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# Evaluating the Level of Some Antioxidants and C-Reactive Activators Protein in a Sample of Iraqi Women with Breast Cancer

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## Abstract

One of the key causes of cancer is the detrimental effect of reactive oxygen species on DNA repair mechanisms. The present study aims to describe the function of oxidative stress in boosting breast cancer and to point out the potential defense role of antioxidants and some trace elements. In addition, it is to estimate the concentration of C - C-reactive protein (CRP), a marker of inflammation. Methods: This study was carried out at the Al-Anbar Oncology Center between January and June 2023. Sixty women with breast cancer and forty healthy women were recruited into this study. Serum antioxidant activity, such as superoxide dismutase. (SOD), Catalase (CAT), vitamin D3, vitamin B12, and some essential chemical elements such as zinc (Zn), copper (Cu), iron (Fe), and selenium (Se). CRP concentration was assessed. Results: The results reveal a significant ($P<0.05$) decrease in serum antioxidant concentrations such as SOD, CAT, vitamin D3, and vitamin B12 concentration in serum blood of women with breast cancer compared to the apparently healthy women group. The results showed a significant increase ($p <0.05$) in the CRP concentration of the blood serum of women with breast cancer compared to the healthy women group. The results showed a significant decrease ($p <0.05$) in the concentration of Zn, Cu and Fe in the serum blood of women with breast cancer compared to the healthy women group. Additionally, there was a significant increase ($p <0.05$) in Se concentration in serum blood in women with breast cancer. The percentage of breast cancer is lower in urban areas than in rural areas. Conclusions Women with breast cancer showed high levels of oxidative stress as evidenced by increased oxidant markers and decreased antioxidant markers.

***Keywords:*** *Breast cancer, Antioxidants, Essential trace elements, CRP*

## Introduction

Cancer is the result of the multistep process by which cells turn into unusual cells and produce additional cells in an unrestrained process (1). Breast cancer starts in cells that form a breast, generally in tubes that transport milk to the nipple or glands that produce milk. Cancerous cells form a mass of tissue known as a malignant neoplasm, originating from cells in the breast (2). Although breast cancer affects mainly women, men can also be affected. Breast cancer is the second most widespread malignant tumor after lung cancer in the world (3).

The harm of cellular oxidative is a well-established public mechanism for cell and tissue harm, and this cellular oxidative harm is caused mainly as a result of free radicals and reactive oxygen species (ROS). ROS can bind to the cellular components; in addition, they interact with unsaturated bonds of denatured proteins, membrane lipids, and attack nucleic acids, causing damage to the structure and function of the cell (4). The alteration of the balance between ROS formation and their removal by different types of antioxidants (enzymes and vitamins) is known as oxidative stress. Cells can restore equilibrium or cause apoptosis if they are in a state of disorder (5). In contrast, cancer cells often take advantage of this disturbance to maintain a proliferative and offensive phenotype, starting from genomic instability to cell metabolism, invasion, and metastasis (6). Antioxidants are the main lines of defense in the body. Under normal circumstances, there appears to be a balance between pro-oxidizing and anti-oxidizing forces (7), antioxidants react with free radicals in numerous ways, controlling damaging chain reactions. These antioxidants are vitamins D3, B12, SOD, and CAT (8). Essential chemical elements possess a primary function in the metabolism of the human body in which they have extremely vital biological effects on antioxidants and the immune system (9). The purpose of this study is to investigate the levels

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of SOD, CAT, vitamins D3, vitamin B12, CRP, and essential chemical elements such as Zn, Cu, Fe and Se in a sample of clinically and histologically confirmed breast cancer in Iraqi women.

# Methods

**Blood Samples**

Blood samples were taken from 100 women, including 60 women with breast cancer (samples were taken before treatment), their mean ages from 29 to 64 years (25 from urban areas and 35 from rural). The Medical Record File System of the Al-Anbar Oncology Center in Ramadi provided information on the demography of the patients. At the same time, the control group included 40 women selected from apparently healthy women, their ages 30-67 years old. No one of the control subjects had acute or chronic diseases. Blood samples were collected and transferred to sterile tubes, then serum was separated, and after that the obtained serum was frozen at -20 C for several biochemical investigations.

Determination of Serum Antioxidants and CRP

The estimated activity of SOD was performed using superoxide dismutase diagnostic ELISA equipment (Biovision, lnc, USA) according to the manufacturer's orders. Catalase activity was determined by using an ELISA kit (Cell Biolab, Inc., USA) according to the manufacturer's instructions. Vitamin B12 was estimated using commercially ready equipment (Roche) according to the company's directions using the Cobas Integra 400+ system. Vitamin D3 was measured using the assay that incorporates an enzyme immunoassay competition method with a fluorescent detection step at the end (ELSA)by (Minividas, Biomerix kit, France). Hypovitaminosis is defined by most experts as a serum 25(OH)D level < 20 ng/ml, whereas a serum 25(OH)D level of > 30 ng/ml is deliberately considered normal. The CRP activity was measured by the ELISA kit based on the principle of the latex agglutination assay.

**Determination of Essential Chemical Elements**

The Beck 200 atomic absorption spectrophotometer (AAS) was used to estimate serum levels of essential chemical elements, as defined by Arinola and Charles-Davies (2008) (10). The approach is based on the idea that when elements are aspirated into AAS, their atoms vaporize and ingest light of the same wavelength as that emitted by the element when in an excited situation.

**Statistical analysis**

Data statistical analysis was performed using SPSS version 20, in which population characteristics were displayed as mean ± SE. The independent t-test was also used to compare between groups of patients. The level of significance used for all analyses was P value ≤ 0.05.

# Results

The results in Table 1 show a significant decrease ($p < 0.05$) of superoxide dismutase (SOD) in serum blood from women with breast cancer compared to the apparently healthy group of women. The results in Table 2 shown a significant decrease ($p < 0.05$) of Catalase (CAT) concentration in serum blood of women suffering from breast cancer in comparison to the apparently healthy women group. The results in Table 3 show a significant decrease ($p < 0.05$) of Vitamin D3 concentration in serum blood of women suffering from breast cancer compared to the apparently healthy women group. The results in Table 4 show a significant decrease ($p < 0.05$) of Vitamin B12 concentration in the serum blood of women suffering from breast cancer in comparison to the apparently healthy women group. Findings in Table 5 show a significant increase ($p < 0.05$) in CRP concentration of blood serum of women suffering from breast cancer in comparison to the apparently healthy women group. The results in Fig 1, showed a significant decrease ($p < 0.05$) in Fe, Cu, and Zn concentration in the serum blood of women suffering from breast cancer compared to apparently healthy women group. While there was a significant increase ($p < 0.05$) in Se concentration in serum blood in women suffering from breast cancer compared to the apparently healthy women group.

**Table 1:** Superoxide dismutase (SOD) concentration in the serum of women with breast cancer and the healthy women group.

| Group | N | SOD Concentration (ng/ml) .Mean ± S.E | Interval of Confidence 95% | | Minimum | Maximum |
|---|---|---|---|---|---|---|
| | | | Lower bound | Upper bound | | |
| **Patients** | 60 | 0.19±0.05 | 0.12 | 0.40 | 0.11 | 0.51 |
| **Healthy Control** | 40 | 0.60±0.06 | 0.56 | 0.71 | 0.48 | 0.93 |
| **Total** | 100 | | | | | |

P<0.05 level. SE: Standard Error

**Table 2:** Catalase (CAT) concentration in the blood serum of women suffering from breast cancer and the group of healthy women.

| Group | N | Catalase Concentration (µm/mol) .Mean ± S.E | Interval of Confidence 95% | | Minimum | Maximum |
|---|---|---|---|---|---|---|
| | | | Lower bound | Upper bound | | |
| **Patients** | 60 | ±0.65 0.89 | 0.73 | 0.86 | 0.56 | 0.90 |
| **Healthy Control** | 40 | 5.01±0.63 | 15.32 | 19.38 | 14.20 | 0.21 |
| **Total** | 100 | | | | | |

P<0.05 level. SE: Standard Error

**Table 3:** Vitamin D3 concentration in blood serum of women suffering from breast cancer and in the healthy women group.

| Group | N | Catalase Concentration (µm/mol) .Mean ± S.E | Interval of Confidence 95% | | Minimum | Maximum |
|---|---|---|---|---|---|---|
| | | | Lower bound | Upper bound | | |
| **Patients** | 60 | 51 .±0 15.06 | 11.82 | 17.24 | 10.75 | 18.17 |
| **Healthy Control** | 40 | 25.61±0.37 | 22.12 | 27.76 | 20.56 | 29.89 |
| **Total** | 100 | | | | | |

P<0.05 level. SE: Standard Error

**Table 4:** Vitamin B12 concentration in the blood serum of women suffering from breast cancer and the group of healthy women.

| Group | N | Vitamin B12 Concentration (pg./mL) Mean ± S.E. | Interval of Confidence 95% | | Minimum | Maximum |
|---|---|---|---|---|---|---|
| | | | Lower bound | Upper bound | | |
| **Patients** | 60 | 166.32±0.76 | 155.34 | 190.45 | 150.93 | 195.67 |
| **Healthy Control** | 40 | 388.08 | 271.26 | 459.54 | 253.43 | 471.43 |
| **Total** | 100 | | | | | |

P<0.05 level. SE: Standard Error

**Table 5:** C-reactive protein (CRP) concentration in the blood serum of women with breast cancer and the healthy women group.

| Group | N | CRP Concentration (mg/l) .Mean ± S.E | Interval of Confidence 95% | | Minimum | Maximum |
|---|---|---|---|---|---|---|
| | | | Lower bound | Upper bound | | |
| **Patients** | 60 | 53.01 ± 1.20 | 43.65 | 58.20 | 39.07 | 60.20 |
| **Healthy Control** | 40 | 9.23± 0.56 | 5.72 | 9.89 | 5.01 | 10.11 |
| **Total** | 100 | | | | | |

P<0.05 level. SE: Standard Error

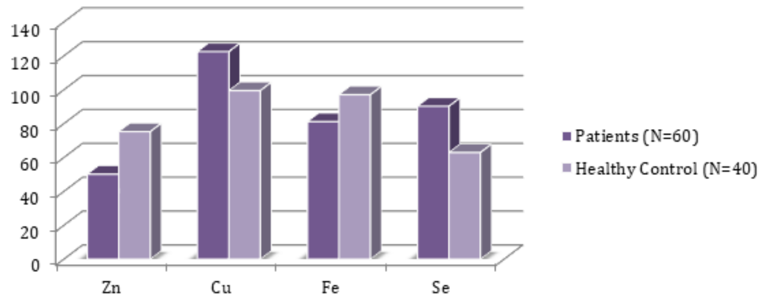


**Figure 1:** Concentration of trace elements levels (µg/dL) concentration in blood serum of women suffering from breast cancer and the group of healthy women.

## Discussion

Risk factors associated with breast cancer may exert their harmful effects through the formation of reactive oxygen species, for example, superoxide radical (O2•- ), hydroxyl radical (•OH), and hydrogen peroxide (H2O2) that cause DNA oxidative harm which can lead to cancer (11). Mean antioxidant levels (SOD, CAT, Vitamin D3 and B12), were significantly ($p<0.05$) decreased in women with breast cancer compared to healthy women, which could be due to free radicals created in body fluids. Vitamins and enzymes exercise an essential function through removing free radicals produced by food oxidation and numerous pollutants, which leads to a decrease in their concentration in serum blood. These results are consistent with studies of (12) (13). There are increasing data for a relationship between vitamin D3 and protection against breast cancer, as many results of research have shown that vitamin D3 inhibits cell proliferation, encourages differentiation and apoptosis, and also has anti-angiogenesis effects in usual and malignant breast cells (14). Previous studies demonstrated that vitamin D3 has anti-inflammatory and antiproliferative effects in tumors, by attaching to the vitamin D3 receptor (VDR), and down-regulation of vitamin D signaling would play a role in the development and progression of mammary cancer, suggesting the possible use of vitamin D supplementation as a preventive agent for breast cancer development in young women (13, 14).

The mean serum vitamin D3 level varies from country to country depending on numerous factors, such as age, season, BMI, exposure to the sun, geographical location, dietary vitamin D3 consumption, everyday activity, and other common issues of ethnic and racial origin (15). The decreases in the concentration of vitamins in patients with cancer can play an important role in tumor growth because antioxidant vitamins expose considerable acts in the physical and chemical quenching of superoxide radicals that are formed by oxidation processes within human cells (16).). Vitamins help stimulate the immune system, also play an important role in energizing cancer suppressor genes and suppressing oncogenes and preventing tumor creation (17).

Outcomes of this research showed that there was a significant increase ($p<0.05$) of CRP concentration in the blood serum of women with breast cancer in compared to the apparently healthy women group, which may be due to reply to swelling necrosis, local tissue harm, or related inflammation with tumor. Similar findings have been mentioned in (18). Also, the malignant process itself causes an increase in CRP concentration despite the existence of systemic bacterial contagion (19). The significant decrease in the level of Zn in women with breast cancer may refer to the metabolic requirements of cancer cells for Zn being significantly higher than of normal cells, therefore this might cause increased uptake from blood (20). In addition, chronic inflammation is a popular hallmark of breast cancer and may lead to a reduced zinc concentration. Other researchers have reported similar results (21). Furthermore, the release of endogenous mediators via tissue damage, such as polymorph nuclear leukocytes, is frequently observed in the development of malignancies, leading to a decrease in Zn concentration and related uptake of Zn through the liver (22).

The significant increase in Cu level in women with breast cancer may be due to the emerging necrosis force. It turns into an increase in the Cu level in the blood as a result of rapid release into the circulation. The high Cu level in blood may reflect the severity of carcinoma (23). Cu and some other trace elements are important cofactors of antioxidant enzymes such as SOD (22). It seems that in the first stages of cancer, when the rate of active free radicals increases slightly, the body tries to increase the levels of some antioxidants, such as SOD (24). SOD will enlist serum Cu, but with increasing intensity of the disease and amount of free radicals, the rate of enzymes decreases. Therefore, more Cu values are seen in the serum of the patients (25). The significant decrease in the Fe level in women with breast cancer may be due to the fact that free iron is used to initiate lipid peroxidation that correlates positively with the progression of breast cancer (26). In addition, insufficient food intake, as a result of burning sensation, could be an important factor, leading to a reduction in serum iron level because a poor diet is produced by neoplasm in cancer patients (26).

The significant decrease in the Se level in women with breast cancer may be due to the ability of selenium as an essential trace element to inhibit growth and induce tumor cell apoptosis as mentioned in (27). Numerous hypotheses have been proposed to describe inhibition of tumor genesis by selenium that include alternative in carcinogen metabolism, effect on endocrine and immune system, production of cytotoxic selenium metabolism, inhibition of protein synthesis, specific enzyme, and tumor growth; Stimulation of apoptosis, and protection against oxidative stress (28).).

This study showed that women living in urban areas have a higher incidence than women living in rural areas, which is similar to previous studies that showed a higher risk of breast cancer among women in geographical areas experiencing intense population mixing (29). Often, this high risk is ascribed to large exposure to aerial benzene, also to several pollutant gases, for example, car traffic flow, and the close presence of industrial plants, or junk incinerators, all of these sources are releasing carcinogenic chemicals (30, 31). Although the study showed a lower risk of breast cancer for women who live in rural areas, this is due to sufficient stimulation of the immune system since childhood (32),(33). Also, there is additional exposure to microbiological factors due to their various lifestyles, such as spending spare time outside houses on the ground floor, unlocking windows for a long time, and larger families), and minimal careful and advanced hygienic conditions contrasted to women living in urban areas (34). Vitamin D3 has some antioxidant properties and has been shown to have protective effects against oxidative stress. Vitamin D3 can control antioxidant enzymes and install antioxidant properties by stimulating the expression of many molecules of the antioxidant defense system, including superoxide dismutase (SOD), glutathione peroxidase (GPX), catalase (CAT), peroxidase (POD) and suppression of the expression of NADPH oxidase (35). Furthermore, many studies have also shown that vitamin D3 stimulates the strength of the antioxidant defense system by increasing antioxidant capacity and controlling ROS. In addition, Vit D3 decreases ROS and pro-inflammatory cytokines, possibly by improving cellular glutathione (GSH) levels (36). One method by which vitamin B12 could affect cancer danger is its role in DNA synthesis and regulation. Suitable levels of vitamin B12 are essential for proper DNA synthesis and repair, which are vital processes in preventing the development of cancerous cells (37).

**Conclusions,** the results of the study indicated an association between a low concentration of antioxidants in the serum blood of women with breast cancer and a higher activity of oxidative stress. This relation confirms the idea that free radical activity increases in malignant cells.

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**Ethical approval**

Ethical permission was obtained from the Al-Anbar Oncology Centre in Ramadi and from all women included in this study . Dated 13-1-2023, the Iraqi Ministry of Health's Ethics Committee approved the study under reference number 72566.

**Authors contribution**

All authors have made equal contributions to this work.

**Conflict of interest**

The author has no conflicts of interest.

## References:

1. Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin DM, Piñeros M, Znaor A, Bray F. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. International journal of cancer. 2019 Apr 15;144(8):1941-53.
2. Waks AG, Winer EP. Breast cancer treatment: a review. Jama. 2019 Jan 22;321(3):288-300.
3. Sant DW, Mustafi S, Gustafson CB, Chen J, Slingerland JM, Wang G. Vitamin C promotes apoptosis in breast cancer cells by increasing TRAIL expression. Scientific reports. 2018 Mar 28;8(1):5306.
4. Katerji M, Filippova M, Duerksen-Hughes P. Approaches and methods to measure oxidative stress in clinical samples: Research applications in the cancer field. Oxidative medicine and cellular longevity. 2019 Mar 12;2019.
5. Seen S, Tong L. Dry eye disease and oxidative stress. Acta Ophthalmologica. 2018 Jun;96(4):e412-20.
6. Cosentino G, Plantamura I, Cataldo A, Iorio MV. MicroRNA and oxidative stress interplay in the context of breast cancer pathogenesis. International journal of molecular sciences. 2019 Oct 17;20(20):5143.
7. Zarrini AS, Moslemi D, Parsian H, Vessal M, Mosapour A, Kelagari ZS. The status of antioxidants, malondialdehyde and some trace elements in serum of patients with breast cancer. Caspian journal of internal medicine. 2016;7(1):31.
8. Singh P, Kesharwani RK, Keservani RK. Antioxidants and vitamins: Roles in cellular function and metabolism. InSustained energy for enhanced human functions and activity 2017 Jan 1 (pp. 385-407). Academic Press.
9. C. Grochowski, E. Blicharska, P. Krukow, K. Jonak, M. Maciejewski, D. Szczepanek, and R. (2019). Maciejewski, "Analysis of trace elements in human brain: Its aim, methods, and concentration levels," Frontiers in Chemistry, Vol. 7, pp. 115.
10. Arinola, O. G., and M. A. Charles-Davies. "Micronutrient levels in the plasma of Nigerian females with breast cancer." African Journal of Biotechnology 7, no. 11 (2008).
11. Moloney JN, Cotter TG. ROS signalling in the biology of cancer. InSeminars in cell & developmental biology 2018 Aug 1 (Vol. 80, pp. 50-64). Academic Press.
12. Kangari P, Farahany TZ, Golchin A, Ebadollahzadeh S, Salmaninejad A, Mahboob SA, Nourazarian A. Enzymatic antioxidant and lipid peroxidation evaluation in the newly diagnosed breast cancer patients in Iran. Asian Pacific journal of cancer prevention: APJCP. 2018;19(12):3511.
13. Kepinska M, Kizek R, Milnerowicz H. Metallothionein and superoxide dismutase—Antioxidative protein status in fullerene-doxorubicin delivery to MCF-7 human breast cancer cells. International Journal of Molecular Sciences. 2018 Oct 20;19(10):3253.
14. Griñan-Lison C, Blaya-Cánovas JL, López-Tejada A, Ávalos-Moreno M, Navarro-Ocón A, Cara FE, González-González A, Lorente JA, Marchal JA, Granados-Principal S. Antioxidants

for the treatment of breast cancer: Are we there yet?. Antioxidants. 2021 Jan 31;10(2):205.

15. de La Puente-Yagüe M, Cuadrado-Cenzual MA, Ciudad-Cabañas MJ, Hernández-Cabria M, Collado-Yurrita L. Vitamin D: And its role in breast cancer. The Kaohsiung journal of medical sciences. 2018 Aug 1;34(8):423-7.
16. Rezaieg NS, Musleh MH. Assessment of the Role of Oxidative Stress and Circulating Biochemical markers in Childhood Leukemia. InJournal of Physics: Conference Series 2019 Sep 1 (Vol. 1294, No. 6, p. 062089). IOP Publishing.
17. Rezaieg NS. Effect of Two Types of Diet on Cholecystokinin (CCK) Level in Three Groups of Males. Journal of the university of Anbar for Pure science. 2021 Jul 1;15(2).
18. Mohammed Awad M, Rezaieg NS. Evaluating the levels of vitamins E, C, Malondialdehyde and some hematological parameters and gamma glutamyl transferase in patients with leukemia. Journal of university of Anbar for Pure science. 2018 Nov 27;12(1):1-8.
19. Rezaieg NS. Consideration of Liver Function test with Erythropoietin Hormone Levels in Iraqi Patients Diagnosed with Lymphoid and Myeloid Leukemia. Iraqi Journal of Cancer and Medical Genetics. 2018;11(1).
20. Mohammed Awad M, Rezaieg NS. Evaluating the levels of vitamins E, C, Malondialdehyde and some hematological parameters and gamma glutamyl transferase in patients with leukemia. Journal of university of Anbar for Pure science. 2018 Nov 27;12(1):1-8.
21. de Vega RG, Fernández-Sánchez ML, Pisonero J, Eiró N, Vizoso FJ, Sanz-Medel A. Quantitative bioimaging of Ca, Fe, Cu and Zn in breast cancer tissues by LA-ICP-MS. Journal of Analytical Atomic Spectrometry. 2017;32(3):671-7.
22. Cabré N, Luciano-Mateo F, Arenas M, Nadal M, Baiges-Gaya G, Hernández-Aguilera A, Fort-Gallifa I, Rodríguez E, Riu F, Camps J, Joven J. Trace element concentrations in breast cancer patients. The Breast. 2018 Dec 1;42:142-9.
23. Blockhuys S, Celauro E, Hildesjö C, Feizi A, Stål O, Fierro-González JC, Wittung-Stafshede P. Defining the human copper proteome and analysis of its expression variation in cancers. Metallomics. 2017 Feb;9(2):112-23.
24. Reehan NS. A comparative study of oxidative stress and Some physiological and biochemical variables in patients with myeloid and lymphoid leukemia in Baghdad city. University of Anbar. 2018.
25. Foo JB, Low ML, Lim JH, Lor YZ, Zainol Abidin R, Eh Dam V, Abdul Rahman N, Beh CY, Chan LC, How CW, Tor YS. Copper complex derived from S-benzyldithiocarbazate and 3-acetylcoumarin induced apoptosis in breast cancer cell. BioMetals. 2018 Aug;31:505-15.
26. Jablonska E, Socha K, Reszka E, Wieczorek E, Skokowski J, Kalinowski L, Fendler W, Seroczynska B, Wozniak M, Borawska MH, Wasowicz W. Cadmium, arsenic, selenium and iron–implications for tumor progression in breast cancer. Environmental toxicology and pharmacology. 2017 Jul 1;53:151-7.
27. Ogut S, Bahtiyar N, Mordeniz C, Cinemre FB, Aydemir B, Karacetin D, Degirmencioglu S, Haciosmanoglu E, Kural A, Kiziler AR, Gunes ME. Effect of breast cancer and breast cancer treatment on the blood serum concentrations of trace elements and selenoproteins. Journal of Elementology. 2022;27(2).
28. Ekoue DN, Zaichick S, Valyi-Nagy K, Picklo M, Lacher C, Hoskins K, Warso MA, Bonini MG, Diamond AM. Selenium levels in human breast carcinoma tissue are associated with a common polymorphism in the gene for SELENOP (Selenoprotein P). Journal of Trace Elements in Medicine and Biology. 2017 Jan 1;39:227-33.
29. Kumar D, Batra U. Epidemiology of breast cancer in indian women: Population and hospital based study. EAI Endorsed Transactions on Pervasive Health and Technology. 2018 Oct 30;4(16).
30. Solikhah S, Promthet S, Hurst C. Awareness level about breast cancer risk factors, barriers, attitude and breast cancer screening among Indonesian women. Asian Pacific journal of cancer prevention: APJCP. 2019;20(3):877.
31. Rodriguez-Gomez M, Ruiz-Perez I, Martin-Calderon S, Pastor-Moreno G, Artazcoz L, Escribà-Agüir V. Effectiveness of patient-targeted interventions to increase cancer screening participation in rural areas: A systematic review. International Journal of Nursing Studies. 2020 Jan 1;101:103401.
32. Montes-Grajales D, Bernardes GJ, Olivero-Verbel J. Urban endocrine disruptors targeting breast cancer proteins. Chemical Research in Toxicology. 2016 Feb 15;29(2):150-61.
33. Rezaieg NS, and MM. Awad. Consideration of Liver Function test with Erythropoietin Hormone Levels in Iraqi Patients Diagnosed with Lymphoid and Myeloid Leukemia. Iraqi Journal of Cancer and Medical Genetics. 2018;11(1)..
34. Trayes KP, Cokenakes SE. Breast cancer treatment. American family physician. 2021 Aug;104(2):171-8.
35. Hashemi SM, Rafiemanesh H, Aghamohammadi T, Badakhsh M, Amirshahi M, Sari M, Behnamfar N, Roudini K. Prevalence of anxiety among breast cancer patients: a systematic review and meta-analysis. Breast Cancer. 2020 Mar;27:166-78.
36. Tagliaferri S, Porri D, De Giuseppe R, Manuelli M, Alessio F, Cena H. The controversial role of vitamin D as an antioxidant: results from randomised controlled trials. Nutrition research reviews. 2019 Jun;32(1):99-105.
37. Lacombe V, Chabrun F, Lacout C, Ghali A, Capitain O, Patsouris A, Lavigne C, Urbanski G. Persistent elevation of plasma vitamin B12 is strongly associated with solid cancer. Scientific Reports. 2021 Jun 25;11(1):13361.