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Ceruloplasmin and some biochemical parameters as a marker for acute myeloid leukemic patients

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ABSTRACT

Acute myeloid leukemia is a second type of leukemia and has more effect on elder patients than adult. This research's objective was to measure the serum levels of ceruloplasmin (CP), ferritin (FR), vitamin B12 (VitB12), folic acid (FA), zinc (Zn), copper (Cu), and iron (Fe) in acute myeloid leukemic patients (AML) (before and after taking chemotherapy) and healthy control groups. In this study, about (160) blood samples (males and females) were collected from acute myeloid leukemic patients in Erbil's Nanakali hospital and they were separated into four groups: Group 1 (G1) including (40) Apparently healthy control group, Group 2 (G2) include (40) acute myeloid leukemic patients before taking chemotherapy (new cases), Group 3 (G3) include (40) acute myeloid leukemia patients taking chemotherapy for one cycle, and Group 4 (G4) include (40) acute myeloid leukemic patients with taking chemotherapy for more than one cycle. The outcomes display a significant increase in serum concentration of ceruloplasmin, ferritin, vitamin B12, and iron in all patient groups when compared with control groups. While the serum concentration of folic acid, zinc, and copper decreased in all patient groups when compared with the healthy control group. In addition, the correlation analysis displays that there was a significant positive correlation between ceruloplasmin with ferritin, vitamin B12, and iron, on another hand have a non-significant negative correlation between ceruloplasmin with folic acid, zinc, and copper. According to the present study, there was a direct correlation between AML patients with the serum levels of CP, FR, VitB12, FA, Zn, Cu, and Fe. A high area under the curve of our data suggests that testing for (CP, FR, VitB12, FA, Cu, and Fe) could be helpful to detect AML. However, zinc is not a good biomarker for detecting AML patients.

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سيرولوبلازمين وبعض المعلمات البيوكيميائية كعلامة دالة لمرضى سرطان الدم النخاعي الحاد

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الملخص

ابيضاض الدم النخاعي الحاد هو ثاني نوع من سرطان الدم وله تأثير كبير على مرضى كبيري السن . الهدف من هذه الدراسة هو قياس مستويات السيرولوبلازمين (CP)والفيريتين (FR)وفيتامين (VitB12)وحمض الفوليك (FA)والزنك (Zn)والنحاس (Cu)والحديد (Fe)في دم مرضى ابيضاض الدم النخاعي الحاد (قبل وبعد تناول العلاج الكيميائي) ومجموعة الاصحاء. في هذه الدراسة ، تم جمع حوالي (160) عينة دم (ذكور واناث) من مرضى سرطان الدم النخاعي الحاد في مستشفى ناناكالي بأربيل وتم تقسيمهم إلى أربع مجموعات: المجموعة الأولى تشمل (40) كمجموعة الاصحاء ، المجموعة الثانية تشمل (40) مرضى ابيضاض الدم النخاعي الحاد قبل تناول العلاج الكيميائي (حالة جديدة) ، تشمل المجموعة الثالثة (40) مريضًا مصابا بسرطان الدم النخاعي الحاد يتناولون العلاج الكيميائي لدورة واحدة ، وتشمل المجموعة الرابعة (40) مريضًا مصابا بسرطان الدم النخاعي الحاد مع استعمال العلاج الكيميائي لأكثر من دورة واحدة. أظهرت النتائج زيادة معنوية في تركيز السيرولوبلازمين ، الفيريتين ، فيتامينB12 ، والحديد في امصال الدم لجميع المرضى المصابين بالمقارنة مع مجموعة السيطرة. بينما انخفض تركيز حمض الفوليك والزنك والنحاس في امصال الدم لجميع المرضى بالمقارنة مع مجموعة السيطرةالاصحاء. بالإضافة إلى ذلك ، أظهر تحليل الارتباط وجود علاقة ارتباط معنوية موجبة بين السيرولوبلازمين مع كل من الفيريتين ، فيتامين(VitB12) ، والحديد ، ومن ناحية أخرى أظهر تحليل الارتباط وجود علاقة ارتباط غير معنوي بين السيرولوبلازمين و كل من حمض الفوليك ،الزنك والنحاس. وفقًا للدراسة الحالية ، كان هناك ارتباط مباشر بين مرضى سرطان الدم النخاعي الحاد بمستويات السيرولوبلازمين والفيريتين وفيتامين B12 وحمض الفوليك والزنك والنحاس والحديد في الدم. تشير المنطقة المرتفعة الواقعة أسفل منحنى بياناتنا إلى أن اختبار) سيرولوبلازمين ، وفيريتين ، وفيتامينB12 ، وحمض الفوليك ، والنحاس ، والحديد (يمكن أن يكون مفيدًا في الكشف عن ابيضاض الدم النخاعي الحاد. ومع ذلك ، اما الزنك فليس له علاقة عند الكشف عن مرضى سرطان الدم النخاعي الحاد .

الكلمات المفتاحية: ابيضاض الدم النخاعي الحاد ، السيرولوبلازمين ، الفيريتين ، فيتامينB12 ، حمض الفوليك ، العناصر النزرة .

Introduction

Leukemia is characterized by the uncontrolled growth of white blood cells in the blood plus bone marrow. There are four kinds of leukemia: CLL, ALL, CML, and AML[1]. The second most typical kind of leukaemia is acute myeloid leukemia (AML) [2]. The illness has an extremely diverse hematology outcome, and the median age of those impacted is sixty-eight years old [3].

Antioxidants are a substance that gives an electron to a rogue free radical and neutralizes it to decrease its ability to cause harm. These antioxidants' primary ability to scavenge free electrons helps them prevent or reduce tissue injury [4]. Antioxidants are divided into enzymatic and nonenzymatic categories depending on their activities. Enzymatic antioxidants work by utilizing coenzymes like Fe, Zn, Cu, plus Mn to transform oxidizing metabolic processes into hydrogen peroxide (H_2O_2) and then into the water via a multi-step process. Non-enzymatic antioxidants prevent plus block free radicals chain processes [5].

Ceruloplasmin, a glycoprotein that can oxidize multiple copper ions, is found in human serum. The liver cells primarily produce ceruloplasmin (CP), later it is released through the bloodstream to contact other organs plus tissues. CP transports (forty-seventy) percent of the copper (Cu) present in plasma and ceruloplasmin promote the conversion from Fe^{2+}/Cu^{1+} to Fe^{3+}/Cu^{2+}, which are observed as less toxic ion forms, Also, CP is involved in an antioxidant defense system and iron metabolism [6, 7].

Except for the yeast, living cells comprise ferritin, a multimeric protein that forms a nanocage configuration and can hold up to 4500–5000 Fe atoms. In addition to serving as a Fe store, ferritin also serves a variety of other roles, such as regulating cells' Fe levels, protecting against oxidative stress (OS), and sequestering Fe from invading pathogenic organisms [8].

Vitamins B is crucial coenzymes plus cofactors in many metabolism processes, & current research suggests that they are also crucial for maintaining immunological equilibrium [9].

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Thiamine, riboflavin, niacin, pantothenic acid, pyridoxine, biotin, folic acid, plus cobalamin, are among the (8) water-soluble vitamins in the vitamins B family [10]. The Vitamin B family includes the chemoprotective micronutrient folic acid (also called vitamin B9) and its derivative, which are commonly referred to as folates. They are water-soluble vitamins that contribute to the manufacture of nucleotides and methylation responses, 2 kinds of enzymatic responses that are necessary for the essential physiological activities of deoxyribonucleic acid production, deoxyribonucleic acid repair, plus deoxyribonucleic acid methylations [11]. Vitamin B_{12}, also known as cyanocobalamin, is a little water-soluble vitamin that is essential for deoxyribonucleic acid production, methylations, erythropoiesis, and cell metabolism. It is a coenzyme that is used by L-methyl malonyl-coenzyme A mutase and methionine synthase [12].

Trace elements are substances that play a critical role in cellular activity. These substances serve as co-factors for numerous enzymes and regulating centers for the shapes of proteins and enzymes [13]. Several trace elements, including zinc (Zn), are important for the body's metabolism activities & are found in the composition of numerous enzymes. Zinc is necessary for the production of deoxyribonucleic acid, ribonucleic acid transcription, cells divisions, and proliferation. Zinc can alter telomerase function in tumor cells [14]. Copper (Cu) is a trace element that is a co-factor for the above Thirty enzymes. Serum Copper concentrations are higher in carcinoma sufferers & are linked to the degree of the illness and how the effective treatments work [15]. For the enzymes implicated in adenosine triphosphate formation (mitochondrial chain complex), deoxyribonucleic acid production (ribonucleotide reductase), antioxidant defense (catalase and peroxidase) , oxygen transfer, and numerous other processes, iron (Fe) is an essential trace element. The capacity of Fe to lose and gain electrons between its oxidized Fe^{3+}-ferric- and Fe^{2+}-ferrous-forms allows it to take part in processes that produce free radicals [16]. The goal of this paper was to evaluate CP, FR, $VitB_{12}$, FA, Zn, Cu, and Fe parameters in sera of acute myeloid leukemic patients (before and after chemotherapy) and correlate with control groups.

Subjects and methods

The study population includes (120) (female and male), their ages are between (18–70 years old) acute myeloid leukemic patients (before and after taking chemotherapy) (Cytosor, Daunorubicin, Decitabine, Dacogen,Cytarabine, Vidaza, Cladribine, and Azacitidine they were used as a chemotherapy) as well as (40) healthy (female and male), their ages are between (18–70 years old) who serve as the control group. About (160) blood samples of males and females were collected from an equivalent number of clinically diagnosed to be acute myeloid leukemia (AML) patients in Erbil's Nanakali hospital and the control group in the period between August (2021) and February (2022). They were classified into four groups: Group 1 (G1) include (40) healthy control group, Group 2 (G2) include (40) acute myeloid leukemic patients before taking chemotherapy (new case), Group 3 (G3) include (40) acute myeloid leukemic patients taking chemotherapy for one cycle, and Group 4 (G4) include (40) acute myeloid leukemic patients taking chemotherapy for more than one cycle. A blood sample was collected in the serum-separating tubes for each group, and serum was separated via centrifugation at 4000 rpm for ten minutes, which was divided into small portions and kept frozen at (-40ºC) until further investigation. A blood sample was used for the determination of ceruloplasmin, ferritin, Vitamin B_{12}, Folic acid, Zinc, Copper, and Iron.

Ceruloplasmin (CP)

The serum ceruloplasmin was estimated by using the Human ceruloplasmin ELISA Kit (SUN LONG Biotech Co., LTD, China) and Elisa (Biotek, USA).

Ferritin

The serum ferritin was determined by Roche diagnostics, GmbH. using the (Roche, Germany) Elecsys Ferritin Cobas kit, which is done by using of Roche/Hitachi fully automated immunoassay analyzer (Elecsys and Cobas e analyzers (Cobas e 411), Germany) REF kit (**03737551** 190) [17, 18].

Vitamin B_{12}

The serum Vitamin B_{12} was determined by Roche diagnostics, GmbH. using the (Roche, Germany) Elecsys Vitamin B_{12} II Cobas kit, which is done by using of Roche/Hitachi fully automated immunoassay analyzer (Elecsys and Cobas e analyzers (Cobas e 411), Germany) REF kit (**07212771** 190) [19-21].

Folic acid

The serum folic acid was determined by Roche diagnostics, GmbH. using the (Roche, Germany) Elecsys Folate III Cobas kit, which done by using of Roche/Hitachi fully automated immunoassay analyzer (Elecsys and Cobas e analyzers (Cobas e 411), Germany) REF kit (**07559992** 190) [22, 23].

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Zinc

The serum zinc was estimated by Colorimetric test, using the (Centronics GmbH/Germany) Zinc fluid Monoreagent kit, and ((UV-Vis) spectrophotometer model 752, China) REF kit (ZF01000050) [24].

Copper

The serum copper was estimated via the Quantitative Colorimetric method, using the (LTA s.r.l., Italy) copper kit, and ((UV-Vis) spectrophotometer model 752, China) REF kit (CC02150) [25, 26].

Iron

The serum iron was determined by Roche diagnostics, GmbH. using the (Roche, Germany) Iron Gen.2 Cobas kit, which is done by using of Roche/Hitachi fully automated immunoassay analyzer (COBAS INTEGRA/ Cobas c systems, Germany) REF kit (03183696 122) [27, 28].

Statistical analysis

The software program Graph Pad-Prism (version 8) and Microsoft excel 2016 were used for data analysis. The results of the data are mean with standard error and probability (P-value). The p-value ≤ 0.05 = significant, p-value > 0.05 = non-significant, p-value ≤ 0.001 = high significant. Ordinary one-way ANOVA test was used for multiple comparisons between the healthy control group and patients The area under the curve (AUC) for the diagnostic accuracy in leukemia patients was calculated using ROC curve (Receiver operating characteristic) analysis. The correlation coefficient was used for the estimation of the correlation between ceruloplasmin with ferritin, vitamin B_{12}, folic acid, Zn, Cu, and Fe in the patient's group.

Results and discussion:

The serum concentrations of ceruloplasmin, ferritin and vitamin B_{12} in each group are shown in Table 1 and Fig.1.

Table 1: Serum concentrations of CP, FR, and Vit B_{12} in control and patient groups.

Groups	CP (pg/ml) Mean ± S. E	P	P*	FR (ng/mL) Mean ± S. E	P	P*	Vit B12 (pg/mL) Mean ± S. E	P	P*
G1	141.1 ± 5.913			132.2 ± 17.66			274.3 ± 11.99		
G2	352.1 ± 11.65	S		1574 ± 81.28	S		964.8 ± 60.50	S	
G3	259.4 ± 7.688	S	S	988.2 ± 43.89	S	S	760.7 ± 25.32	S	S
G4	260.3 ± 12.41	S	S	1491 ± 104.2	S	N. S	691.1 ± 76.91	S	S

Where: G1: Group 1 (control Group), G2: Group 2 Patients group (before chemotherapy-new cases), G3: Group 3 (Patients group after chemotherapy- one cycle), and G4: Group 4 (Patients group after chemotherapy-more than one cycle), CP: ceruloplasmin, FR: ferritin, and VitB12: Vitamin B12, P: Probability between G1 and G2, G3, G4, P*: Probability between G2 and G3, G4, S: Significant, N.S: Non-Significant.

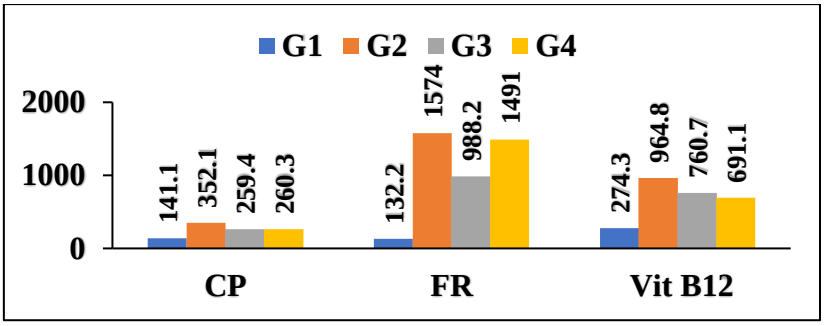

Figure 1: CP, FR, and Vit B_{12} concentration in sera of AML patients' group (before and after taking chemotherapy) with the healthy control group.

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The concentration of Ceruloplasmin for all studied groups was shown in table 1 and figure 1, The mean± S.E of CP in G1 was (141.1 ± 5.913), G2 was (352.1 ± 11.65), G3 was (259.4 ± 7.688), and for G4 was (260.3 ± 12.41). The data was shown a highly significant increase of CP in all group patients (G2, G3, and G4) when compared with G1. Also, there was a higher significant decrease of CP in G3 and G4 when compared with G2.

Ceruloplasmin a mammalian ferroxidase is a glycoprotein binding with copper, which has antioxidant properties due to its capability to react with scavenging toxic oxygen species such as hydrogen peroxide and superoxide. The higher formation of ROS plays a role in the pathogenesis of various human diseases such as atherosclerosis, allergy, and cancer [6, 29, 30]. Based on previous literature, it's clear that our finding is in agreement with Al-Kazzaz, 2011. Al-Kazzaz described a significant increase in serum CP levels among AML patients, a comparative study between these patients and healthy subjects revealed a higher level of CP among AML patients. This is because the increased serum level of CP results from its increased synthesis by the liver and is secreted into the bloodstream to reach other tissues. One of the acute phase proteins, CP, sees a rise in concentrations with several diseases, including malignancies [31, 32].

The mean ± S.E of Ferritin for G1 was (132.2 ± 17.66), G2 was (1574 ± 81.28), G3 was (988.2 ± 43.89), and G4 was (1491 ± 104.2). This table, there were shows that the concentrations of ferritin statistically highly significant increase in all AML patient groups than the control group. In addition, there is a highly significant decrease in G3 when compared with G2, and a non-significant decrease in G4 when compared to G2.

A study of the serum ferritin level is utilized to identify Fe overload, particularly in cases of hematological malignancy undergoing chemotherapy or repeated blood transfusions [33]. The level of ferritin is significantly higher increase at AML diagnosis newly. Under several pathological conditions similar to liver damage, malignant tumor, inflammation, etc., the significant increase in the level of serum ferritin shows the severity of the disease rather than the quantity of stored Fe and these results are consistent with previous reports [34, 35]. Additionally, higher ferritin levels upon identification might be an indicator of malignancy load in acute myeloid leukemia patients & a poorer predictor of event-free survival in the high-risk group [36]. Tachibana et al stated that ferritin at diagnosis is not influenced via Fe overload or chemotherapy and simply reflects the clinical properties of acute myeloid leukemia [36].

The mean ± S.E for Vit.B_{12} in G1 was (274.3 ± 11.99), G2 was (964.8 ± 60.50), G3 was (760.7 ± 25.32), and G4 was (691.1 ± 76.91). In table 2, we observed that there was a high significantly increased in G2, G3, and G4 when compared with G1, while G3 and G4 were statistically significantly decreased as compared with G2.

Vitamin B_{12} is the only vitamin that does not present in plant sources but exists in dietary sources such as shellfish, fish, meat, and milk [37]. Also, Vit B_{12} is formed by bacteria in the human colon [38]. Vitamin B_{12} is required for normal cell division, and its deficiency reasons many diseases such as macrocytic anemia, and megaloblastic anemia [39].

The findings of our research were in line with Liu et al. Liu et al show that patients with liver illnesses and leukaemia frequently have elevated vitamin B_{12} levels, suggesting that this could be a useful indicator for the diagnosis of the condition. Vitamin B_{12} metabolism was faulty in leukemia patients, and excessive vitamin B_{12} levels could encourage the formation of leukemic cells, which might be prevented by a vitamin B_{12} antagonist [34]. Our finding disagrees with a previous study that was done by Goff and Levyq, in which the vitamin B_{12} tests display outcomes within the normal range [40].

The concentration of folic acid in patient groups and control group are illustrated in Table 2, and Fig. 2.

Table 2: Folic acid concentration (ng/mL) in all studied groups

Groups	FA (ng/mL) Mean ± S. E	P	P*
G1	**4.903 ± 0.2747**		
G2	**3.772 ± 0.1880**	**N. S**	
G3	**3.530 ± 0.4814**	**S**	**N. S**
G4	**2.876 ± 0.2571**	**S**	**N. S**

FA: folic acid

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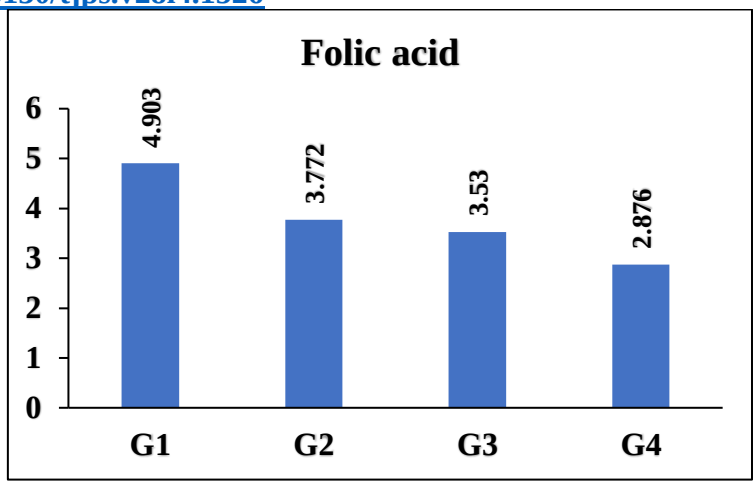

Figure 2: Folic acid concentration (ng/mL) in sera of AML patients with control groups.

Table 2 and Figure 2, show the concentration of folic acid in patient groups and control group. The mean ± S.E of FA for G1 was (4.903 ± 0.2747), G2 was (3.772 ± 0.1880), G3 was (3.530 ± 0.4814), and G4 was (2.876 ± 0.2571). There was a statistically non-significant decrease of folic acid in G2 when compared to G1, while a significant decrease of folic acid in G3, and G4, when compared with the control group, was detected.

Folic acid functions as a cofactor in the one-carbon metabolism of deoxyribonucleic acid production and deoxyribonucleic acid methylation. A lack of certain micronutrients might interfere with one-carbon metabolism, increasing the risk of hematologic malignancy [41]. Particularly, a deficiency in folic acid can cause deoxyribonucleic acid damage and result in chromosome disorders, which are known to be a marker of malignancy and leukaemia [11]. Our results revealed a lower concentration of folic acid in AML patients; this outcome was in agreement with Liu et al in 2011. The active state of acute leukemia and malignant loads may be correlated with reduced levels of folate [34]. In addition, decreased levels of folic acid in AML patients may be due to using chemotherapy for these patients.

The serum concentrations of trace elements such as zinc, copper, and iron in patients and control groups are described in Table 3 and Fig.3.

Table 3: Serum concentrations of Zn, Cu, and Fe in control and patient groups.

Groups	Zn (µg/dL) Mean ± S. E	P	P*	Cu (µg /dL) Mean ± S. E	P	P*	Fe (µg/dL) Mean ± S. E	P	P*
G1	132.9 ± 2.304			135.2 ± 1.779			78.25 ± 5.319		
G2	128.1 ± 5.622	N. S		129.9 ± 3.884	N. S		109.7 ± 11.21	S	
G3	112.9 ± 3.528	S	N. S	126.5 ± 4.770	N. S	N. S	117.9 ± 5.638	S	N. S
G4	114.8 ± 4.806	S	N. S	123.2 ± 1.650	N. S	N. S	96.58 ± 7.946	N. S	N. S

Zn: Zinc, Cu: Copper, and Fe: Iron

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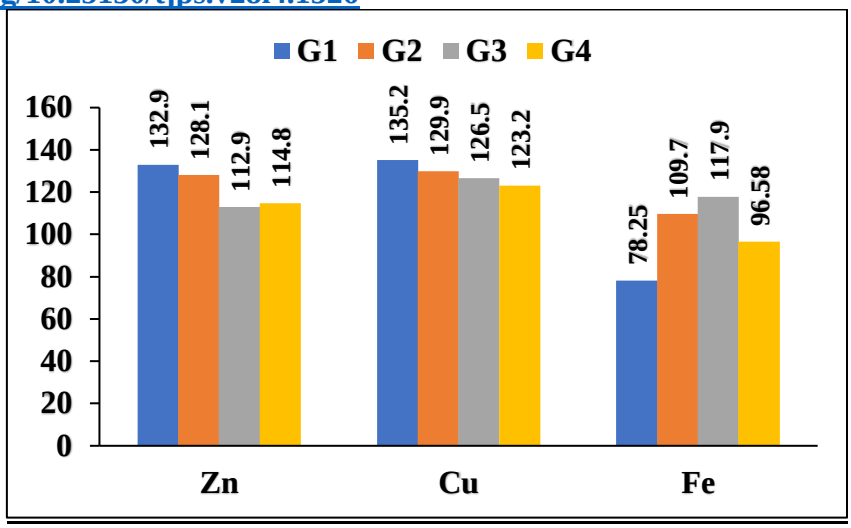

Figure 3: Zn, Cu, and Fe concentration in sera of AML patients' group (before and after taking chemotherapy) with the healthy control group.

Table 3 and Figure 3 show the concentration of zinc in the AML groups and the control group. Mean ± S.E for Zn in G1 was (132.9 ± 2.304), G2 was (128.1 ± 5.622), G3 was (112.9 ± 3.528), and G4 was (114.8 ± 4.806). This data shows that there was a non-significant deceased in G2 when Compared with G1, while G3 and G4 were statistically highly significantly decreased as compared with G1. In addition, G3, and G4 were non-significantly lower than G2.

Zinc is a necessary trace element with a variety of basic physiological actions, including anti-inflammatory and apoptosis properties [42]. Zinc is a co-factor of deoxyribonucleic acid damages responsive proteins, and evaluated malignancy risk have been linked with deficiency of micronutrients. zinc is a trace element, which impacts the proliferation and impacts development, and integrity of the immunological process. Also, zinc acts as an antioxidant and plays a role in the protection against oxidative stress (OS) in organisms [43]. Zn also takes a role in the production and breakdown of lipids, proteins, carbohydrates, and nucleic acids [44]. Due to zinc's participation in numerous immunological processes, a Zn deficit causes natural killer cell dysfunction, decreased biological immunological systems activities, including decreased phagocytosis, and decreased lymphocyte quantity and activity [45]. Serum levels of Zinc in acute myeloid leukemic patients for our study were significantly lower than in healthy control subjects, this finding were agree with some previous studies [46]. Although the precise processes through which zinc deficiency promotes tumorigenesis are unknown and understudied, substantial evidence indicates that raising dietary or supplemented Zn not only helps malignancy prevention but also has the potential to reduce the number of already existing cancers. Additionally, data suggest that acute myeloid leukemia has abnormalities in the DNA damage response [47]. Asfour et al and Olaniyi et al. also compared the levels of Zn AML patients with healthy control individuals; they found no statistically significant difference in serum zinc between patients and controls either before or after induction chemotherapy. This can be attributed to Zn mobilization from tissues in response to chemotherapy [48, 49].

The mean ± S.E of Cu in G1 was (135.2 ± 1.779), G2 was (129.9 ± 3.884), G3 was (126.5 ± 4.770), and G4 was (123.2 ± 1.650). A statistically non-significant decrease in G2, G3, and G4 was detected when compared with G1. On the other hand, a non-significant decrease found in G3, and G4 when compared with G2 found.

Copper is an essential element for various metalloenzymes such as albumin, CP, bis-histidine complex, α-2-macroglobulin, cytochrome oxidase, and dopamine hydroxylase. In normal situations, about 96% of serum Cu is bound to CP [50, 51]. The imbalance in Cu levels, either deficiency or overload, was associated with various diseases such as thrombocytopenia, anemia, neutropenia, cancer aggressivity, and tumor development. These changes might be due to chemotherapy as well as changing lifestyle of AML patients toward healthy eating nutrition [52]. Serum levels of copper non significantly decreased in AML patients before and after chemotherapy when compared with the healthy control group, this may be due to using chemotherapy as a treatment [50]. Our data is agree with a study that was done by [46]. While our data disagreed with the result of Valadbeigi et al, they found that the serum levels of Cu increase in AML patients when compared with healthy control subjects [14].

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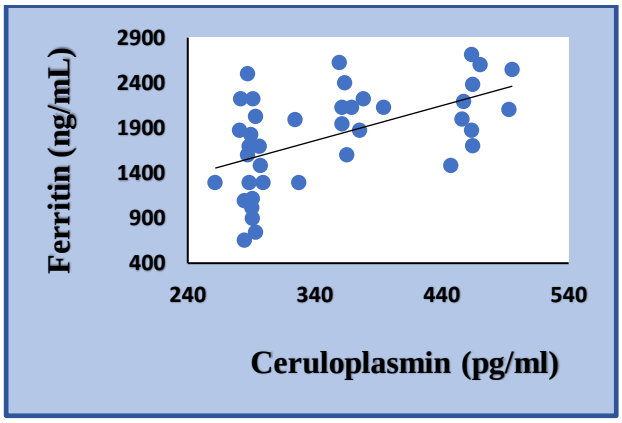
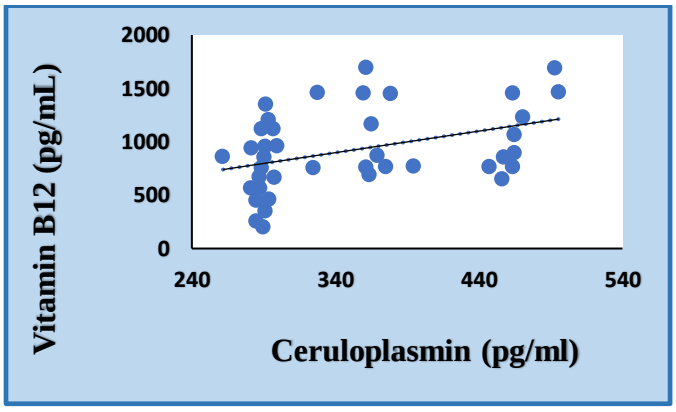
The mean ± S.E for Fe in G1 was (78.25 ± 5.319), G2 was (109.7 ± 11.21), G3 was (117.9 ± 5.638), and G4 was (96.58 ± 7.946). There is a highly significant increase in G2, and G3 when compared with G1, and G4 non-significant increase when compared with G1. While a non-significant increase in G3 and a non-significant decrease in G4 when compared with G1 were found.

Iron promotes cell growth, and proliferation, and causes OS damage. The overload of Fe and dysregulation of Fe metabolism are carefully linked with the occurrence and development of leukaemia. In particular, excessive iron accumulation accelerates the development of leukaemia because of iron's oxidative effects & its harmful effects on deoxyribonucleic acid [53]. Elevated levels of Iron, which are directly linked to transfusion, can aggregate in several organs and have harmful impacts on the heart and liver. In acute myeloid leukemic patients, iron overload begins earlier; the difference vanishes after six months of chemotherapy. It is vital to stress that iron overload, particularly in cases of acute myeloid leukemia, is a significant contributor to pretransplant illness [54]. Our detections showed that Fe levels were significantly higher in the acute myeloid leukemic patients than in the healthy control subjects. Yokus et al also confirmed the results above, where noted that the levels of Fe are significantly higher in the acute myeloid leukemic patients than in the healthy control subjects. The slightly enhanced plasma level of superoxide activity, which released Fe^{2+} from ferritin and catalyses the generation of hydroxyl radicals from H_2O_2 via the Haber-Weiss process, may be the cause of the reported slightly increased level of Iron. Additionally, this breaks down lipid peroxides into radicals called peroxyl and alkoxyl, which help lipid oxidation propagate.

The correlation relation between CP and FR showed there is a positive correlation relation (r=0.5401) (P-value = 0.0003), which was statistically highly significant showed in figure 4A. In addition, figure 4B showed a statistically significant positive correlation between CP and Vit.B_{12} (r=0.4009) (P-value =0.0104), and figure 4C showed a statistically non-significant negative correlation between CP and FA (r= -0.2059) (P-value = 0.2023). Figure 4D showed a statistically non-significant negative correlation between CP and Zn (r= -0.2917) (P-value = 0.0678), figure 4E showed a statistically non-significant negative correlation between CP and Cu (r= -0.1753) (P-value = 0.2793), and figure 4F showed a statistically significant positive correlation between CP and Fe (r= 0.4181) (P-value = 0.0073).



A



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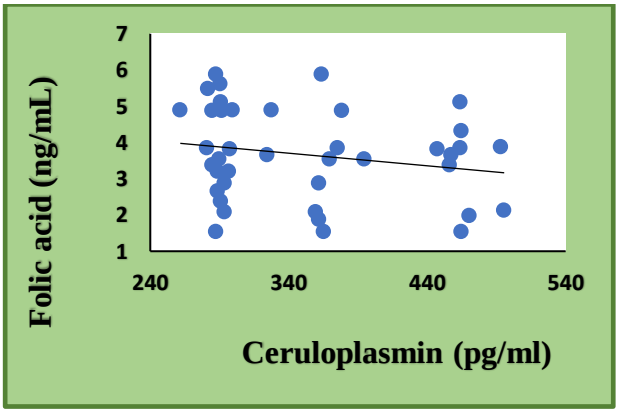

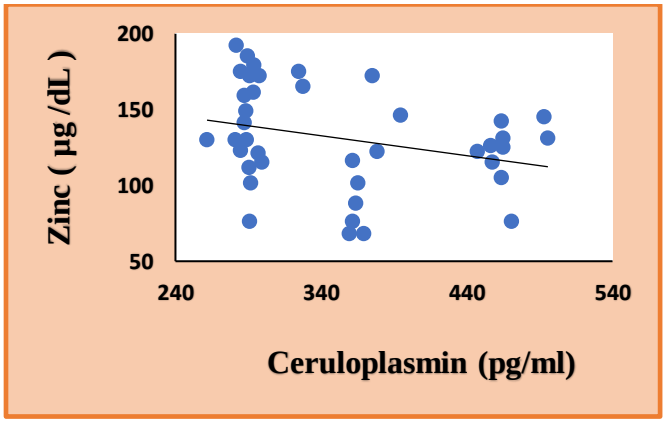

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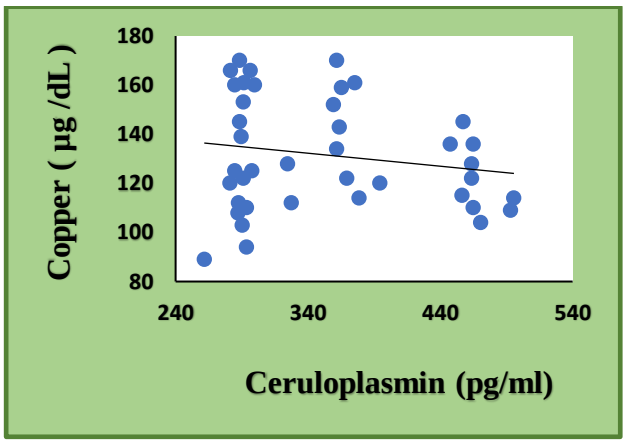
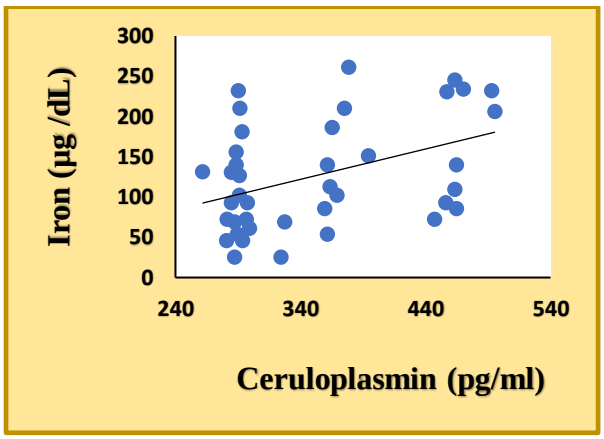
C



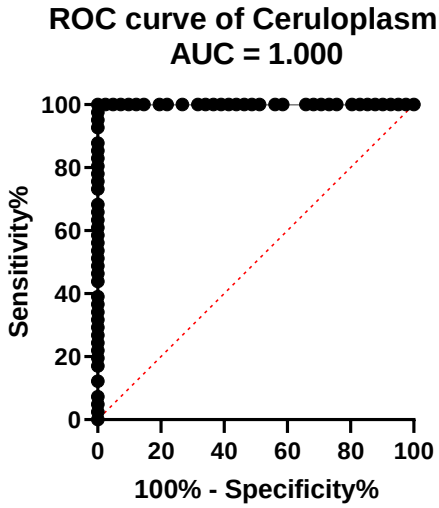
D



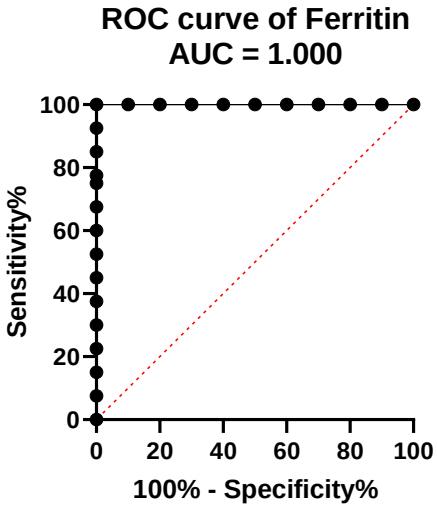
E F

Figure 4: A- Correlation between CP and FR, B- Correlation between CP and Vit.B_{12}, C- Correlation between CP and FA, D- Correlation between CP and Zn, E- Correlation between CP and Cu, F- Correlation between CP and Fe.

Figure.5A, 5B, 5C, 5D, 5E, 5F, and 5G display the receiver operating characteristic curve (ROC) curve of ceruloplasmin, ferritin, vitamin B_{12}, folic acid, zinc, copper, and iron performance as a potential diagnostic marker for AML. A high area under the curve (AUC=1.000) suggests that testing for ceruloplasmin, ferritin, and vitamin B_{12} were excellent biomarkers and could help detect AML patients and a high area under the curve (AUC = 0.8425), this means that folic acid is a very good biomarker for detecting AML patients. Also, the area under the curve (AUC = 0.7831, 0.7863) means that copper and iron were good biomarkers while (AUC = 0.6984) mean zinc is not a good biomarker for the detection of AML patients.



A



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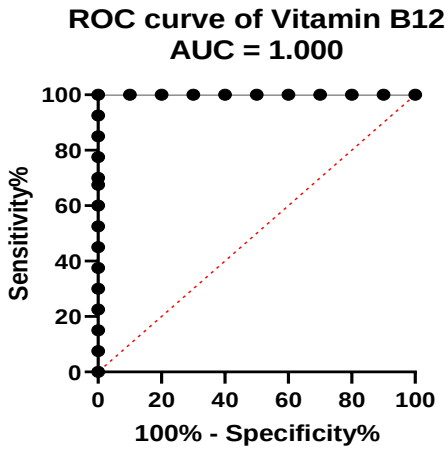

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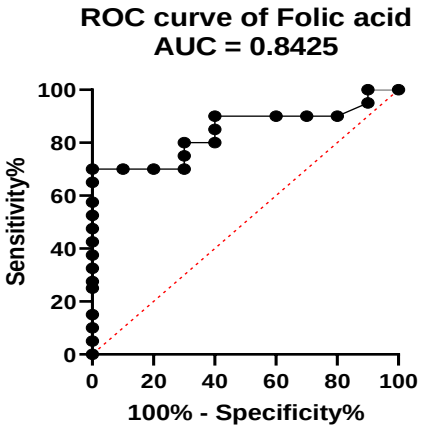

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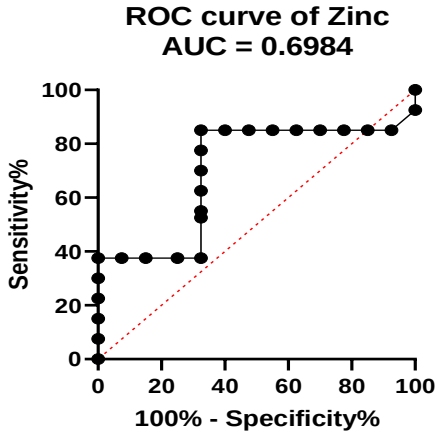
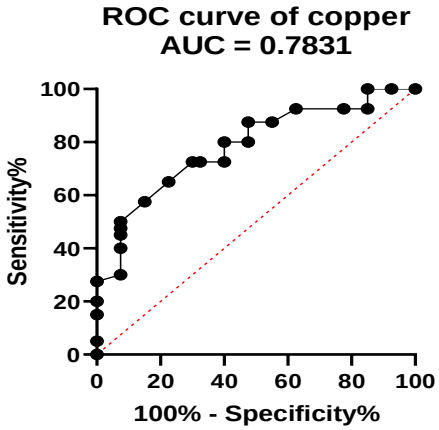
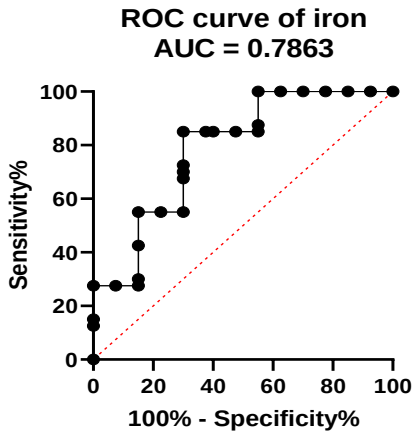


E



F



G

Figure 5 (A, B, C, D, E, F, and G): ROC curve illustrates the sensitivity and specificity of ceruloplasmin, ferritin, vitamin B_{12}, folic acid, zinc, copper, and iron for the detection of acute myeloid leukemia.

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Conclusion

Our detections in this research propose that there was a significant increase in serum concentration of ceruloplasmin, ferritin, vitamin B_{12}, and iron in all patient groups when compared with control groups. While the serum concentration of folic acid, zinc, and copper was decreased in all patient groups when compared with the control. There was a significant positive correlation between ceruloplasmin levels with ferritin, vitamin B_{12}, and iron, on another hand there was a non-significant negative correlation between ceruloplasmin with folic acid, zinc, and copper. A relatively high AUC suggests that testing for CP, FR, Vit B_{12}, and iron, could help detect AML, while a low AUC suggests that testing for zinc is not a good biomarker for the detection of AML disease.

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