Available online at **www.joac.info**

ISSN: 2278-1862

Journal of Applicable Chemistry

2017, 6 (3): 433-447

(International Peer Reviewed Journal)

Assessment of the Cellular Balance for Production of Oxidants – Antioxidants In Serum Samples of Patients with Advanced Stages of Cancer Tumors

Noor Sabah Matlab and Rasha Hasan Jasim*

*Department of Chemistry, Factually of Education for Girls, University of Kufa, **IRAQ**

Email: dr.rashahussainee@yahoo.com

Accepted on 24th May 2017, Published online on 27th May 2017

ABSTRACT

Carcinogenesis is a chronic and multistep process, resulting from mutagenic damage to growth-regulating genes and their products, that ultimately leads to development of invasive or metastatic cancers. Under normal conditions ROS and RNS are produced. This production balanced by number of acceptor electron molecules that synthesized cellular. An injured tissues caused by disorders in the balance between the production of reactive species of known as free radicals and antioxidants which is the defensive mechanism, through this status the raise in the oxidation processes will occur in contrast to the reduction in the synthesis of defense molecules. 201 patients with malignant tumors, 74 patients with different benign tumors and, 83 healthy individuals were enrolled in the present study. Evaluation of the MDA concentrations revealed a significant increase ($p < 0.05$) in patients of malignant tumors when compared with those of benign tumors and healthy individuals. According to ANOVA test, significant differences ($p < 0.05$) were noticed at the two tumoral groups (malignant and benign) were compared together, when both of ceruloplasmin oxidase activity and concentration were examined. Statistical analysis of ceruloplasmin oxidase activity of malignant tumor cases as well as benign tumor cases compared to healthy persons failed to show same findings. MDA levels is affected during malignancy and treatment. Cp acts as acute phase protein in response to cancer occurring and invasion, in addition to it's an antioxidant role to accommodate the overflow of electrons (free radicals) formed during the malignancy.

Keywords: Cancer, oxidative stress, MDA, Cp.

INTRODUCTION

Specifically; cancer is a genetic disorder consequent uncontrolled and abnormal genetic changes [1], it is the main cause of death in economically developed countries and the second leading cause of death in poor countries. The heaviness of cancer is increasing in economically developing countries in consequence of growth and population aging also increasingly, an adoption of cancer-associated lifestyle choices including smoking, physical inactivity, and type of diets [2].

Cellular, about 1-3% of the inhaled oxygen human turn into **Reactive Oxygen Species** (**ROS**)[3], these species divided into two groups: ***Free Radicals*** such as superoxide radicals, and ***Non Radical*** like

hydrogen peroxide. The essential source of the cellular ROS is **mitochondria** where continuous production of ROS takes place. When the result of the electron transport chain which can be found in the mitochondrial membrane, which is important for the energy production inside the cell [4, 5]. Moreover, several cytochrome 450 enzymes are also known as stimulators for ROS production [6]. In addition to their production inside cells which can happen by numerous mechanisms, ROS can be found in the environment, such as in pollutants, tobacco smoke, iron salts, and radiation [3, 7]. Normally, cells protect themselves against damage by ROS and other radicals "like reactive nitrogen species (RNS)" through **repair processes, compartmentalization** of free radical production, **defense enzymes,** and **endogenous and exogenous antioxidants (free radical scavengers).** The defense enzyme superoxide dismutase (SOD) removes the superoxide free radical. Catalase and glutathione peroxidase remove hydrogen peroxide and lipid peroxides. Vitamin E, vitamin C, and plant flavonoids act as antioxidants [8]. Oxidant and antioxidant are very important species in metabolic processes, signal transfer and regulation of cellular functions, therefore, each cell in the human body reservation condition of the balance between the oxidant and antioxidant species [3]. Hyperactivity in the oxidation pathways may lead to cellular stress, then,

Cellular Oxidative Stress occurs when the rate of ROS generation exceeds the capacity of the cell for their removal, so it is a disorder in the balance between free radicals (ROS) and antioxidant defense mechanisms, which can be described as predilection of the oxidant environment, so that can lead to a discomfort in the balance between oxidant-antioxidant compounds [3, 9].

Oxidative stress can cause injury to numerous cellular components such as proteins, DNA and membrane lipids, which confirms it participating role in the most of physiological and pathological processes, that involve DNA damage, proliferation, cell adhesion, and survival [10]. In addition to, there are many experimental and clinical information that are highlighted enough prove responsible of a large number of pathological states including: Atherogenesis, cerebrovascular disorders, emphysema bronchitis, ischemia/reperfusion injury, Duchenne-type scular, neurodegenerative disorders dystrophy, amyotrophic lateral sclerosis (Lou Gehrig's disease), pregnancy/preeclampsia, Alzheimer's disease, Down's syndrome, alcohol-induced liver disease, Ischemia/reperfusion injury following stroke, hemodialysis, Oxphos diseases (mitochondrial DNA disorders), diabetes, multiple sclerosis, acute renal failure, Parkinson's disease, aging, retrolental fibroplasias, and cancers [8]. There are complex interactions between ROS generation, ROS signaling, ROS-induced damage, and carcinogenesis. ROS responsible for regulatory pathways in cells and variety aspect of signaling pathways induced by oxidative stress cross-links and single or double-stranded DNA break by ROS. There are cancer-causing pathways lead to DNA damage such as induction of signal transduction pathways, arrest or induction of transcription, replication errors, and genomic instability [11, 12].

Malondialdehyde (**MDA**) is ***bisdimethylacetal*** with molecular weight of 164.2 g mol^{-1}, it consists of three carbons low molecular weight aldehyde and spontaneous breakdown product of peroxides that can be produced from free radical attack on poly unsaturated fatty acids[13]. MDA is the main product of membrane lipid peroxidation; it can also be generated during prostaglandin biosynthesis in cells [14]. MDA circulates in plasma either bound to protein or in free form. Another portion of MDA is generated in vitro, from decomposition of lipid hydro peroxides during sample preparation. MDA is a significant by-product during enzymatic synthesis of prostaglandin [15]. It can be removed by renal clearance. It plays a significant role in DNA damage, sister- chromatid exchanges and carcinogenesis [16].

MDA is the major metabolite of arachidonic acid and serves as a reliable biomarker for oxidative stress. It is considered as a mutagenic and tumorigenic therefore, it was interesting to determine its activity as a complete carcinogen, a tumor initiator, or a tumor promoter and a co-carcinogenic agent [17-19]. In chronic inflammation MDA elevated because it represents a biomarker to estimation of free radical damage and it is used to measure of ROS [20]. In molecules MDA can combine with several functional groups including proteins, lipoproteins, RNA and DNA. The monitoring of MDA levels in biological materials can be used as an important indicator of lipid peroxidation in vitro and in vivo for various diseases. This will mainly focus on MDA chemistry, biochemistry, routes of formation, detection, and

biological health aspects [14, 21]. The MDA –modified proteins are potentially as deleterious as free MDA, and could be involved in aging as well as in degenerative complications of diseases with increased oxidative stress such as diabetes mellitus, atherosclerosis and cancer [22].

Ceruloplasmin (**EC:1.16.3.1**) is α2-globulinknown as blue oxidases with a molecular weight 132 KDa that binds six copper ions, it contains 90-95% of serum copper [23,24]. It is a metalloenzyme belongs to the iron (II) oxygen oxido-reductase class, and to the multicopper oxidases family, also known as blue oxidases. Ceruloplasmin has a single chain structure; It has a six-domain formula [25]. Human ceruloplasmin has a high homology to type-A domains of clotting factors involving a threefold repeat and those domains 2, 4 and 6 should bind mononuclear coppers with a possible trinuclear site between domains 1 and 6. Ceruloplasmin isoform is synthesized with six atoms of copper incorporated during biosynthesis in the Golgi complex [(26-28)].Serum Ceruloplasmin has a half-life of 5.5 days with little or no exchange of human ceruloplasmin bound copper after synthesis. Although copper has no effect on the rate of synthesis or secretion of ceruloplasmin, failure to incorporate Cu during synthesis results in apo-ceruloplasmin, this apo-protein is rapidly catabolized in 5 h and an unstable with no ferroxidase activity [25]. Predominantly, ceruloplasmin detected in the liver as an apo-form with 1046 amino acids protein, but extra hepatic gene expression has been described in brain, spleen, lung and testes. The amino acid sequence of ceruloplasmin is obtained by protein chemistry and demonstrated abundant expression of the ceruloplasmin gene in the liver [29]. Cp has an important role in hormones and neurotransmitters levels regulation in brain and bloodstream. Ceruloplasmin can be used as substrates epinephrine, norepinephrine, dopamine, DOPA and serotonin. Human ceruloplasmin was described as being related to neurodegenerative processes in humans. In CNS, ceruloplasmin is involved in oxidation of epinephrine and serotonin and the protein was detected in the brain, then the details of its synthesis in glial cells were described [30- 32]. It is expressed in 9neurons and as troglial cells, e.g. cerebral microvascular network involving dopaminergic neurons in substantia nigra. Ceruloplasmin of plasma cannot cross the blood brain barrier because the synthesis of ceruloplasmin is inadequate or its decreased activity in the cells of the CNS is regarded as one of the mechanisms underlying the development of a number of neurodegenerative disorders [25]. Ceruloplasmin plays an important role in the metabolism and development of nervous tissue as its deficiency, its impaired function, or the failure of copper metabolism can lead to severe neurodegenerative diseases as Parkinson's disease, Alzheimer's disease or a ceruloplasminaemia. Serum ceruloplasmin concentration increases during processes of inflammation, infection or trauma as a result of increased gene transcription in hepatocytes mediated by inflammatory cytokines [33, 34]. Previous studies indicate that the Cp has a role in iron homeostasis. It has ferroxidase activity, oxidizing Fe^{2+} to Fe^{3+} and incorporating it into Apo transferrin and has an essential role in iron metabolism (It is involved in iron transport across the cell membrane. This protein oxidizes ferrous iron and incorporates the ferric form into apo transferrin. The role of human ceruloplasmin may be an efficient control of the level of ferrous iron oxidation without the production of hydrogen peroxide as an end product [35]. It is also an acute phase reactant having antioxidant properties and being capable of removing H_2O_2 .However, studies show that this protein can also act as a pro oxidant promoting LDL (low density protein) oxidation. It is known that chloride inhibits human ceruloplasmin ferroxidase activity at pH 5.5, but it is thought that at neutral pH chloride might enhance the oxidase activity of human ceruloplasmin and this enzyme might even exhibit an important role in the oxidation of several substrates present in the serum plasma. A group of scientists showed that such anions as chloride or azide increase the amin oxidase activity of human ceruloplasmin and that this effect is observed with non-iron substrates, while Fe^{2+} oxidation remains unaffected [36-38]. In human body, ceruloplasmin has many functions such as ferroxidase activity, eliminating free iron in the plasma, protecting blood and lipidic membranes from per oxidative damage (antioxidant), and/or mobilizes iron from cells for transporting via transferrin. In addition to that, it's having amine oxidase activity for controlling the levels of biogenic amines in the plasma, spine cord and interstitial fluids and works on the copper transport for metal distribution for extra hepatic tissues [25].

MATERIALS AND METHODS

During the period from the beginning of March 2016 to the end of September 2016; **358** individuals were enrolled in the present study and classified in three groups. **The first group** involved **201** patients with different malignant tumors, while **the second group** included **74** patients underwent benign tumors ***were used as a pathological controls***, and **the last group** included **83** healthy individuals. The enrolled patients (malignant and benign tumors), were collected from several public and private hospitals in addition to centers in Al-Najaf Al-Ashraf governorate; involved: Al-Sadder Medical City, Al-Zahra Teaching Hospital, Al- Ameer Privet Hospital, Al-Ghadeer Hospital, Middle Euphrates Cancer Center, and Daily Specialized Najaf Clinic. Patients with malignant tumors were the basic group of the present study. Cancerous patients group were classified into six general subgroups (**Breast, Lung, Brain, Bladder, Lymphoma,** and **Acute Lymphocytic Leukemia (ALL)**) ***according to the cases that have been followed during treatment with chemotherapy or radiotherapy***

5mL of venous blood samples were collected from the patients and healthy individuals, after fasting period more than 8h. Samples were allowed to clot at lab temperature, centrifuged at 5000 xg for 5 min. Sera were collected and divided to two parts: the first was used for evaluating oxidative stress parameters, and the second part was used for tests of the immunoassay, then these parts were stored at -18˚C until used.Thiobarbituric Acid Reactive Substances (**TBARS**) assay is one of few methods used for estimation of malondialdehyde level.

The *p*-phenylenediamine is a substrate of ceruloplasmin oxidase, so the oxidation process of *p*-phenylenediamine by ceruloplasmin oxidase at moderate acidic media (~5-5.4) to produce colored production made modified Rice method for evaluation of ceruloplasmin oxidase levels[39, 40].

RESULTS AND DISCUSSION

Table 1: Levels of Malondialdehyde Concentration (mM)
In Sera of Tumoral Patients and Controls Subjects (Mean ± S.D.)

Groups (n)	Malondialdehyde Concentration (mM) Mean ± S.D.	Range	*P*
Malignant 201	0.399±0.406	0.016-1.860	0.034 Malignant vs Benign 0.030 Malignant vs Healthy 0.479 Benign vs Healthy
Benign 74	0.263±0.278	0.036-1.161	
Healthy 83	0.227±0.092	0.136-0.408	

When the three study groups were subjected to **Analysis of Variance (ANOVA) test**, the results revealed significant elevation (**$p < 0.05$**) of **Malondialdehyde** levels in patients with malignant tumors when they were compared with those of benign tumor, and healthy controls groups. On the other hand, no-significant variations were observed at benign tumor patients were compared with healthy individuals, as shown in **table 1**.

The sensitivity of malondialdehyde as predictor biomarkers was **94.53%**, on the other hand; this parameter was recorded **93.24%** specificity. With more details, the sensitivity of malondialdehyde as a marker for the present study cancers was seemed to be so approximate when it ranged from 85.71% for bladder cancer to 100% for lung cancer and Acute Lymphocytic Leukemia.

The arise in the level of malondialdehyde at patients with cancerous tumors in comparison to those of benign tumors and healthy controls could be attributed to the abnormal activity of aerobic metabolism as well as surviving pathways in the malignant cells, leads to overproduction of ROS molecules, malondialdehyde especially. ROS excess leads to imbalance in the oxidants-antioxidants system, that promote alteration redox homoeostasis within cell occurring. The rise in the level of malondialdehyde in the neoplasm may be due to reduction in the synthesis of endogenous antioxidant system components, which will cause inefficiency of cellular and extracellular antioxidant defense system.

Elevation of malondialdehyde levels in the serum of patients with cancerous tumors were mentioned in many previous studies, the nearest among them to the present study were: the study of **Badri G.** [41] that was carried out on the oral cancer patients, she proved presence of significant (elevation) difference between oral malignant tumor patients and healthy controls, at malondialdehyde levels were evaluated as a parameter for lipid peroxidation. In the study focused on lung cancer, **RafiqKhan M. and Sellapa S**. [42] found highly significant elevation ($p < 0.001$) in the levels of malondialdehyde at smoker patients with lung cancer in comparison to healthy controls, while this differentiation was less significant ($p < 0.05$) at group of non-smoker patients with lung cancer in comparison to healthy controls. With the same manner **Topdaq S. *et al.***[(43)] found high malondialdehyde concentrations (2.8 ± 1.66 U mol g^{-1} of malignant tissue) in the patients with lung carcinoma in contrast to their levels at controls (1.025 ± 0.59 U mol g^{-1} of healthy tissue).

At 2009 a team of researchers in the University of Baghdad evaluated several of bio parameters, involved malondialdehyde, in the group of female patients with breast tumors, this study revealed significant elevation of this parameter in malignant breast tumor in comparison to benign breast tumors and healthy control [44]. In the Iraqi center for cancer and medical genetic researches, recent study was carried out to evaluate malondialdehyde and glutathione-s-transferase in colorectal cancer and healthy control, this study illustrated a significant increase in malondialdehyde ($p < 0.001$) in the patients group in comparison to healthy controls [45].

Recently, **Lorente L. *et al***[46] recorded high concentrations of malondialdehyde at patients with hepatocellular carcinoma and those of liver transplantation patients in comparison to non tumoral liver diseases. This study recorded malondialdehyde as a survival one year parameter after liver transplantation for hepatocellular carcinoma patients. Local study was carried out in Babylon University on the patients with developing urinary bladder cancer to measure malondialdehyde levels in addition to several trace elements, this study showed significant increase of malondialdehyde concentration at patients when compared to control individuals [(47)]. Same results were recorded at work of **Al-Kufy D**. [48] when malondialdehyde and glutathione levels as biomarkers for oxidative stress. With same manner, **El-Far M.** and his colleagues [49] observed significant increases in the several oxidative stress parameters (malondialdehyde is one of them)in the samples of patients with bladder and renal tumors when compared with their corresponding in the sera of healthy individuals. **Bilal K.** [50] evaluated various biomarkers in the purpose of finding their efficiency as predictors of uterine cancer, this study revealed high malondialdehyde concentrations in serum samples of uterine cancer patients during diagnosis stage when compared with healthy women.

Several lipid peroxidation parameters included malondialdehyde in addition to super oxidase dismutase and several vital cofactors were measured in the Nigerian study applied on patients suffering from acute leukemia, this study showed significant elevation ($p < 0.05$) in the malondialdehyde concentration at patients group when compared to healthy individuals [51]. **Al-Ubadi N. *et al.*** [52] studied levels of some oxidant and antioxidant in samples of patients at 16 years old only who suffered from leukemia, this work demonstrated elevation in the malondialdehyde concentration ($p < 0.01$) and others oxidant parameters in contrast to the levels of several enzymatic antioxidant parameters that were measured in the same work. Same findings (increased of malondialdehyde levels at cancer patients) were shown at malondialdehyde

(as an over-oxidation parameter) and several endogenous non enzymatic antioxidant parameters were evaluated at patients with acute and chronic myeloid leukemia patients [53]. **Al-Hammami S.**[54] designed study for investigating some biochemical parameters (involved malondialdehyde) in the serum and CNS samples of children with acute lymphoblastic leukemia at diagnosis and during chemotherapy. The study showed increase in the concentration of malondialdehyde at patients in comparison to its levels at healthy controls.

On the other hand, the present study disagreed with the study of **Abdel-Salam O.** and his team [55], they recorded significant decrease in the malondialdehyde concentrations at patients with local breast cancer (49.50 ± 2.80µM) and 46.6 ± 1.7µM at patients with metastasis breast cancer comparison with healthy control (62.50 ± 1.70µM).

Generally, **figure 1** shows levels of malondialdehyde in the serum of cancer patients after treatment by chemotherapy or radiotherapy didn't illustrated statistical variations than their corresponding levels before treatment.

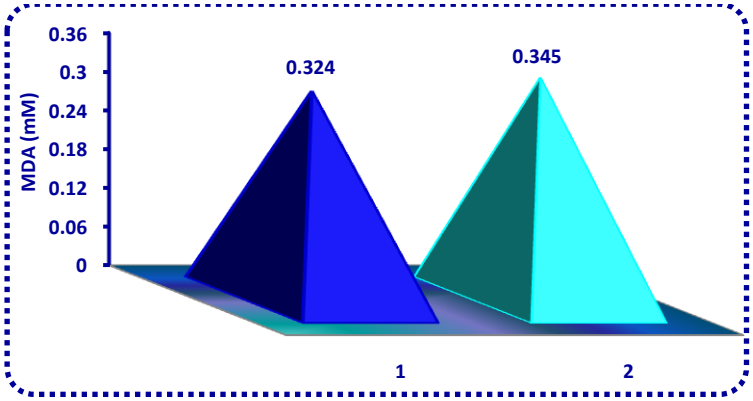

Figure 1: Comparison Levels of Malondialdehyde in The Sera Samples of Cancerous Patients a Detection firstly, then after Treatment with Chemotherapy (Radiotherapy)

General results showed that malondialdehyde concentration after treatment seemed to approximate to those at diagnosis, this result could be explained due to the side effect of induction therapy treatment that act as toxic compound to the malignant as well as normal body cells, cellular injure will occur leading to keep the oxidative stress situation.

Levels of malondialdehyde concentration didn't show statistical significant differences between their levels at diagnosis time (pre-treatment) and after chemotherapy (radiotherapy), the **only exception** was noted at subgroup of patients with **lymphoma**, as shown in **figure 2**.

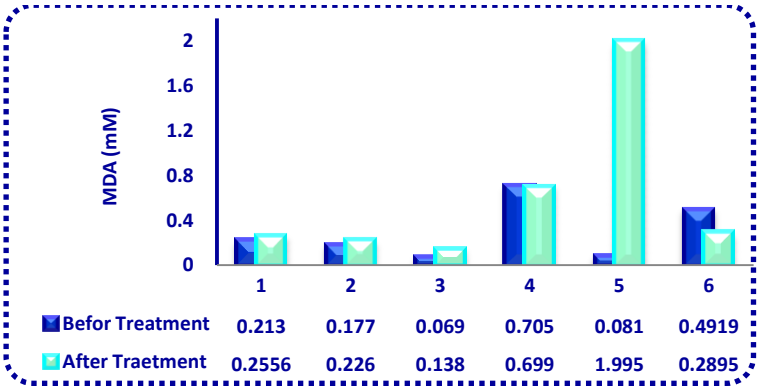

Figure 2: Malondialdehyde Concentration In The Sera Samples of Patients with Different Malignant Tumors at Detection and After Treatment with Chemotherapy (Radiotherapy)

Elevation of malondialdehyde at patients with lymphoma after treatment among the types of tested cancers may be reflex to the activation of immune system caused toxic compounds used in the chemotherapy or radiation with the high frequency in the radiotherapy treatment which caused free radicals overproduction and formation of high levels of malondialdehyde as a final result.

Several previous studies deal with determination of malondialdehyde concentration as one of the important parameters for following cellular oxidative stress during treatment of different cancers with chemotherapy/radiotherapy or combined therapies.

A study to evaluate serum lipid peroxidation and trace elements levels in ovarian cancer patients before and after cisplatin and doxorubicin chemotherapy[56] showed significant decrease ($p<0,05$) in the malondialdehyde concentration after the first course of the chemotherapy, followed by significant increase in their levels after the second course of chemotherapy to achieve to their levels before treatment.

Recent study was carried out to evaluate the effect of radiotherapy on the oxidative stress, biological and hematological parameters in women with breast cancer, results of this study showed no significant increase in the levels of malondialdehyde at the end course of radiotherapy [57]. Same results were recorded at the study of **Al-Sarraf*et al.***[58] which study the effect of valsartan on echocardiographic ejection fraction, brain natriuretic peptide and malondialdehyde in trastuzumab treated females with breast cancer, this study showed a significant decrease in the malondialdehyde after surgical treatment followed by slightly gradual no significant increases in the malondialdehyde concentrations during the treatment courses. These findings agreed exactly with the present study results. On the other hand, outresults of the present study were disagreed with several previous studies, for example: the study of **Thanoon I. *et al***. [59] in which they observed significant increase ($p<0.001$) in the levels of malondialdehyde at women with breast cancer underwent to treatment by surgical interference and chemotherapy, sequently with progress of the chemotherapy doses. While study of **Abdel-Salam O. *et al.***[55] revealed significant decreases in the levels of malondialdehyde at breast cancer women undergoing chemotherapy in the final course of therapy.

According to **ANOVA test,** significant differences (**$p < 0.05$**) were noticed at the two tumoral groups (**malignant and benign**) were compared together, when both of ceruloplasmin oxidase activity and concentration were examined, as shown in **tables 2** and **3**; respectively. Statistical analysis of ceruloplasmin oxidase activity in malignant tumor cases as well as benign tumor cases compared to healthy persons failed to show same findings **(Table 2)**.

Table 2: Levels of Ceruloplasmin Oxidase Activity (U / L) In Sera of Tumoral Patients and Controls Subjects (Mean ± S.D.)

Groups (n)	Ceruloplasmin Oxidase Activity(U / L) Mean ± S.D.	Range	*P*
Malignant 201	117.138±78.186	26.806-383.944	0.046 Malignant vs Benign 0.526 Malignant vs Healthy 0.056 Benign vs Healthy
Benign 74	87.230±27.832	38.394-148.691	
Healthy 83	104.712±31.535	26.806-383.944	

Table 3: Levels of Ceruloplasmin Oxidase Concentration (g / L) in Sera of Tumoral Patients and Controls Subjects (Mean ± S.D.)

Groups (n)	Ceruloplasmin Oxidase Concentration(g / L) Mean ± S.D.	Range	*P*
Malignant 201	33.618±19.398	10.500-83.125	0.048 Malignant vs Benign 0.045 Malignant vs Healthy 0.001 Benign vs Healthy
Benign 74	25.443±15.152	2.625-52.675	
Healthy 83	45.369±10.713	34.125-75.250	

From other side, only ceruloplasmin oxidase concentration levels illustrated good statistical variations (**p = 0.045**) when malignant tumor patients and healthy individuals groups were compared. With same manner, evaluation of ceruloplasmin oxidase concentration revealed high significant differences (**p = 0.001**) when the comparison has been done between benign tumor patients and healthy individuals groups **(Table 3).**
The current study indicated a decrease in the concentration of the excreted enzyme in the malignant tumor patient samples compared with the marked increase in the ceruloplasmin oxidase activity as noted in the **tables 2** and **3**; respectively. These findings can be explained based to the different roles of this enzyme. Deficiency in the concentration of ceruloplasmin oxidase may be returned to the reduction of manufacture function in the liver which is represented as one of the features of the simultaneous imbalance with the progress of cancer. From other side, an elevation in the activity of ceruloplasmin oxidase could be attributed to the defense role of this enzyme as one of the acute phase proteins against presence of malignant cells, in addition to that, during invasion of malignant tumor, ceruloplasmin oxidase seemed to be more active because of its an antioxidant role, so its elevated levels refluxed the cellular oxidative stress (unbalanced production of ROS) which is associated with carcinogenesis and metastasis. These roles were absent at benign tumors group.

Ceruloplasmin oxidase activity and concentration were evaluated in numerous non tumoral diseases included: immune and iron metabolism disorder [60], Alzheimer's disease [61], Wilson's disease [62], Parkinson's disease (63), systemic zoonotic disease [64], burn and non-burn trauma cases [65], cardiovascular diseases [66], renal diseases [67], and hepatitis virus [68]. Moreover, ceruloplasmin oxidase was assessed in several unsatisfactory cases, i.e.: commonly used methods of contraception [69], pregnancy [70], cigarette smoking individuals [71], diet style [72], and during lactation [73]. Findings of the present work agreed with many previous studies that were carried out in the cancer researches, the nearest among them to present work were: the study of **Gadjeva V. *et al.***[74] that recorded significant elevation ($p<0.001$) in the ceruloplasmin activity levels in patients with malignant hematological diseases in comparison to healthy control. **Abdul-Barry J.** and his team [75] evaluated ceruloplasmin activity and two reheated trace elements in the serum of different malignancies types, they found that levels of this enzyme were arise at cancerous patients especially those with age more than 45 years, and suggested activity of this enzyme as useful marker for measurement of the severity of malignancy. In the bladder cancer, ceruloplasmin activity with other antioxidant enzymes was studied in the plasma samples of 66 patients, this study proved that activity of this enzyme was elevated at smoker and nonsmoker patients in comparison to healthy individuals [76].

Al-Kazzaz F.[77] measurement levels of ceruloplasmin activity in patients with different leukemia types (ALL, AML, and CML) and multiple myeloma before and during treatment, she found significant increase in the activity of this enzyme ($p < 0.05$) in comparison to healthy individuals at same age range. Same findings were recorded by **Mehdi W.** and her colleagues [78] when ceruloplasmin oxidase activity was tested in children with acute lymphoblastic leukemia (ALL) comparing to the activity of this enzyme at healthy children.

Highly significant elevation at $p \leq 0.05$ in the activity of ceruloplasmin oxidase in the serum of patients with liver and lung cancers comprising with control group [79]. When ceruloplasmin oxidase concentrations were evaluated [80] in the group of patients with colorectal cancers high levels of this protein were observed at progressive stages of disease (stage III and IV) in comparison to group of healthy individuals. **Upadhya S.** and his team observed high elevation of ceruloplasmin concentration as one of the acute phase proteins that were examined in the patients with cancer of uterine cervix at primary as well as advanced stages [81]. In a previous study to evaluate ceruloplasmin concentration and CA125 at ovarian cancer patients, this study showed increase in the enzyme concentrations at different stages (prime stages "I, II" and "III, IV" as advanced stage) when compared with healthy individuals, these levels were increased gradually with the invasion of disease [82]. The present work disagreed with **Al-SaadiN.** study that showed no significant decrease in the ceruloplasmin activity levels at patients with colon cancer comparing with controls group [83].

Student's t – test illustrates there are no significant differences in the levels of serum **Ceruloplasmin**

Oxidase Activity at pre- and post- treatment samples of the malignant tumor patients, as shown in **figure 3.**

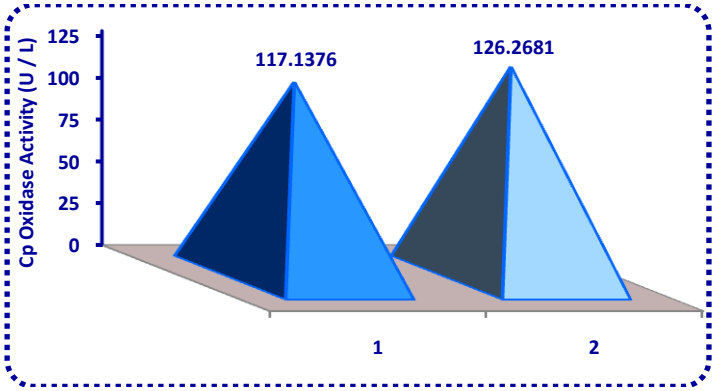

Figure 3: Comparison Levels of Ceruloplasmin Oxidase Activity in The Sera Samples of Cancerous Patients a Detection firstly, then after Treatment with Chemotherapy (Radiotherapy)

The statistical analysis of **Ceruloplasmin Oxidase Concentration** in the pre- and past treatment samples for the patients suffered from different malignant tumors which was done using ***student's t – test*** illustrated that no significant differences between two analyzed groups, as shown in **Figure 4**.

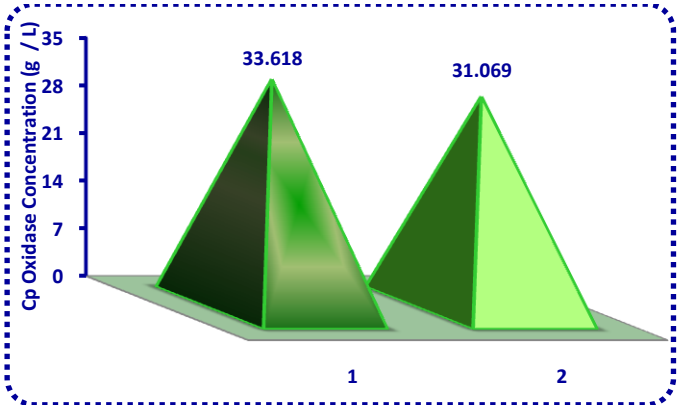

Figure 4: Comparison Levels of Ceruloplasmin Oxidase Concentration in The Sera Samples of Cancerous Patients a Detection firstly, then after Treatment with Chemotherapy (Radiotherapy)

The current study showed approximate levels of activity and concentration of ceruloplasmin oxidase in the malignant tumor samples at diagnoses (pretreatment) and after treatment, as observed in the **figures 3** and **4**, respectively. Activity and concentration of serum ceruloplasmin oxidase after treatment are related to their levels prior of treatment due to the continued of cellular stress that was happen as reflect for exposure to chemotherapy (toxic chemicals) or radiotherapy (high frequency radiation), in this status ceruloplasmin oxidase remains as an extracellular scavenger of free radicals and superoxide ions.

Earlier, many studies have focused on the follow-up of biochemical changes associated with chemotherapy or radiotherapy. **Al-Ghazally M. *et al.*** [80] observed significant elevation in the ceruloplasmin oxidase concentration during treatment with chemotherapy comparison to the enzyme levels at diagnosis of colorectal cancers, while the enzyme concentrations were seemed to be approximate during the treatment period, where this study was designed to compare the enzyme concentration at the first and second dosages. **Gadjeva V. *et al.***[74] mentioned to stay put of plasma ceruloplasmin oxidase concentration (not significant differences at $p<0.05$) in patients with malignant hematological diseases during treatment in comparison to their levels at diagnosis. **Al-Kazzaz F.**[77] study found the levels of ceruloplasmin oxidase activity in the group of different types of leukemia and multiple myeloma, before chemotherapy were significantly higher than that after chemotherapy ($p<0.05$) moreover, the sera of ceruloplasmin oxidase levels of patients who passed away were higher than other patients. **Hegde M. *et al.***[82] observed highly significant decrease in the levels of ceruloplasmin oxidase in the sera samples of women suffered from ovarian cancer after chemotherapy in comparison to their enzyme levels before treatment, these findings were in all of malignant tumor patients regardless stage of malignant tumors, but levels of this enzyme were elevated concurrently with the malignancy progression. Out results of ceruloplasmin oxidase in the current work agreed with most of the previous studies.

Highlight **Ceruloplasmin Oxidase Activity** levels in sera samples of patients with various types of cancers at diagnosis period and after chemotherapy or radiotherapy (**Figure 5**) demonstrates that no significant alterations in the activity of this enzyme when its levels compared using ***Student's t-test***, except **lung cancers patients subgroup** who illustrated a moderate significant decrease in the levels of **Ceruloplasmin Oxidase Activity** after treatment, in addition to that levels of this type of malignant tumors showed the highest levels of examined enzyme activity at the diagnosis. Actually, these results need extensive and separate study; especially results of lung cancer.

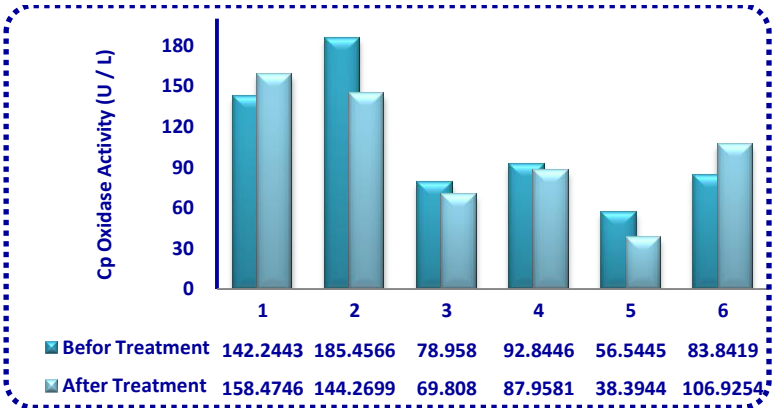

Figure 5: Ceruloplasmin Oxidase Activity in the Sera Samples of Patients with Different Malignant Tumors at Detection and after Treatment with Chemotherapy (Radiotherapy)

Results of the statistical analysis were clearer whenthe levels ofserum **Ceruloplasmin OxidaseConcentration** in the prior and post-treatment were tested using ***student's t-test***, as shown in **Figure 6**. Groups of lung, brain, and bladder cancers illustrated significant decrease in the concentration of this enzyme after treatment with chemotherapy or radiotherapy, while group of patients with lymphoma

showed a significant increase in the concentration of ceruloplasmin oxidase in the post-treatment sera samples, this unusual increase may be caused by aggressive immune response toward toxin chemical used in chemotherapy.

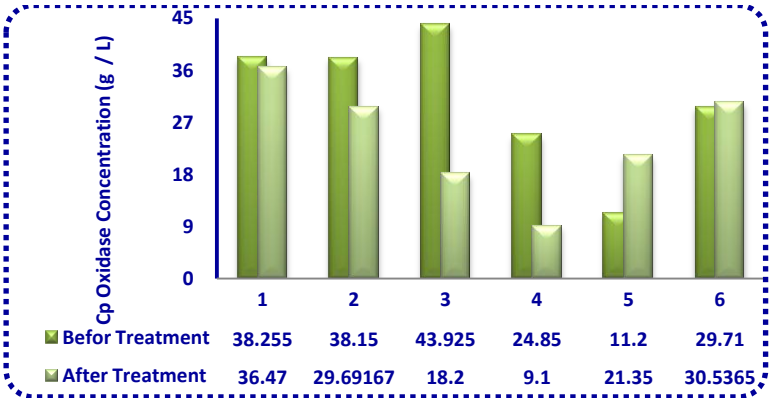

Figure 6: Ceruloplasmin Oxidase Concentration in The Sera Samples of Patients with Different Malignant Tumors at Detection and after Treatment with Chemotherapy (Radiotherapy)

REFERENCES

[1] H D A. Abbas, Physiological and Immunohistochemical Study of Some Biomarkers in Bladder Carcinoma, University of Kufa , faculty of Science, Biology Department, *Thesis*, **2003.**

[2] DVM. Jemal A, F.Bray, M.M.Center, J. Ferlay, E.Ward, D. Forman, Global Cancer Statistic, *CA Cancer J. Clin*, **2011,** 61, 69-90**.**

[3] A.A. Dayem, H.Y. Choi, J.H. Kim, S.G. Cho, Role of Oxidative Stress in Stem, Cancer, and Cancer Stem Cells, *Cancers*, **2010,** 2, 859-884.

[4] C.J.Rhodes, J.Moncol, M. Izakovic, M. Mazur, Free radicals, metals and antioxidants in oxidative stress-induced cancer, *Chem. Biol. Interact*, **2006,** *160*, 1-40.

[5] M. Inoue, M. Nishikawa, A.M. Park, Y. Kira, I. Imada, K. Utsumi, Mitochondrial generation of reactive oxygen species and its role in aerobic life, *Curr. Med. Chem*, **2003,** 10, 2495–2505.

[6] D.V. Parke, Chemical toxicity and reactive oxygen species, *Int. J. Occup. Med. Environ. Health*, **1996,** 9, 331–340.

[7] A. Agarwal, A.A.Mellado, B.J.Premkumar, A.Shaman, S.Gupta, The effects of oxidative stress on female reproduction: a review, *Reproductive Biology and Endocrinology*, **2012,** 10(49), 1-31.

[8] C.Smith, A.D. Marks, M.Lieberman, Oxygen Toxicity and Free Radical Injury In Marks' Basic Medical Biochemistry: A Clinical Approach, 2nd Edition. p: 439.

[9] A.AbdalDayem, H.Y. Choi, J.H. Kim, S.G.Cho, Role of Oxidative Stress in Stem, Cancer, and Cancer Stem Cells, *Cancers*, **2010,** 2, 859-884.

[10] C.K. Pillai, K.S. Pillai, Antioxidants in health, *Int. J. Physiol. Pharmacol*, **2002,** 46, 1–5.

[11] G.Waris, H. Ahsan, Reactive oxygen species: Role in the development of cancer and various chronic conditions, *J. Carcinog*, **2006,** 5, 1–8.

[12] O.A. Martin, S. Nowsheen, S.Siva, K.Aziz, V.I. Hatzi, A.G. Georgakilas, Inflammation and Oxidative DNA Damage: A Dangerous Synergistic Pathway to Cancer In: Cancer: Oxidative Stress and Dietary Antioxidants, 1st Edition. Elsevier Inc. United States of America. p:63-74, **2014.**

[13] N. Tukozkan, H. Erdamar, I. Seven, Measurement of Total Malondialdehyde in Plasma and Tissues by High-Performance Liquid Chromatography and ThiobarbituricAcid Assay, *Fırat.Tıp.Dergisi*, **2006,** 11(2), 88-92.

[14] J. Suwimol, Malondialdehyde (MDA), a lipid oxidation product, *Free Radicals in Biology and Medicine*, **2005,** 77(222), 1 -10.

[15] B H J. Juurlink, Can dietry phase II enzymes induces a melarate disease withan underling chronic inflammatory component to them?, 6th Edition, Internet word congress for Biomedical Sciences, **2000.**

[16] P.H. Saifullah, F.F. Al-Kazzaz, N.N. Zayzafoon, Study of Malondialdehyde Levels in sera, RBCs and Tissues homogenate of Iraqi Women With Breast Tumors, *Baghdad Science Journal,* **2009,** 6 (3), 553-562.
[17] G.H. Badri, Lipid Peroxidation In Oral Cancer, *Basrah Journal of Surgery*, **2003,** 9, 98-100.
[18] R.A. Bitla, E.P.Reddy, K.Sambasivaih, M.M.Suchitra, V.S.Reddy, P V L N S.Rao, Evaluation of Plasma Malondialdehyde as a Biomarker in Patients with Carcinoma of stomach, *Biomedical Research,* **2011,** 22 (1), 63-68.
[19] Z. Singh, I.P. Karthigesu, P. Singh, R. Kaur, Use of Malondialdehyde as a Biomarker for Assessing Oxidative Stress in Different Disease Pathologies: a Review, *Iranian. J. Publ Health,* **2014,** 43(3), 7-16.
[20] M.H. Shohag, M.Ashik Ullah, M.A. Azad, M.S.Islam, S.Qusar, S.F.Shahid, A. Hasnat, Serum Antioxidant Vitamins and Malondialdehyde Levels in Patients with Obsessive-Compulsive Disorder, T*he German Journal of Psychiatry,* **2012,** 1433-1055.10-14.
[21] A.A. Lefta, Biochemical Evaluation of the Levels of Oxytocin, Serotonin and Some Oxidative Stress Parameters in Sera of Patients with Morbid Obesity, University of Kufa, the Faculty of Education for Girls, Department of Chemistry, *Theses*, **2017.**
[22] N M Al-Ubuda, L M. Al-Naama, A.H. Al-Hashimi, Profile study of some oxidant and antioxidant levels in leukemic patients, *The Medical Journal of Basrah University*, **2012,** 30 (2), 115-121.
[23] V.L. Avila, W. H. Robinson, K. Lokits, Ceruloplasmin levels in human sera from various diseases and their correlation with patient's age and gender, Sci. Res. Copyright, **2009,** 1(2), 104-110.
[24] Z L. Harris, L W. Klomp, J.D. Gitlin, ceruloplasminemia: an inherited neurodegenerative disease with impairment of iron homeostasis, *Am J. Clin. Nutr,* **1998,** *67*, 972-977.
[25] D M. Moutinho, Human ceruloplasmin and neurotransmitters: complex stabilization and crystallization, Faculty of Sciences and Technology, Universidad Nova de Lisboa, *Dissertation*, **2013.**
[26] Z.L. Harris, Aceruloplasminemia, *J. Neurol. Sci*, **2003,** *207*, 108-109.
[27] C. G. Holmberg, C.B. Laurell, Investigations in serum copper II, isolation of the coppercontaining protein and a description of some of its properties, *ActaPhysiologica. Scandinavica,* **1948,** *2*, 550-556.
[28] H. Miyajima, Aceruloplasminemia, an iron metabolic disorder, *Neuropathology*, **2003,** *23*, 345-350.
[29] L.W. Klomp, J.D. Gitlin, Expression of the ceruloplasmin gene in the human retina and brain: implications for a pathogenic model in aceruloplasminemia, *Hum. Mol. Genet*, **1996,** 5, 1989-1996.
[30] B. C. Barrass, D. B. Coult, P. Rich, K.J. Tutt, Substrate specificity of caeruloplasmin. Phenylalkylamine substrates, *Biochem. Pharmacol,* **1974,** 23, 47-56.
[31] M C Linder, J.R. Moor, Plasma ceruloplasmin. Evidence for its presence in and uptake by heart and other organs of the rat, Biochim. Biophys. Acta, **1977,** *499*, p: 329-336.
[32] B.N. Patel, R.J. Dunn, S. David, Alternative RNA splicing generates a glycosyl phosphatidyl inositol-anchored form of ceruloplasmin in mammalian brain, *J. Biol. Chem*, **2000,** *275*, 4305-4310.
[33] K. Kaneko, K. Yoshida, K.Arima, S.Ohara, H.Miyajima, T.Kato, M.Ohta, S.L.Ikeda, Astrocytic deformity and globular structures are characteristic of the brains of patients with aceruloplasminemia, *J. Neuropathol. Exp. Neurol,* **2002,** *61*, 1069-1077.
[34] Z. B. Friedenberg C.T. Brighton, Bioelectric potentials in bone, *J Bone Joint Surg Am,* **1966,** *48*, 915-923.
[35] C.D. Vulpe, Y.M. Kuo, T.L.Murphy, L.Cowley , C.Askwith, N.Libina, J.Gitschier, G.J. Anderson, Hephaestin, a ceruloplasmin homologue implicated in intestinal iron transport, isdefective in the sla mouse, *Nat Genet*, **1999,** 21, 195-199.
[36] N. Giurgea, M.I. Constantinescu, R. Stanciu, S. Suciu, A. Muresan, Ceruloplasmin – acutephase reactant or endogenous antioxidant? The case of cardiovascular disease, *Med. Sci. Monit,* **2005** 11, 48-51.

[37] C.K. Mukhopadhyay, B. Mazumder, P. F. Lindley, P. L. Fox, Identification of the prooxidant site of human ceruloplasmin: a model for oxidative damage by copper bound to protein surfaces, *Proc. Natl. Acad. Sci, USA*, **1997**, *94*, 11546-11551.
[38] G. Musci, G.C. Bellenchi, L. Calabrese, The multifunctional oxidase activity of ceruloplasmin as revealed by anion binding studies, *Eur. J. Biochem*, **1999**, *265*, 589-597.
[39] F. W. Sunderman, S. Nomoto, Measurement of Human Serum Ceruloplasminby Its p-Phenylenediamine Oxidase Activity, *Clinical Chemistry*, **1970**, 16, 11, 903-910.
[40] J. Ceron, S. M. Subiela, An automated spectrophotometric method for measuring canine ceruloplasmin in serum, *Vet. Res*, **2004,** 35, 671-679.
[41] G.H. Badri, Lipid Peroxidation in Ora Cancer, *Basrah Journal of Surgery*, **2003**, 9, 98-100.
[42] M. RafiqKham, Sellappa, Serum malondialdehyde levels in lung cancer patient, *Journal of Applied Biology & Biotechnology*, **2013**, 1, 4, 032-034.
[43] E. P. Rombach, P. S. Barboza, J. E. Blake, Utilization of copper during lactation and neonatal development in muskoxen, *Canadian Journal of Zoology*, **2002**, 80, 8, 1460-1469.
[44] A. Topdag, C. Aslaner, Z. Tataroglu, Ilce, Evaluation of antioxidant capacity in lung carcinoma, *I. J.T C VS*, **2005**, 21, 269-271.
[45] N.A.Mahmood, Glutathion-S-transferase Enzyme and Malondialdehyde (MDA) in Colorectal Cancer and in Healthy Control, *Iraqi Journal of cancer and Medical Genetics*, **2010**, 3, 1, 21-25.
[46] L. Lorente, S. T. Rodriguez, P. Sanz, P. A. González, D. Díaz, A. M. Moreno, E. Borja, M. M. Martín, A. Jiménez M. A. Barrera, Association between Pre-Transplant Serum Malondialdehyde Levels and Survival One Year after Liver Transplantation for Hepatocellular Carcinoma, *Int. J. Mol. Sci.*, **2016**, 17, 500, 1-10.
[47] T.M. Juda M.J. Ewad, K.J. Alhamdani, Role of Oxidative Stress by Lipid Peroxidation in Developing Urinary Bladder Cancer and Correlation between Malondialdehyde and Trace Elements Copper and Zinc, *Medical Journal of Babylon*, **2009**, 6, 1, 45-53.
[48] D. A. F. Al-Kufy, Measuring MDA & GSH as Biomarkers for Oxidative Stress in Bladder Cancer Patients, *Journal of Kerbala University*, **2009**, 7, 3, 127-131.
[49] M. El-Far, H. Abol-Enein, A. Zakaria, M. El-Gedamy, Evaluation of Nitric Oxide and Malondialdehyde levels in Serum of Egyptian Patients with Bladder and Renal Tumors: Potential use as Medicinal Biomarkers, World *Journal Pharmacy and Pharmaceutical Sciences*, **2014**, 8, 6, 87-101.
[50] K.M. Bilal, Measurement of some Biochemical Parameters in Serum of Uterine Cancer, *Raf. J. Sci.*, **2013**, 24, 6, 37-44.
[51] A. O. John, A. Agnes, A. Oluyemi, O.A.Emmanuel, K.R. Sheu , O.A.Ganiyu, Antioxidant Levels of Acute Leukaemia Patients in Nigeria, *Sierra Leone Journal of Biomedical Research*, **2011,** 3(30, 133-137.
[52] N. M. Al-Ubuda, L. M. Al-Naama, A.H. Al-Hashimi, Profile study of some oxidant and antioxidant levels in leukemic patients, *MJBU*, **2012,** 30(2), 115-121.
[53] U. Rajeshwari, I. Shobha, R.Raghunatha, B. Andallu, Oxidative Stress and Antioxidant Status in Acute and Chronic Myeloid Leukemia Patients, *Open Journal of Blood Diseases*, **2013,** 3, 17-22.
[54] S A. Al- Hammami, Study of Some Biochemical Parameters in Iraqi Children with Acute Lymphoblastic Leukemia, *Baghdad Science Journal*, **2015,** 12 (2), 371-378.
[55] O. M. E Abdel-Salam, E R Youness, H.F Hafez, The antioxidant status of the plasma in patients with breast cancer undergoing chemotherapy, *Open Journal of Molecular and Integrative Physiology*, **2011,** 1, 29-35.
[56] H.R.Hasan, S.A. Al-Shammaree, T.H. Mathekoor, Serum lipid peroxidation and trace elements levels in ovarian cancer patients before and after cisplatin and doxorubicin chemotherapy, *Journal of College of Education*, **2011,** 5, 119-136.
[57] R A R. Abulkassim, D K Ismael, N A M Numan, N N, Al-Shawi, S A R. Hussain, The Effect of Radiotherapy on Oxidative Stress, Biochemical and Hematological Parameters in Women with Breast Cancer, *AJPS*, **2014,** 14 (2), 1-9.

[58] A. M. Al-sarraf1, H M Hashim, H B Sahib, H N. Salih, A A .Al-zubaidy, I K Alwan, I S. Rabeea, Effect of Valsartan on Echocardiographic Ejection Fraction, Brain Natriuretic Peptide and Malondialdehyde in TrastuzumabTreated Females with Breast Cancer, *Int. J. Pharm. Sci. Rev. Res.,* **2014,** 29, 2, 205-209.
[59] I A J .Thanoon, K R, Jadoa, F A. Ahmed, Oxidant/antioxidant status in serum of breast cancer women treated by surgical interference and chemotherapy, *Iraq J Pharm*, **2013,** 13(1), 7-12.
[60] J. Banha, L. Marques, R.Oliveira, F.Martins M de , E.Paixão, D.Pereira, R.Malhó, D.Penque, L. Costa, Ceruloplasmin expression by human peripheral blood lymphocytes: A new link between immunity and iron metabolism, *Free Radical Biology & Medicine*, **2008,** 44, 483-492.
[61] J H Park, D W Lee, K.S. Park, Elevated serum copper and ceruloplasmin levels in Alzheimer's disease, *ASI.PACIFIC. PSYCHIATRY*, **2014,** 6(1), 38-45.
[62] R. Cholakova, M.Drangov, K.Markova, V.Zidarova, M.Avramova, Surgical treatment in patients with Wilson's disease, *J of IMAB*, **2017,** 23(1), 1447-1450.
[63] M. Barbariga, F.Curnis, A. Andolfo, A.Zanardi, M.Lazzaro, A.Conti, G.Magnani, M.A.Volontè, L.Ferrari, G. Comi, A.Corti, M. Alessio, Ceruloplasmin functional changes in Parkinson's disease-cerebrospinal fluid, *Molecular Neurodegeneration*, **2015,** 10 (59), 1-12.
[64] O.Demirpençe, B.Sevim, M.Yıldırım, N.A.Nurlu, D.Mert, O.Evliyaoğlu, Serum paraoxonase, TAS, TOS and ceruloplasmin in brucellosis, *Int. J. Clin. Exp. Med*, **2014,** 7 (6), 1592-1597.
[65] M.A. Dubick, J.L. Barr, C.L. Keen, J.L. Atkins, Ceruloplasmin and Hypoferremia: Studies in Burn and Non-Burn Trauma Patients, *Antioxidants*, **2015,** 4, 153-169.
[66] M.Hammadah, Y. Fan, Y. Wu, S.L.Hazen, W.H.W.Tang, Prognostic Value of Elevated Serum Ceruloplasmin Levels in Patients with Heart Failure, *J Card Fail*, **2014,** 20, 12, 946-952.
[67] L. Brandi,1alpha(OH)D3 One-alpha-hydroxy-cholecalciferol--an active vitamin D analog. Clinical studies on prophylaxis and treatment of secondary hyperparathyroidism in uremic patients on chronic dialysis, *Dan Med Bull*, **2008,** 55, (4), 186-210.
[68] R H Jasim, A Biochemical Study to Estimate Malonaldehyde and Ceruloplasmin Oxidase Activity As Parameters Express Oxidation – Antioxidation Balance for Patients with Acute Hepatitis Virus Type C, *International Journal of Computers & Technology*, **2014,** 12(5), 3508-3514.
[69] A.N. Sontakke, U. More, Changes in Serum Ceruloplasmin Levels with Commonly used Methods of Contraception, *Indian Journal of Clinical Biochemistry*, **2004,** 19 (1)), 102-104.
[70] S.Burrows, B.Pekal, Serum copper and ceruloplasmin in pregnancy, *American Journal of Obstetrics and Gynecology*, **1971,** 109 (6), 907-909.
[71] H.D.Jenifer, S. Bhola, V.Kalburgi, S.Warad, V.M.Kokatnur, The influence of cigarette smoking on blood and salivary super oxide dismutase enzyme levels among smokers and non smokersd A cross sectional study, *Journal of Traditional and Complementary Medicine*, **2015,** 5, 100-105.
[72] M. Broderius, E.Mostad, K.Wendroth, J.R. Prohaska, Levels of plasma ceruloplasmin protein are markedly lower following dietary copper deficiency in rodents, *Comp Biochem Physiol C Toxicol Pharmacol*. **2010,** 151 (4), 473-479.
[73] E.P.Rombach, P.S. Barboza, J.E. Blake, Utilization of copper during lactation and neonatal development in muskoxen, *Canadian Journal of Zoology*, **2002,** 80 (8), 1460-1469.
[74] V Gadjeva, D. Kutchukova, E. Aladjov, R. Georgieva, Correlation Between Plasma Malondialdehyde and Ceruloplasmin Activity in Patients with Malignant Hematological Diseases, *Trakia Journal of Sciences*, **2005,** 3 (2), 29-33.
[75] J.Abdul-Barry, L.M. Al- Naama, Z.A. Al- Manaseer, H.S. Al- Khayat, Serum Ceruloplasmin, Copper, Zinc and Copper Zinc Ratio Levels in Different Types of Malignancy, *Medical Journal of Babylon*, **2009,** 6 (2), 377-391.
[76] I G Zainal, M.AL-Dori, A N M Abdul, Study of some Antioxidants in plasma of patients with bladder cancer, *Eng. &Tech. Journal*, **2009,** 27 (4), 751-758.
[77] F F. Al-Kazzaz, A Comparative study of Ceruloplasmin Oxidase with Copper and Renal Function Tests in Sera of Leukemia and Multiple Myeloma Patients during the Treatment, *Iraqi Journal of Science*, **2011,** 52 (1), 1-10.

[78] W A Mehdi, F.Yusof , A.A.Mehde, J.W. Zainulabdeen, R.A.Raus, A.S.Abulbari, Effects of Acute Lymphoblastic Leukemia on Ceruloplasmin Oxidase, Copper and Several Markers of Oxidative Damage, in Children, *Asian. Pac. J. Cancer. Prey,* **2015,** 16 (13), 5205-5210.
[79] R S H .Al Hussain, S.H. Assi, R.R.ismaeel, E.M.Kadhem, A.S. Salman, Evaluation of levels Ceruloplasmin, Copper, Zinc, Calcium and Non Ceruloplasmin_bound Copper in Lung and Liver cancer Patients, The 2nd Scientific Conference of the College of Science, Iraq, p: 90-96, **2014.**
[80] M E Al-Gazally, A S. Al-Awad, H.H. Kzar, Assessment of Antioxidant Status and Ceruloplasmin in Early and Advanced Stages of Sporadic Colorectal Cancer Patients whom Receiving Adjuvant Chemotherapy, *Medical Journal of Babylon,* **2015,** 12 (3), 780-791.
[81] S.Upadhya, K.S. Prabhu, Serum Glycoconjugates and ceruloplasmin in Cancer of Uterine Cervix, *Indian Journal of Clinical Biochemistry,* **2002,** 17 (1), 20-24.
[82] M. Hegde, Y.R. Chianeh, J.Shetty, D.J. Fernandes, P. Rao, CA-125 and Ceruloplasmin Levels in Ovarian Cancer Patients, *Cukurova Medica Journal*, **2015,** 40 (3), 510-516.
[83] N H Al-Saadi, M K Al-Naqib, Z.H. Ali, Investigated of Ceruloplasmin Activity and Related Elements, Copper and Zinc in Patients with Colon Cancer, *International Journal of Current Engineering and Technology,* **2014,** 4 (3), 2112-2115.

AUTHOR ADDRESS

1. **Rasha Hasan Jasim**
Department of Chemistry,
Factually of Education for Girls,
University of Kufa, Iraq
E-mail: dr.rashahussainee@yahoo.com