويات قبل العلاج الكيميائي اعلى بصورة ملحوظة عن تلك مابعد العلاج الكيميائي($P<0.05$).بلغ معدل CP في امصال المرضى القدماء اعلى عن بقية المرضى .

تناول الجزء الثاني من هذه الدراسة متابعة التغيرات في بعض المعاملات الكيميا حيوية المتضمنة قياس تراكيز الكرياتينين في الدم (Cr)، واليوريا (U) وحامض اليورك (U.A.) والنحاس (Cu) لتقييم وتحديد وظيفة عمل الكلى كاحد التعقيدات المصاحبة للمرضى قيد الدراسة. فيما يلي محصلة النتائج :-

كانت مستويات حامض اليورك والنحاس في امصال المرضى قبل وبعد اخذ العلاج الكيميائي اعلى ($P < 0.05$)عن تلك مجموعة السيطرة وبصورة ملحوظة ، بينما بلغت تلك المستويات من التراكيز قبل العلاج الكيميائي اعلى($P < 0.05$) عن تلك بعد تناول العلاج الكيميائي بصورة ملحوظة.

- بلغ مستوى تركيز اليوريا والكرياتينين في امصال المرضى قبل وبعد اخذ العلاج الكيميائي اعلى($P >0.05$) مقارنة بمجموعة السيطرة بصورة غير ملحوظة بينما ازدادت مستويات كلا المعاملين قبل اخذ العلاج الكيميائي بصورة ملحوظة($P < 0.05$) مقارنة فيما بعد تناول العلاج الكيميائى
- في دراسة لمعرفة وجود علاقة مابين فعاليةCP مع جميع المعاملات اعلاه قبل تناول العلاج الكيميائى، فقد تم الحصول على علاقة موجبة ملحوظه مابين CP و U.A ($r > 0.5$)بينما كانت العلاقة موجبة ضعيفة وغير ملحوظة مابينCP وCr و U ($r < 0.35$..).
- ان الاستنتاج لمحصلة النتائج اعلاه في هذه الدراسة هو مقدرة الشخص ان يستخدم قياسCP، Cu، U.A. في المصل علاوة على استخدام U و Cr كدالة كيميا ء حياتية للمساعدة في متابعة مرض سرطان الدم خلال فترة العلاج الكيمياوى.

وكذلك نستنتج ان المرضى بسرطان الدم يجب ان يتابعوا وظيفة الكلى خلال تناول علاجهم الكيميائي (لاسيما عند الجرعة الاولى) بقياس CP و Cu و U.A. في امصالهم.

Introduction

Leukemia, in common with most other cancers, is the second disease in 2004 - 2005 which causes death in Iraq [1] ,it refers to a group of malignant disorders of the hematopoietic tissues characteristically with the increasing number of primitive white cells (blasts) in the bone marrow. There is a failure of cell maturation in leukemial proliferation of cells, which are not mature, and this leads to an increasing accumulation of useless cells which take up more and more marrow space at the expense of the normal hematopoietic elements. Leukemia is a disease that starts in the bone marrow and extends from there to the blood and then to the tissues. There is no tissue that is immune from being invaded by the malignant cells. The course of leukemia may vary from a few days or weeks to many years, depending on its type [2].

Multiple Myeloma is a malignant proliferation of plasma cells. Normal plasma cells are derived from B cells and produce immuno globulins which contain heavy and light chains. Normal immuno globulins are polyclonal. Myeloma plasma cells produce immuno globulins of single heavy and light chain a monoclonal protein commonly referred as a para protein. In some cases only light chain is produced, a small number of malignant plasma cells are present in the circulation, the majority are present in the bone marrow [3].

Cerulopasmin is one of the acute phase protein,it is a single glycoprotein, has a molecular weight of (135000)Daltons with 6 or 7 copper atoms per molecule [4],it represents an example of "a moon lighting" protein that overcomes the one gene-one structure function concept to follow the changes of the organism in its physiological and pathological condition [5] Copper has enzymatic activities, 90% or more of total serum copper is associated with ceruloplasmin [6] and the remaining 5-10 % of copper is believed to be fairly loosely attached to albumin and histidine and only a trace of copper is present as free Cu++ [7,8].CP, synthesized in the liver, is a multifunctional protein that has feroxidase activity [9]. It was reported that ceruloplasmin plays an important role in protecting a variety of tissues from free radical injury, also the antioxidant protection of CP drives
mainly from its ability to oxidize polyamines,by controlling the levels of highly toxic iron. Most evidence points to CP ferroxidase activity as an antioxidant activity, conversion of Fe^{+2} to Fe^{+3} may reduce the oxidation by inhibition of the Fenton reaction(which requires reduced metal) , by decreasing the amount of the pro-oxidant Fe^{+2} ,Fe^{+2} /Fe^{+3} complex or by causing iron sequestration by apo-transferrin [10] . The antioxidant protection of CP is derived mainly from its ability to oxidize highly toxic ferrous iron to the relatively non toxic ferric form [11],and that helps in preventing oxidative damage of proteins, lipids and DNA[12]. Copper is the 3rd most abundant trace elements in human body (following Zn and Fe) and is essential to all organisms [13, 14].

Subjects and methods

1-Patients

Samples were collected from 87 patients (44 male and 43 female) aged (5-62) years old who attending (National Center of Hematology –Baghdad) during the period (2004 to 2005) and diagnosed by the physicans Dr.Ali Muslem Al Amamrii. Study samples were classified as shown in table(A):-

Table A: The host information of patients &control

Patients	Groups	Age (years)	Female (no)	Male (no)	Total (no)
Leukemia	AML	14-56	20	14	34
	ALL	5-55	8	12	20
	CML	5-59	3	10	13
Multiple myeloma		47-62	12	8	20
Total		**5- 62**	**43**	**44**	**87**
Control of AML		18-58	20	14	34
Control of ALL		22-60	8	12	20
Control of CML		10-45	3	10	13
Control of Multiple myeloma		25-55	12	8	20
Total		**10-60**	**43**	**44**	**87**

No =number of cases
ALL = acute lympholastic leukemia
CML= chronic myeloblastic leukemia
AML=acute myeloblastic leukemia

The criteria of inclusion in this study are:-

1. All patients were newly diagnosed.
2. The samples were collected before any chemotherapy treatment and after the first course of chemotherapy treatment, (about 6 weeks).
3. Eighty seven house hold relatives were taken as a control.
4. Six of patients with chronic myeloblastic leukemia died during the first course of chemotherapy treatment.

Venous blood samples (5 ml) were drawn from the control and each patient before and after chemotherapy treatment, transferred into plain tube then the blood was left to clot and serum was obtained by centrifugation at 3000 xg for 10 min then serum was removed and kept at (-20ºC) till analysis.

2-Methods

Ceruloplasmin Concentration Assay:

The activity of ceruloplasmine was determined in serum using, the modified Rice method, whereas ceruloplasmine catalyzed the oxidation of p-phenylenediamine (substrate) to give blue-violet color that measured at 525 nm.[15].

Copper Concentration Estimation:

Serum copper concentration was determined using .Shimadzu flame atomic absorption spectrophotometer type (AA 680 G) at 324 nm [16].

Urea Concentration Estimation:

The urea concentration was determined in serum samples of control and patients by enzymatic method (urease-modified Berthelot reaction), in an alkaline medium, the ammonium ions react with the salicylate and hypochlorite to form a green colored indophenol (2,2 dicarboxyl indophenol) [17].

Creatinine Concentration Estimation:

Kinetic was carried out using the complex formed by creatinine and picric acid in an alkaline medium forming a red complex. The rate of alteration in absorbance was proportional to the creatinine concentration [18].

Uric acid concentration Estimation:

Serum uric acid concentration was determined using, the modified Barham method whereas uric acid was oxidized by uricase to allantoine and hydrogen peroxide .In the presence of peroxidase,a mixture of N-ethyl-N-sulphopropyl-m-anisidine and 4-aminoantipyrin was oxidized by H_2O_2 to form a quinoneimine dye that was proportional to the concentration of uric acid in the sample[19].

3-Statistical methods

The results were analyzed statistically, and the values were expressed as (mean ± standard deviation). The level of significance was determined by employing (student t-test).When (P value) was less than 0.05 then the difference between two groups is considered statistically significant. Overall values were performed according to program SPSS version10

Results and Discussion

I- CP and Cu levels

Table (1) and (2) showed the mean of serum CP and Cu levels of the patients before and after treatment compared to the control.

Table 1:-Mean ± SD, P value of serum CP for patients before (B), after (A) c treatment and control groups (C).

Type	No.	CP activity mg/L Mean ± SD				
		C	B	A	B-C	B-A
AML	34	365.2±84.9	1121.6±111.4	799.0±93.4	P<0.05	
Response	8	375.3±98.2	1103.6±140.0	700.3±133.5	P<0.05	P<0.05
Resistant	26	367.2±81.2	1125.9±112.5	893.6±119.2	P<0.05	P<0.05
ALL	20	376.2±91.8	1099.9±93.4	794.2±119.5	P<0.05	P<0.05
Response	12	377.4±99.4	1118.1±106.6	703.5±130.4	P<0.05	P<0.05
Resistant	8	370.0±79.1	1180.0±68.2	866.2±107.1	P<0.05	P<0.05
CML	7	375.8±42.9	886.0±46.3	464.1±19.7	P<0.05	P<0.05
M.M	20	374.7±82.1	1109.1±83.8	578.1±66.6	P<0.05	P<0.05
Death	6	375.6±87.5	1183.8±71.7	……	P<0.05	……

AML=acute myeloblastic leukemia ALL= acute lympholastic leukemia
CML= chronic myeloblastic leukemia

Table 2: Mean ± SD, P value of serum Cu concentration for patients with AML, ALL, CML, MM. before (B), after (A) chemotherapy treatment and control groups(C).

Type	No.	Cu. Concentration mg/L Mean ± SD			P Value	
		C	B	A	B-C	B-A
AML	34	1.078±0.10	1.36±0.14	1.13±0.16	P<0.05	P<0.05
Response	8	1.075±0.11	1.28±0.06	1.04±0.10	P<0.05	P<0.05
Resistant	26	1.01±0.11	1.35±0.08	1.117±0.07	P<0.05	P<0.05
ALL	20	1.01±0.09	1.42±0.09	1.149±0.10	P<0.05	P<0.05
Response	12	0.98±0.05	1.44±0.099	1.16±0.10	P<0.05	P<0.05
Resistant	8	1.04±0.10	1.43±0.05	1.14±0.07	P<0.05	P<0.05
CML	7	1.01±0.02	1.19±0.08	1.01±0.08	P<0.05	P<0.05
M.M	20	1.05±0.03	1.28±0.14	1.06±0.10	P<0.05	P<0.05
Death	6	1.06±0.12	1.49±0.28	……	P<0.05	……

These results show that:-

1- Mean serum CP and Cu concentrations in the patients with all types of blood cancer before and after treatment were statistically significantly higher than that of the control groups ($P< 0.05$).
2- Mean serum CP and Cu concentrations in the patients with all types of blood cancer before treatment were statistically significantly higher than their levels after treatment ($P<0.05$).
3- Mean serum CP and Cu concentrations of patients with CML was less than serum CP and Cu concentrations of other patients.
4- Mean serum CP and Cu concentrations of patients who response to treatment were less than their concentrations in patients who resist to treatment.
5- Serum CP and Cu concentrations of patients died was more than serum CP and Cu concentrations of other patients.

Table (3) showed the mean +S.D serum Cu /CP ratio with P values of patients before treatment compared to control and of same patients before and after treatment .It was found that

1- Mean serum Cu /CP ratio was the same in all patients with blood cancer before and after treatment and control groups.
2- Mean of serum Cu /CP ratio of patients before treatment was statistically insignificant than that of control groups ($P> 0.05$) .
3- Serum Cu /CP ratio in patients before treatment was statistically insignificant than serum Cu /CP ratio of patients after treatment ($P>0.05$).

Table 3: Mean ± SD, P value of serum Cu/CP raio for patients with AML, ALL, CML, MM. before (B), after (A) chemotherapy treatment and control groups (C).

Type	No.	Cu /CP ratio Mean ± SD				
		C	B	A	B-C	B-A
AML	34	0.01±0.01	0.01±0.04	0.01±0.03	P>0.05	P>0.05
Response	8	0.01±0.01	0.01±0.03	0.01±0.005	P>0.05	P>0.05
Resistant	26	0.01±0.01	0.01±0.01	0.01±0.02	P>0.05	P>0.05
ALL	20	0.01±0.02	0.01±0.04	0.01±0.002	P>0.05	P>0.05
Response	12	0.01±0.01	0.01±0.009	0.01±0.004	P>0.05	P>0.05
Resistant	8	0.01±0.02	0.01±0.05	0.01±0.02	P>0.05	P>0.05
CML	7	0.01±0.02	0.01±0.005	0.01±0.04	P>0.05	P>0.05
M.M	20	0.01±0.03	0.01±0.04	0.01±0.01	P>0.05	P>0.05
Death	6	0.01±0.02	0.01±0.02	…….	P>0.05	…….

AML=acute myeloblastic leukemia ALL= acute lympholastic leukemia
CML= chronic myeloblastic leukemia

Ceruloplasmin is considered as one of the positive acute-phase reactants. Increased CP concentration in serum result from its increased synthesis by liver, as one of the acute phase proteins which their concentration increase upon different disease including tumors [20]. Ceruloplasmin is an enzyme which has a role as an antioxidant [21]. The unbalanced production of reactive oxygen intermediates have been postulated to play a role in the pathogenesis of cancer [22].

Copper and ceruloplasmin are usually closely correlated with each other, since ceruloplasmin is the major copper-binding protein (over 95% of plasma copper is bound to CP)[21]. One symptoms of copper deficiency include anemia, sever anemia may reflect the reduced ceruloplasmin activity(23)

The Cu/CP ratio reflects the concentration of Cu that is either bound to albumin or free copper. This form of Cu is consider to be one of the pro-oxidants in the body, where transition metals such as Fe^{+2} or Cu^{+} ,catalyze formation of the hydroxyl radical(OH) from hydrogen peroxide in the enzymatic Fenton reaction [24]. The results of this study are in agreement with previous studies to the Cu, CP and Cu/CP of the leukemia, lymphoma (Hodghkin's and non Hodghkin's desease) and multiple myeloma

II-Study Renal Function Test

Table (4) showed the mean serum U concentration of patients before and after treatment compared to control .It is clear that:-

1- Mean of serum U concentration in patients with the all types of blood cancer before and after treatment was statistically significantly higher than control groups ($P< 0.05$).
2- Mean serum U concentration in patients with the all types of blood cancer before

treatment was statistically significant less than serum U concentration after treatment (P<0.05).

3- Mean serum U concentration of patients with CML was less than serum U concentration of other patients.
4- Mean serum U concentration of patients who response to treatment was less than serum U concentration of patients who resisted the treatment.
5- Mean serum U concentration of patients who died was more than serum U concentration of other patients.

Table 4: Mean ± SD, P value of serum U. concentration for patients with AML, ALL, CML, MM. before, after chemotherapy treatment and control groups.

Type	No.	U. Concentration mmol/L Mean ± SD				
		C	B	A	B-C	B-A
AML	34	4.43±0.70	5.15±2.15	7.33±3.30	P<0.05	P<0.05
Response	8	3.96±0.73	4.56±0.90	5.98±1.27	P<0.05	P<0.05
Resistant	26	4.34±0.71	5.10±2.12	7.27±3.39	P<0.05	P<0.05
ALL	20	4.31±0.78	5.15±2.1	5.90±2.20	P<0.05	P<0.05
Response	12	4.20±0.79	5.09±2.02	5.78±2.27	P<0.05	P<0.05
Resistant	8	4.35±0.80	4.82±2.15	6.48±1.96	P<0.05	P<0.05
CML	7	3.97±1.46	4.30±0.54	5.08±0.77	P<0.05	P<0.05
M.M	20	4.45±0.72	5.18±2.01	6.96±3.14	P<0.05	P<0.05
Death	6	4.30±0.52	6.85±2.45	……	P<0.05	…….

Table (5), showed the mean of serum U.A concentrations in the patients before and after treatment compared to control .It was found that

1- Mean serum U.A concentrations in patients with the all types of blood cancer before treatment was statistically significantly higher than control group (P< 0.05).
2- Mean serum U.A concentrations in all types of blood cancer before treatment was statistically significant higher than their concentrations after treatment (P<0.05).
3- Mean serum U.A concentrations of patients with CML was less than serum U.A concentrations of other patients.
4- Mean serum U.A concentrations of patients who response to treatment less than serum U.A concentrations of patients who resist to treatment.
5- Mean serum U.A concentrations of patients who dead were more than serum U.A concentration of other patients.

Table 5: Mean ± SD, P value of serum U.A concentration for patients with AML, ALL, CML MM. before, after chemotherapy treatment and control groups.

Type	No.	U.A Concentration µmol/L Mean ± SD				
		C	B	A	B-C	B-A
AML	34	245.3±41.8	597.5±51.4	309.9±48.0	P<0.05	P<0.05
Response	8	240.6±32.0	588.1±61.1	307.1±58.0	P<0.05	P<0.05
Resistant	26	246.0±37.7	617.2±32.2	419.0±43.3	P<0.05	P<0.05
ALL	20	247.1±37.5	601.2±14.3	312.5±50.8	P<0.05	P<0.05
Response	12	244.9±38.6	594.8±38.2	298.1±38.2	P<0.05	P<0.05
Resistant	8	242.5±33.6	609.5±15.1	431.8±66.4	P<0.05	P<0.05
CML	7	216.5±23.6	450.1±144.9	248.4±33.7	P<0.05	P<0.05
M.M	20	199.0±18.1	411.4±107.4	307.9±55.2	P<0.05	P<0.05
Death	6	259.1±69.8	607.5±6.4	……..	P<0.05	…….

AML=acute myeloblastic leukemia **ALL= acute lympholastic leukemia**
CML= chronic myeloblastic leukemia

Table (6) showed the mean serum Cr concentration of patients before and after treatment compared to control .It was found that:-

1- Mean serum Cr concentration in patients with the all types of blood cancer before treatment was statistically insignificant higher than control groups (P> 0.05).

2- Mean serum Cr concentration in patients with the all types of blood cancer before treatment was statistically insignificant less than serum Cr concentration after treatment (P>0.05).
3- Mean serum Cr concentration of patients with CML was less than serum Cr concentration of other patients.
4- Mean serum Cr concentration of patients who response to treatment less than serum Cr concentration of patients who resist to treatment.
5- Mean serum Cr concentration of patients who dead was more than serum Cr concentration of other patients.

Table 6: Mean ± SD, P value of serum Cr. concentration for patients with AML, ALL, CML, MM. before, after chemotherapy treatment and control groups.

Type	No.	Cr. Concentration µmol/L Mean ± SD			P Value	
		C	B	A	B-C	B-A
AML	34	89.7±13.7	95.3±25.5	109.4±29.1	P>0.05	P>0.05
Response	8	82.5±3.7	91.8±14.8	94.1±17.8	P>0.05	P>0.05
Resistant	26	89.6±13.4	96.5±29.7	105.8±31.3	P>0.05	P>0.05
ALL	20	88.0±9.1	88.8±19.2	96.3±15.8	P>0.05	P>0.05
Response	12	85.2±18.4	89.1±11.5	96.6±17.5	P>0.05	P>0.05
Resistant	8	87.0±2.9	95.2±15.18	99.5±15.6	P>0.05	P>0.05
CML	7	87.5±13.5	88.1±14.9	92.9±15.2	P>0.05	P>0.05
M.M	20	94.2±18.5	88.7±11.3	110.1±12.4	P>0.05	P>0.05
Death	6	89.5±13.9	107.3±18.7	……	P>0.05	…….

AML=acute myeloblastic leukemia ALL= acute lympholastic leukemia
CML= chronic myeloblastic leukemia

Increase protein diet leads to increase the ammonium level in the blood [29]. A high concentration of ammonium ions shifts the equilibrium of the reaction catalyzed by glutamate dehydrogenase towards the formation of glutamine, then the elevated levels in glutamine is found in the cerebrospinal fluid of patients with hyperammonemia and may lead directly to brain damage [17]. In sever liver disease, the ability of liver cells to form urea is impaired,ammonia accumulate and urea level fall. The rate of urea removal depends upon urea concentration in the plasma and capacity of the kidney to remove urea from the plasma (renal function),in most clinical situation changes in urea levels are more dependent upon renal function than upon liver function[30, 31]. So the results of this study are agreement with the thought presence disorders in kidney capacity of the patients after treatment.

Creatinine is a catabolism end product occur in kidney and liver it excreted from the body via the urine [31, 32].

Uric acid is a catabolism end product of the purines (adenine and guanine) 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 especially with extensive neucrosis.Uric acid seems to be a major protective antioxidant against NO_2 and HOCl[31]. In this study U, U.A and Cr were increased; due to the rate of turnover of nucleic acid, tissues damage or starvation. The result of our study is in agreement with previous studies of U, U.A and Cr in blood malignancies [33].

Table (7), showed the mean of serum CP, U., Cr and U.A concentrations of patients who response and resistant to the treatment .It was found that

1- Mean serum CP and U.A concentrations in AML and ALL patients who were resistant to the treatment were statistically significantly higher than of patients who response (P< 0.05).
2- Mean serum U. and Cr concentrations in AML and ALL patients who was resistant to the treatment were statistically insignificantly higher than that of patients who response to the treatment (P> 0.05).

Table 7: Mean ± SD, P value of serum CP, U., Cr, U.A concentration for patients with AML, ALL response and resistant.

	Type	Response Mean ± SD	Resistant Mean ± SD	P Value
AML	CP mg/L	700.3±133.5	893.6±119.2	P<0.05
	U. mmol/L	5.98±1.27	7.27±3.39	P>0.05
	U.A µmol/L	307.1±58.0	419.0±43.3	P<0.05
	Cr µmol/L	94.1±17.8	105.8±31.3	P>0.05
aA ALL	CP mg/L	703.5±130.4	866.2±107.1	P<0.05
	U. mmol/L	5.78±2.27	6.48±1.96	P>0.05
	U.A µmol/L	298.1±38.2	431.8±66.4	P<0.05
	Cr µmol/L	96.6±17.5	99.5±15.6	P>0.05

Correlation coefficients

The correlation test done by using statistical programme SPSS version10. Figures (1-3) show correlations between serum CP levels with parameters of renal functions i.e.(U,Cr and U.A) with their values of correlation coefficient (r). Data observed that:-

- A significant positive correlation was found between CP and U.A in patients with ALL, AML, M.M ($p<0.05$), as shown figures 1-b ,2-b, 3-b.
- A non-significant positive correlation was found between CP and U ,Cr in patients with ALL , AML, M.M ($p>0.05$), as shown in figures 1-a,2-a,1-c,2-c,3-a,3-c.

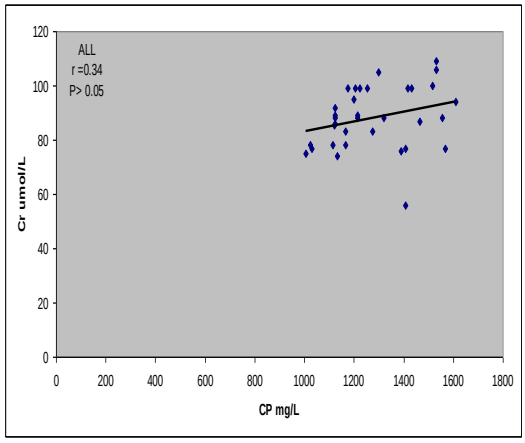

Figure 1-c: Correlation between Cr and CP in ALL

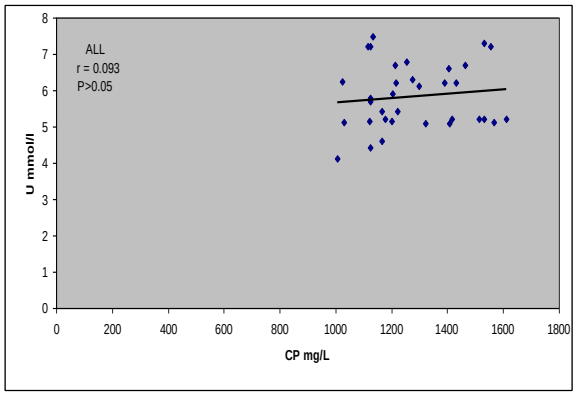

Figure 1-a: Correlation between U and CP in ALL

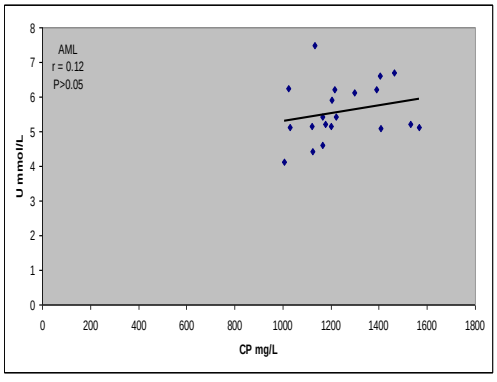

Figure 2-a: Correlation between U and CP in AML

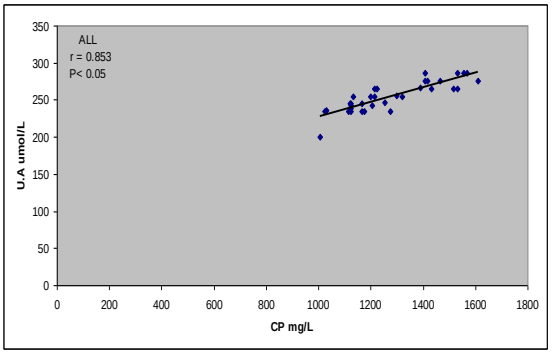

Figure 1-b: Correlation between U.A and CP in ALL

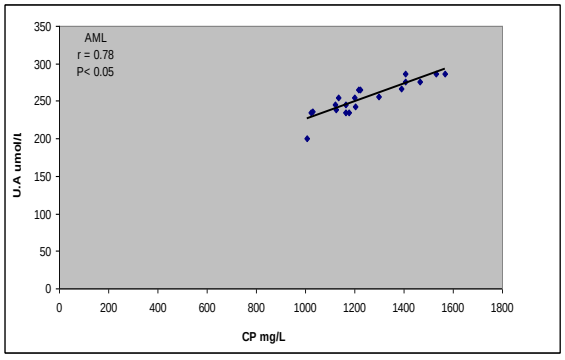

Figure 2-b: Correlation between U.A and CP in AML

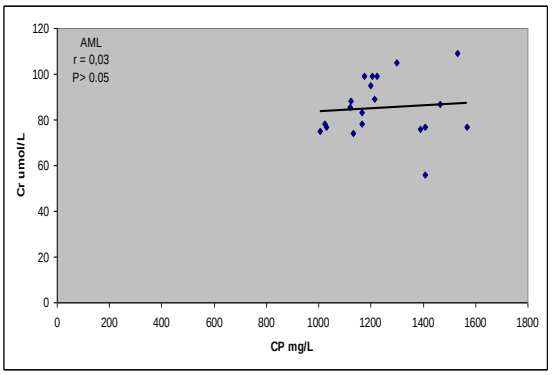

Figure 2-c: Correlation between Cr and CP in AML

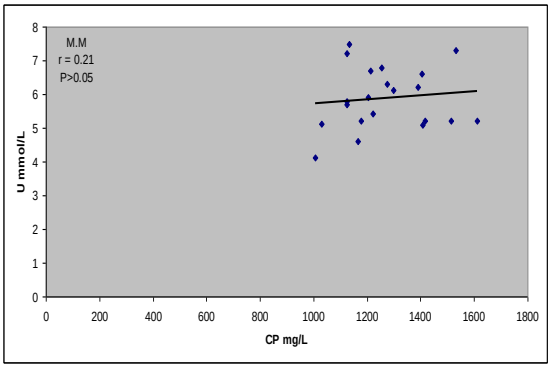

Figure 3-a: Correlation between U and CP in M.M

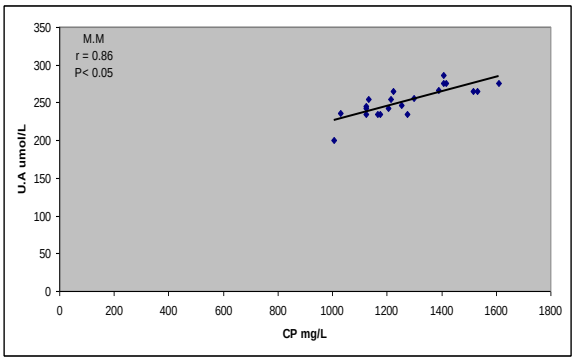

Figure 3-b: Correlation between U.A and CP in M.M

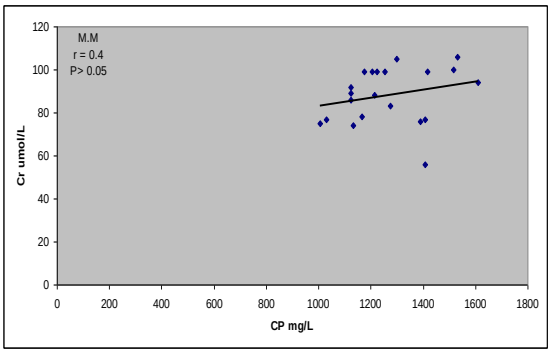

Figure 3-c: Correlation between Cr and CP in M.M

In those observations the author can conclude that, patients with blood cancer disease their CP activity has a positive correlation with U.A due these both parameter antioxidant agents, therefore it can use CP and U.A as an evaluations marker along side rather than other biochemical parameters i.e., U. or Cr.

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