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Evaluation of interleukin-7 and lipid profile in breast cancer women

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Abstract--Breast cancer is one of the most common cancerous tumors and one of the main causes after lung cancer that leads to death, and the most common type of breast cancer is adenocarcinoma and is usually detected either during the examination before symptoms appear or after the woman notices the presence of the tumor. Breast cancer is one of the most common diseases in Iraq recently. This study was designed to measure the level of interleukin-7 and its role in cancer, as well as to find out the Level of lipids (cholesterol, triglycerides, and high-density lipoproteins) in breast cancer women and compare them with the control group. The results showed a significant increase ($P \leq 0.05$) in the level of interleukin-7 and high-density lipoprotein cholesterol ($357.505 \pm 89.921 \mu\text{g/L}$, $104.383 \pm 20.865 \text{mg/dl}$) respectively among patients with breast cancer compared with the control group ($150.705 \pm 39.559 \mu\text{g/L}$, $114.782 \pm 14.139 \text{mg/dl}$) respectively, , and the results showed a significant decrease ($P \leq 0.05$) in the level of cholesterol and triglycerides in patients with breast cancer ($104.383 \pm 20.865 \text{mg/dl}$, $110.388 \pm 18.180 \text{mg/dl}$) respectively compared with the control group ($114.782 \pm 14.139 \text{mg/dl}$, $138.925 \pm 23.178 \text{mg/dl}$) respectively.

Keywords--breast cancer, interleukin-7, lipid profile, cholesterol, lipoprotein.

Introduction

The incidence of breast cancer in Western societies is greater than the rate of infection in Eastern societies, because women in Western societies use hormones as well as contraceptive methods in addition to the different nature of life (1). The

incidence of cancerous diseases increases every year due to the presence of uncontrolled canned food and environmental pollution, and the lack of culture among some, which may contribute to the high number of injuries and the important role of preparing for the genetic factor in the family (2). Breast cancer begins when breast cells grow abnormally, as mass of tissue form as a result of rapid cell division and multiplication, and these masses are called tumors, and these tumors may be cancerous and called malignant tumors, or these tumors may be non-cancerous, called tumors Benign, malignant tumors multiply and destroy healthy tissues in the body and also it is possible for some tumor cells to separate and spread to other areas of the body and this spread is called metastasis (3).

Breast cancer develops in the lobules that supply the milk ducts, and breast cancer is in the lining of the milk ducts. The first type is known as lobular carcinomas, and the second type is known as non-lobular carcinomas. In addition, there are other types of breast cancer that are considered subtypes (4). There are several methods for early detection of breast cancer, and the most important of these methods used are (Mammogram and Magnetic Resonance Imaging (MRI), resonance imaging is considered the most accurate (5). The diagnosis of breast cancer is confirmed by taking (Biopsy) of the tumor (6). There are several ways to treat breast cancer, and the most important of these methods used is surgery. Medicines can also be used as a treatment for breast cancer. The most important of these drugs are radiation therapy, hormonal therapy, chemotherapy, and immunotherapy. (7), and the surgery is considered one of the most useful methods, which is represented by a high rate of recovery, and after the surgery, radiation is used, which is used to increase the incidence of improvement and reduce relapse rates (8).

Interleukin-7 causes the lymphatic properties of breast cancer cells to be induced by regulating vascular endothelial growth factor-D (VEGF-D), which has a significant effect on the lymphatic proliferation of breast cancer (9). The tumor surrounding environment contains cancer-associated fibroblasts that act as key modulators of cancer progression, distinct subsets of cancer-associated fibroblasts influence breast cancer growth, fibroblasts expressing recombinase enzymes under the control of interleukin-7 promoter mainly occupied the tumor margin where they interact “physical” with cancer cells, as intra-tumoral ablation of fibroblasts expressing interleukin-7 impairs breast tumor growth and reduces the ability of cancer cells to proliferate (10).

Materials and Methods

Samples collection

90 blood samples were collected from patients with breast cancer and healthy women, whose ages ranged between (40-70) years, and samples were collected from the Cancer Tumor Center at Baquba General Hospital in Diyala Governorate for the period from 31/10/2021 to 30/12/2021. Then the samples were divided according to the study design into the following:

- The first group: which included 40 blood samples from healthy women (control group).
- The second group: which included 50 blood samples from patients with breast cancer. this group subdivided in the following subgroup:

Blood collection

Samples for the current study were collected by withdrawing 5 ml of venous blood from both patients and healthy subjects after an overnight fasting. the blood sample was 5ml and put it in test tubes and left it for several minutes to coagulate and then the serum was separated from it using a centrifuge at 3000 rpm for 10 minutes.

Estimation of the concentration of interleukin-7 in the blood serum:

The Principle

The level of IL-7 in serum was determined by a ready-made assay kit from Mybiosource of America.

Estimation of lipid profile in the serum of study group

Determination of serum cholesterol concentration

The concentration of cholesterol in the blood serum was measured using an analysis kit (kit) (11).

The principle

The enzyme cholesterol oxidase oxidizes cholesterol in the presence of the enzyme peroxidase and in the presence of a hydrogen donor, the colorless substrate is oxidized to the pink pigment quinonimine.

Determination of serum Triglycerides concentration

The concentration of triglycerides in the blood serum was estimated using the readyKit (12).

The Principle

This method is based on enzymatic decomposition of triglycerides into glycerol, which passes through a chain reaction to eventually produce a pink complex.

Determination of serum High Density Lipoprotein Cholesterol (HDL-C)

The concentration of high-density lipoprotein (HDL) in serum was estimated using the ready Kit (13). The working done by application the instructor of the kit.

The principle

The measurement of the concentration of (HDL-C) was based on the use of the enzymatic method, which includes the quantitative precipitation of low-density lipoproteins (LDL-C, VLDL-C) and chylomicrons when adding phosphotriestane

acid in the presence of magnesium chloride ions. And that the filtrate obtained after the centrifugal separation process contains (HDL-C) only, as it was estimated using the enzyme solution of cholesterol.

Determination of serum low density lipoprotein-cholesterol (LDL-C)

LDL-C in serum was estimated based on the following relationship (13)

$$\text{LDL-C concentration (mg/dl)} = \text{Total cholesterol} - (\text{HDL-C}) - \text{VLDL-C}.$$

Determination of serum very low density lipoprotein-cholesterol (VLDL-C)

The concentration of (VLDL-C) in the blood serum was estimated based on the following relationship (13)

$$\text{VLDL concentration (mg/dl)} = (\text{Triglycerides} / 5) .$$

Results and Discussion

Table (1) shows that the level of interleukin-7 (IL-7) \pm standard deviation in patients with breast cancer was $(357.505 \pm 89.921 \mu\text{g} / \text{L})$ while the control group was $(150.705 \pm 39.559 \mu\text{g} / \text{L})$.

Table 1
 Mean \pm standard deviation of the serum interleukin-7 (IL-7) in the two groups of the study

Groups	Sample	Mean \pm SD $\mu\text{g} / \text{L}$	P- value
Patients	50	357.505 ± 89.921	$P \leq 0.05$
Control	40	150.705 ± 39.559	

The results showed a strong significant elevation ($P \leq 0.05$) in the level of interleukin-7 (IL-7) in patients with breast cancer ($357.505 \pm 89.921 \mu\text{g} / \text{L}$) compared the control group ($150.705 \pm 39.559 \mu\text{g} / \text{L}$). The results agreed with what was reached by Li Zhang et al (14), Maximilian et al (15), and Al-Rawi et al (16), which showed higher levels of IL-7 in women with breast cancer compared with healthy ones, as IL-7 is a known cytokine since a long time in immunology, especially with regard to its effects on T- cells and B- cells, as well as the fact that it is necessary for the proliferation of B and T cells and its deficiency causes inhibition of the immature immune cells. Interestingly, some studies have strongly suggested that the role of IL-7 is beyond the field of immunology, as it may have a direct or indirect effect on cancer (17), especially breast cancer through its action on inhibiting programmed cell death and stimulating angiogenesis in tumors (18). IL-7 is a potent pro-inflammatory cytokine that has the ability to destabilize chromosomes and induce tumorigenesis. In addition, it can control the spread of malignant tumors by affecting the tumor microenvironment and the immune system (19). The level of IL-7 in the sera of patients with breast cancer increases with the progression and spread of the disease because the action of IL-7 is anti-inflammatory and as the disease progresses, the body tries to counteract the tumor by increasing the level of IL-7 in the serum.

Where cytokines collect with white blood cells at the site of the tumor to start the process of tissue repair which leads to an increase in the level of IL-7 in the serum (20). The high level of IL-7 is due to the immune response of patients in this stage of the tumor and that T cells and B cells work to enhance the activity of IL-7 in the serum, or the reason for the increase may be due to the treatments given to them and the progression of infection as well as the resistance of cancer stem cells to radiotherapy and chemotherapy (21). Table (2) shows that the cholesterol mean \pm standard deviation of patients with breast cancer which was (104.383 \pm 20.865mg\dl) while the control group, (114.782 \pm 14.139mg\dl)

Table 2

Average \pm standard deviation of cholesterol level in the two groups of the study

Groups	Sample	Mean \pm SD mg /dL	P- value
Patients	50	104.383 \pm 20.865	P \leq 0.05
Control	40	114.782 \pm 14.139	

The results showed a significant decrease (P \leq 0.05) the level of cholesterol (104.383 \pm 20.865mg\dl) in patients with breast cancer compared with the control group (114.782 \pm 14.139mg\dl), this may be due to the fact that women with breast cancer follow a diet during cancer. This study agrees with Seema and his group (22) and Fagherazzi et al. (23), where a significant decrease in the level of total cholesterol was observed in breast cancer patients compared to the control group due to its increased use by tumor cells to build a new biofilm. The present results do not agree with Al-Faraji (24), Mahmoud et al (25), Al-Rabee et al (26), Wehbe et al (27), and Alacacioglu et al (28), where a significant increase was observed in the level of cholesterol in women with breast cancer and this it may be due to metabolism and increased fat oxidation, which may be associated with cancers because it has an important role in maintaining cell integrity. The cholesterol formation pathway may also produce different tumor compounds. Cholesterol serves as a precursor to the synthesis of many sex hormones associated with an increased risk of various cancers, and the mechanism of the link between cancer and cholesterol is still controversial because both hyperlipidemia and hypercholesterolemia may also be associated with malignancies, not only carcinogenic but also antineoplastic as well as therapeutics has an effect on the lipid profile. Cholesterol is essential in maintaining the structure and functional integrity of all biological membranes. It is also involved in various other biological functions including; Cell growth and division of both normal and malignant tissues, activity of membrane-associated enzymes and DNA double-helix stabilization. High cholesterol may lead to malignancies (29). Table (3) shows the mean of triglycerides \pm standard deviation in patients with breast cancer was (110.388 \pm 18.180mg\dl) while the control group, was (138.925 \pm 23.178mg\dl).

Table 3

Mean \pm standard deviation of Triglyceride levels in the two groups under study

Groups	Sample	Mean \pm SD mg /dL	P- value
Patients	50	110.388 \pm 18.180	P \leq 0.05
Control	40	138.925 \pm 23.178	

The results showed significant decrease ($P \leq 0.05$) in the level of triglycerides ($110.388 \pm 18.180 \text{ mg/dl}$) in patients breast cancer women compared to control group ($138.925 \pm 23.178 \text{ mg/dl}$). The current study did not agree with the findings of Al-Rubaie et al (26) and Custodio et al (30), as the high concentration of T.G may lead to a decrease in the level of sex hormones binding, which leads to an increase in the amount of free estradiol. Chemotherapy does not affect cancer cells only; but leads many side effects such as indigestion, nausea, inflammation of the oral mucosa, dry mouth...etc, which can affect nutritional intake and nutritional results (31). Sharma et al. demonstrated that chemotherapy affects the liver and increases the concentration of triglycerides. (32). These results also did not agree with Ali (33), who found a significant elevation in the level of triglycerides in breast cancer patients compared to the control group. The increase may be due to tamoxifen treatment. Tamoxifen is known to be prescribed chemotherapy for breast cancer patients and increases the concentration of triglycerides in the blood.

Umesh et al. (34), explains that a high-fat diet is an important factor in the progression of breast cancer according to the Master Nutrition Theory. Chemotherapy can reduce liver productivity, which may be the cause of high triglycerides. The reason for the decrease in fat for cancer patients is due to the nature of the cancerous tumor, which withdraws all useful substances for the body and causes a decrease in glucose, fats and hemoglobin, which causes weight loss in addition to the psychological and psychological state of the cancer patient, causing a kind of depression, which causes abstinence from eating and isolationist behavior, and thus a decrease in fat and weight. Table (4) shows that the mean of high-density lipoproteins \pm standard deviation in patients with breast cancer was ($26.642 \pm 6.086 \text{ mg/dl}$) while the control group, it was ($41.520 \pm 2.641 \text{ mg/dl}$).

Table 4
Mean \pm standard deviation of HDL level in the two groups under study

Groups	Sample	Mean \pm SD mg / dL	P- value
Patients	50	26.642 ± 6.086	$P \leq 0.05$
Control	40	41.520 ± 2.641	

The results showed a significant decrease ($P \leq 0.05$) in the level of high-density lipoproteins HDL in patients ($26.642 \pm 6.086 \text{ mg/dl}$) with breast cancer compared with the control group ($41.520 \pm 2.641 \text{ mg/dl}$). These results agree with TIAN et al (35), who showed in their study that the level of HDL-C decreased in chemotherapy patients compared to the control group and was prone to malignant tumors (36). The precise mechanism by which blood lipids are increased and HDL cholesterol concentration decreases occurs in patients with cancer is unknown. (37). However, it has been suggested that lipoprotein lipase (LPL) may normalize clearance of T.G from blood to tissue and its activity in white adipose tissue and decrease in cancer patients contributing to hypertriglyceridemia. HDL-C precursor particles are believed to be derived from lipolysis in T.G and thus LPL activity is decreased in cancer (38). This estrogen action is not shared by tamoxifen therapy (39). Table (5) shows that the mean of low density lipoproteins \pm standard deviation in patients with breast cancer

was (55.662 ± 15.466mg\dl) compared with the control group, it was (45.477 ± 12.624mg\dl).

Table 5
Mean ± standard deviation of LDL in serum in of two groups under study

Group	Sample	Mean ± SD mg /dl	P- value
Patients	50	55.662 ± 15.466	P≤ 0.05
Control	40	45.477 ± 12.624	

The results showed a significant increase (P≤ 0.05) in the level of low-density lipoproteins in patients with breast cancer (55.662 ± 15.466mg\dl), compared with the control group (45.477 ± 12.624mg\dl). Our result agrees with WU, Jing and his group (40) who found that serum LDL-C significantly increased in breast cancer patients. Where the results indicated that the level of LDL-C increases in patients who are not undergoing treatment. LDL-C acts as a prognostic indicator for breast cancer. Kumar and his group also demonstrated the role of blood lipid content in 100 breast cancer patients and a control group. Their results revealed that breast cancer patients had higher levels of LDL-C, compared to healthy women (41). Table (6) shows that the mean of very low density lipoprotein ± standard deviation in patients with breast cancer was (22.077±3.636mg\dl) compared with the control group, it was (27.784±4.635mg\dl).

Table 6
Mean ± standard deviation of VLDL in serum of the two groups under study

Group	Sample	Mean ± SD mg /dL	P- value
Patients	50	22.077±3.636	P≤ 0.05
Control	40	27.784±4.635	

The results showed a slight decrease (P≤ 0.05) in the level of very low density lipoproteins in patients (22.077±3.636mg\dl) with breast cancer compared with the control group (27.784±4.635mg\dl). The results of the current study do not agree with Al-Faraji et al. (24), and Al-Attar. (42), where it was found that VLDL levels are elevated in women with breast cancer compared with the control group. Previous studies have shown that VLDL is significantly elevated in breast cancer patients compared to the control group (43). Because of the nature of the cancerous tumor, which withdraws all the useful substances for the body and causes a decrease in sugars, fats and hemoglobin, which causes weight loss, in addition to the psychological and psychological state of the cancer patient, it causes a kind of depression, which causes abstinence from eating and isolationist behavior, and thus a decrease in fat and weight.

Conclusions

Through the results obtained, it was found that interleukins have an important role in combating breast cancer, as they are inflammatory cells and part of the immune system. It also appears that breast cancer affects the levels of fat in the body as a result of the damage caused by cancer cells, which leads to an imbalance in the fat levels in women compared to healthy women.

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