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STUDY OF SOME BIOCHEMICAL VARIABLES IN WOMEN WITH BREAST CANCER

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Abstract

Cancer ranks among the leading causes of death across the global population. Breast cancer, stands as the main cancer in the female and the main cause of death in western world. In Iraq, it is mentioned that it is the second cause of death after cardiovascular diseases. The research sample comprise of 60 samples from women with breast cancer while the control group was 30 samples; biochemical variables which included hormones; estradiol, progesterone and prolactin, enzyme glutathione peroxidase, alkaline phosphatase, and lipid profile. The results depicted that estradiol, progesterone and prolactin, alkaline phosphatase, cholesterol, triglyceride, LDL, vLDL concentration in the serum of women with breast cancer was elevated compared to control. Indications were observed that women with breast cancer were found to have decreased level of HDL and glutathione peroxidase (GPx) in serum at probability level of $P \leq 0.05$ when compared with control group.

Keywords: Estradiol, Progesterone, Prolactin, Reduced Glutathione Peroxidase, Alkaline phosphatase, lipid profile.

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Introduction

Breast cancer is among the leading and most common diseases affecting women globally. It is a multifactorial anatomico-pathological condition involving repeated abnormal cell proliferation in the breast tissue with hormonal, genetic and environmental modifiers [1]. In this case, they include estradiol, progesterone, and prolactin hormones and metabolic and biochemical markers are influential in the development of breast cancer. Knowledge of the relationship of these factors with breast cancer is important in enhancing diagnosis, treatment and prevention [2].

Estradiol is the most potent estrogen receptor available to women and has significant responsibilities concerning reproductive and breast tissues. However, increased estradiol level has been found to be highly correlated with occurrence of breast cancer disease [3]. It is well-established that that estradiol serves as a stimulant to the growth of cancerous breast cells through the estrogen receptors; the growth of cells is accelerated and tumors develop as a result [4]. High estradiol levels especially in post menopausal women put them at a higher risk of hormone receptor positive breast cancer. This provides further support to the hypothesis that hormone balance is very important in the prevention of breast cancer [5].

Also the role of, progestogen, another hormone associated with female reproductive functions has been known to play role in development of breast cancer, albeit not a very clear one. It must be noted that progesterone influences the effects of estrogen in the breast tissue to act as a protective or protecting agent in the growth of the breast tissue [6] In certain circumstances particularly with hormone receptor-positive breast cancer Progesterone can actually promote cancer cell proliferation in the presence of estradiol. In other settings, progesterone is known to have protective effects. This dual function demonstrates a delicate hormonal that characterizes breast cancer formation and progression [7].

There is that hormone called Prolactin which is mostly associated with breastfeeding; this hormone has also been cited to pose a risk to breast cancer patients. High prolactin levels may promote the development of breast tissue proliferation as well as the progression of breast cancer especially that of hormone receptor positive type [8]. Prolactin may support the proliferation and anti-apoptoticsis of neoplastic cells through specific signaling antenna, which add value to the neoplastic process [9]. This fact proves the importance not only of the reproductive hormones but also those involved in other physiological processes, particularly breast cancer [10].

Thus, apart from hormonal effects, it is also established that the effects of oxidative stress are able to have a conceptually critical impact on cancer in general, including breast cancer. Lowered glutathione peroxidase (GPx) is one antioxidant enzyme responsible for averting cell dysfunction due to oxidative stress through disposal of dangerous ROS [11]. In breast cancer patients, different variant is the lowered activity of the antioxidant enzyme glutathione peroxidase that results in the increased oxidative stress, which in turn may have detrimental effects on DNA and stimulate cancer growth [12]. Decreased activity of GPx mirrors just how critical it is to achieve optimal redox ratios to reduce cellular damage that spawns cancerous changes begin [13].

Another biochemical marker which is worth mentioning here is Alkaline Phosphatase (ALP), enzyme which is associated with the bone and liver, may has relationship in breast cancer, especially at the terminal stage [14]. Patients with breast cancer with bone metastasis commonly present with high levels of ALP because the enzyme is shed to reflect higher bone turnover. Similarly elevated levels of ALP can suggest involvement of the liver due to metastasis of cancer. It can, therefore, be used as a marker of disease progression in a variety of metastatic breast cancer cases [15].

A particularly robust relation with BC risk and progression is the metabolic health of an individual. Lipid profile in terms of cholesterol, triglycerides and lipoprotein have been reported to play a role in cancer incidence [16]. Lipid metabolism abnormalities, including hypercholesterolaemia or hypertriglyceridaemia, are not rare in patients with breast cancer. Lipid in cancer cell membranes can be

derived from raised cholesterol levels which alter signaling pathways that aid tumor growth. Also, the metabolic disorder of lipids can cause a chronic inflammation and that is a key factor in cancerous diseases. There is also possibility to investigate lipid profiles in breast cancer patients in order to reveal metabolic alternations associated with cancer disease progression [17].

It is postulated that hormones involved in breast carcinogenesis include estradiol, progesterone and prolactin, while the oxidative stress breast cancer biomolecules include reduced glutathione peroxidase, while alkline phosphatase and lipid profiles also play a role in the development of breast malignancies. Knowledge of these relationships is crucial in trying to create new diagnostic methods that are specific for female breast cancer and also in establishing new intervention techniques for prevention and treatment of the disease [18].

Aim of study

The purpose of this research is to measure biochemical indices in women with breast cancer by studying the concentration of hormones; estradiol, progesterone, prolactin; antioxidant enzyme; glutathione peroxidase; and metabolic indicators; alkaline phosphatase and lipid profile. The study aims to know the variation of these variables from a control group with emphasis to know variation in hormonal, enzymatic, lipid variables that might be related to the development and progression of breast cancer. Besides, the study seeks to establish possible significance of these biochemical markers in the field of orienting the pathophysiology of breast cancer and the creation of the individualized treatment methods.

Statistical Analysis

For statistical analysis of the collected data all the study results were calculated using the XL-STAT and SPSS version 23. An independent samples T-test and one way ANOVA-Dunnett's Test were conducted to show the difference of mean between the groups at the probability level of 0.05 ($P \leq 0.05$). Results were analysed and presented using mean and Standard Deviation or numbers and frequencies according to the variable type. Prior to parametric testing, data was checked for normality with the Shapiro-Wilk test. Multiple comparisons were done using Bonferroni correction. Potential confounding factors were controlled in a multivariate regression analysis

Materials and Methods

Data for this study were collected from a sample of 60 patients whose ages ranged between (25-40 years). Additionally, 30 control subjects whos ages ranged between (25-40) were collected. Patients who had localized, non-metastatic breast cancer (Stages I-III) were included in the study. A post-hoc power analysis was carried out to justify the number of patients and controls included (60 patients, 30 controls) and to check the power of the study. The samples were obtained from Baghdad Private Laboratories. Both patients and controls had 5 mL of venous blood collected. The blood samples were then left to clot for 10 minutes at room temperature. The serum was subjected to centrifugation for ten minutes at a speed of 3000 revolutions per minute (rpm), resulting in its division into three equal portions called aliquots. The specimens were stored at a temperature of -20°C in microcentrifuge tubes with a capacity of 1.5 mL until they were analysed using ELISA kits and a flameless atomic absorption spectrometer. Serum hormones were measured in duplicate by commercial ELISA kits for reproducibility. A 12-hour overnight fasting period was followed by blood samples. LDL and vLDL estimation according to the Friedewald standardized equation.

Results and Discussion:

Table 1. mean ± standard deviation of the measured biochemical variables.

Group	Estradiol (pg/ml)	Progesterone (ng/ml)	Prolactin (ng/ml)	GSH (µmol/l)	Alkaline phosphatase (U/l)
Patient	272.5 ± 20.63	13.09 ± 0.7	23.13 ± 0.55	3.75 ± 0.19	88.56 ± 1.85
Control	90.58 ± 5.6	6.66 ± 0.58	11.11 ± 0.46	5.83 ± 0.17	63.1 ± 2.0
P-Value			P≤0.05		

The table compared biochemical markers between breast cancer patients and healthy control subjects which demonstrated major changes that occurred because of the disease. The research conducted by Asthana et. al. revealed that women with breast cancer exhibited an elevation in estradiol level, our results showed that the estrogen level in patient group were 272.5 ± 20.63 pg/ml which exceeded that of control group (90.58 ± 5.6 pg/ml) and were statistically significant ($P \leq 0.05$) as shown in figure 1. The development of estrogen receptor-positive breast cancer cells depends on estradiol which explains why breast cancer patients show elevated levels of this hormone. The body experiences increased cell growth because high estradiol levels trigger cancer formation through cell proliferation and cell death reduction [20].

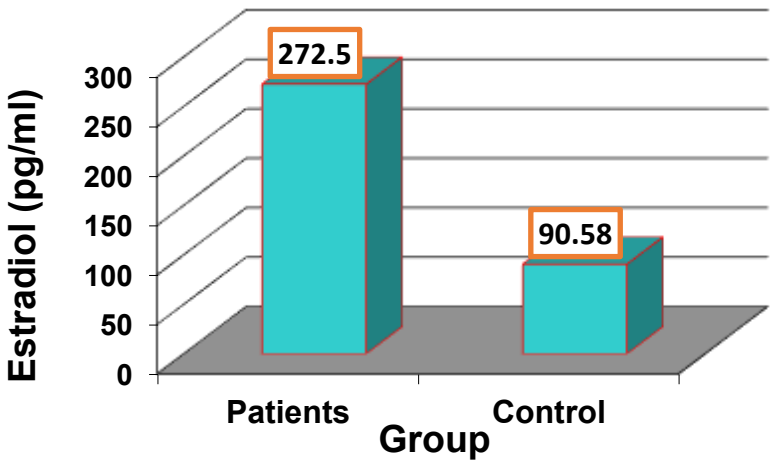


Figure 1. Estradiol level in patients and control groups

The results of previous study by Kossman et al. demonstrated that breast cancer patients showed higher progesterone levels, our results in table 1 and figure 2 showed statistically significant ($P \leq 0.05$) higher progesterone levels in patients group 13.09 ± 0.7 ng/ml compared to 6.66 ± 0.58 ng/ml in the control group. The body needs progesterone for reproductive status but this hormone interacts with estrogen to trigger breast cancer cell growth in hormone receptor-positive breast cancer cases, the combination of high progesterone levels with high estradiol might drive breast tumor development and cancer spread in breast which is sensitive to estrogen and progesterone hormones [21].

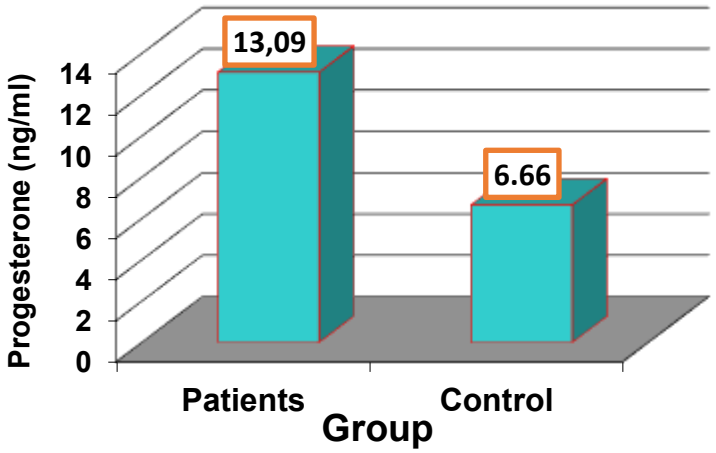


Figure 2. Progesterone level in patients and control groups

Research findings demonstrated that breast cancer patients developed major hormonal imbalances which affected their body. The patient group showed Prolactin levels which reached 23.13 ± 0.55 ng/ml while control subjects had levels of 11.11 ± 0.46 ng/ml and it was statistically significant ($P \leq 0.05$) (Table 1 and Figure 3) which matched the findings of Carrero et al., Prolactin major function to develop breast tissue and produce breast milk but higher hormone concentrations lead to breast cancer cell growth in hormone receptor-positive breast tumors. The hormone prolactin appears to drive breast cancer cell development which suggests it might contribute to cancer advancement. [22].

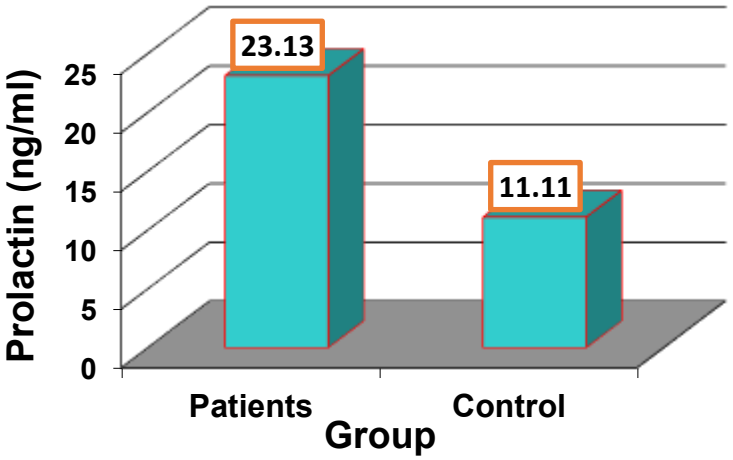


Figure 3. Prolactin level in patients and control groups

Didžiapetrienė et al.'s study also found a significant decrease in antioxidant enzymes, glutathione peroxidase (GPx) in breast cancer patients, this was consistent with the findings of our study shown in Table 1 and figure 4 where the GPx level was (3.75 ± 0.19 µmol/L) in patients and were statistically significant ($P \leq 0.05$) higher than in controls (5.83 ± 0.17 µmol/L). The GSH antioxidant plays a pivotal role in protecting body cells from oxidative stress caused by free radicals. Increased oxidative damage in breast cancer patients due to decreased antioxidants such as GSH can result in DNA mutations that further lead to proliferation of cancer cells. Hence, this discrepancy between oxidative stress and antioxidant systems can be important for the progression of breast cancer [23].

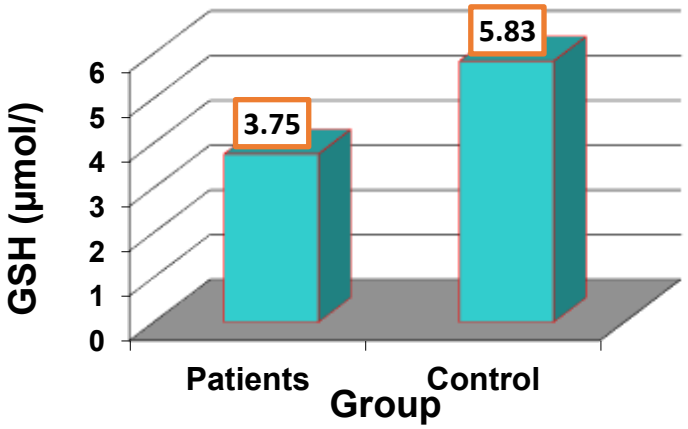


Figure 4. Comparison between patients with breast cancer and control in GSH

Similar study by Chauhan et al. showed that alkaline phosphatase (ALP) levels were markedly higher in the breast cancer, the results of ALP level in this study showed that it was statistically significant ($P \leq 0.05$) higher in patient group (88.56 ± 1.85 U/L) compared to the control group (63.1 ± 2.0 U/L) (Table 1 and figure 5). This enhanced enzyme activity is related to increase in bone turnover or liver dysfunction common in metastatic breast cancer to bones and liver respectively [24]. ALP proved to be a marker for both skeletal and hepatic complications and the increase in its level in breast cancer patients may be due to the body's reaction to tumor load [25]. All these compared differences we observed between the breast cancer and control groups achieved a statistical significance of $P \leq 0.05$. This makes it rather evident that breast cancer begins and develops as an effect of hormonal changes, oxidative stress as well as be metabolism disorders. Higher ALP may indicate metastasis or liver involvement, and lower antioxidant enzyme activity and increased hormone level (PRL, PGE2, and E2) may indicate that oxidative damage and hormone-stimulated tumor growth in breast cancer women are related. These findings highlight the necessity of monitoring these biochemical markers not only for diagnosis and assessment of breast cancer pathogenesis, but also for evaluating treatment efficacy and monitoring prognosis. [26].

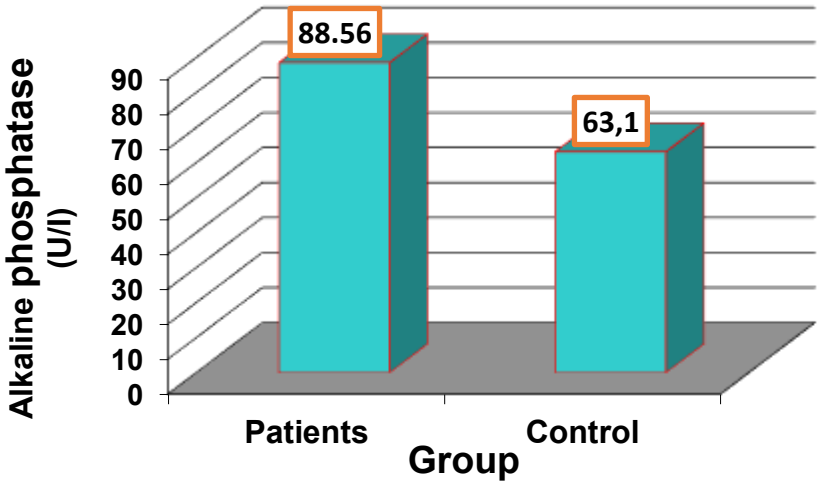


Figure 5. Alkaline phosphatase level in patients and control groups

Table 2. Shows mean ± standard deviation of lipid profile

Group	Mean ± SD (mg/dl)				
	Cholesterol	**Triglyceride**	**HDL**	**LDL**	**vLDL**
Patients	189.9 ± 33.0	228.1 ± 31.8	42.1 ± 8.4	48.21 ± 9.80	29.6 ± 4.4
Control	139.6 ± 24.0	122.3 ± 25.3	55.9 ± 7.4	16.53 ± 3.01	20.5 ± 3.1
P-Value		P ≤ 0.05			

Lipid profile in this research had significant differences in both groups of patients (breast cancer patients) and controls in all parameters measured. The level of cholesterol in patients was significantly higher than in controls (189.9 ± 33.0 mg/dl vs. 139.6 ± 24.0 mg/dl) (Table 2, Figure 6). In the study by González-Ortiz et al., suggesting dyslipidemia, which is a common factor in the progression of cancers. Increased levels of cholesterol can influence the development of cancer through modulation of cellular membranes and signaling pathway [27].

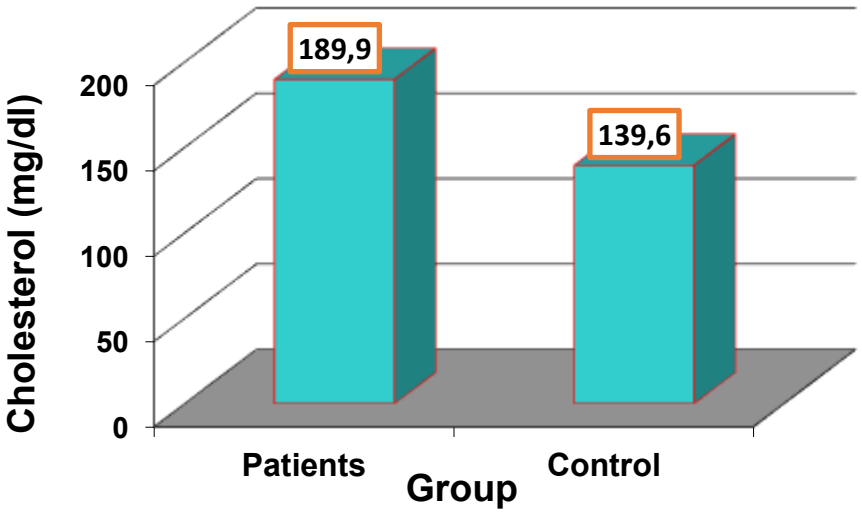


Figure 6. Cholesterol level in patients and control groups

The findings by Lofterød et al. indicated that Triglyceride levels in breast cancer patients were much higher than those in the control group (P ≤ 0.05), the results of our study for triglyceride shown in (Table 2, Figure 7) were 228.1 ± 31.8 mg/dl in the patient group and 122.3 ± 25.3 mg/dl in the control group. The increase in triglycerides could result from changes in lipid metabolism of cancer cells where lipogenesis is increased to facilitate fast division of cancerous cells. This alteration is common in various forms of cancer, including breast cancer [28].

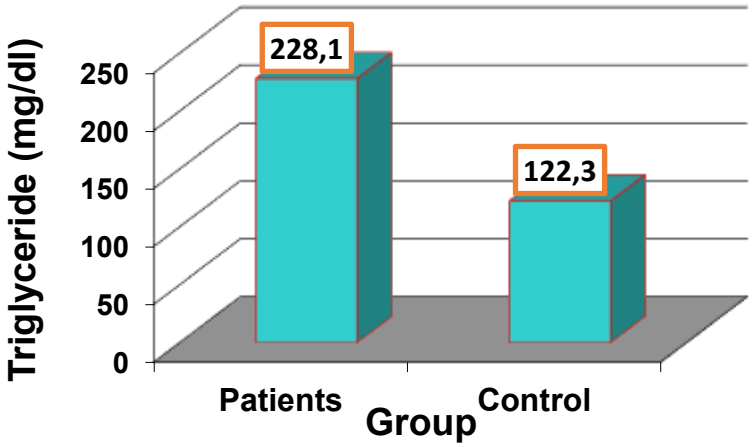


Figure 7. TG level in patients and control groups

The high-density lipoprotein (HDL) known as "good cholesterol" that had significantly ($P \leq 0.05$) lower levels in breast cancer patients (42.1 ± 8.4 mg/dl) compared to the healthy group (55.9 ± 7.4 mg/dl). According to Jung et al., the study also believed that HDL protects against diseases by removing cholesterol from the cells as well as reducing inflammation. In this case, the reduction of HDL levels in breast cancer patients could interfere with increase of inflammatory and oxidation mechanism thus promoting further cancer development. [30].

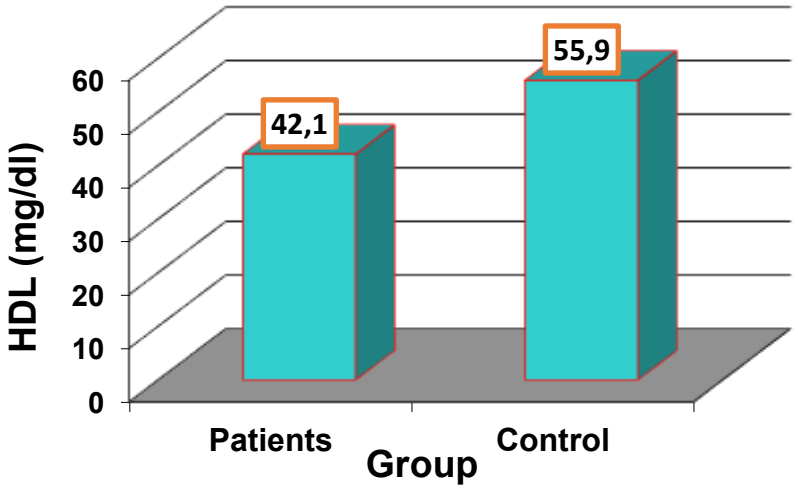


Figure 8. HDL level in patients and control groups

According to Guan et al., the study showed that low-density lipoprotein (LDL) levels were significantly higher in breast cancer patients, this is consistent with the findings of our study shown in table 2 and figure 9, where the level of LDL in patients group (48.21 ± 9.80 mg/dl) were statistically significant ($P \leq 0.05$) higher than in the control (16.53 ± 3.01 mg/dl). High levels of LDL are described as bad cholesterol due to its role in inducing oxidative stress and promoting inflammation thereby increasing cellular proliferation. Thus, an elevated LDL in breast cancer patients indicate the occurrence of dyslipidemia and pathological changes that contribute to disease progression. [30].

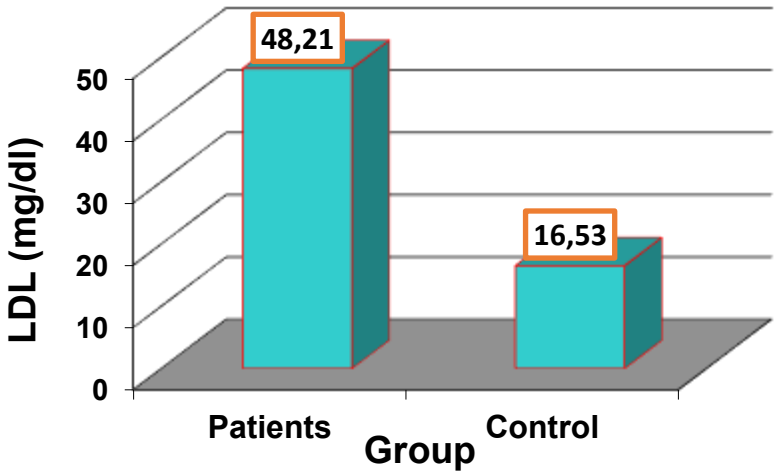


Figure 9. LDL level in patients and control groups

On the same basis, Lu et al. stated that the concentration of very low-density lipoprotein (vLDL) are elevated in breast cancer patients, this was demonstrated by the findings in our study (Table 2 and figure 10) in which the level of vLDL was statistically significant ($P \leq 0.05$) elevated in the patients (29.6 ± 4.4 mg/dl) compared to the control group (20.5 ± 3.1 mg/dl). As vLDL is accountable for transporting triglycerides in the blood circulation, it promotes higher fat storage and can contribute to altered lipid metabolism in breast cancer. The enhanced levels of vLDL imply an advanced lipid transportation system that might facilitate tumor growth and malignancy [31].

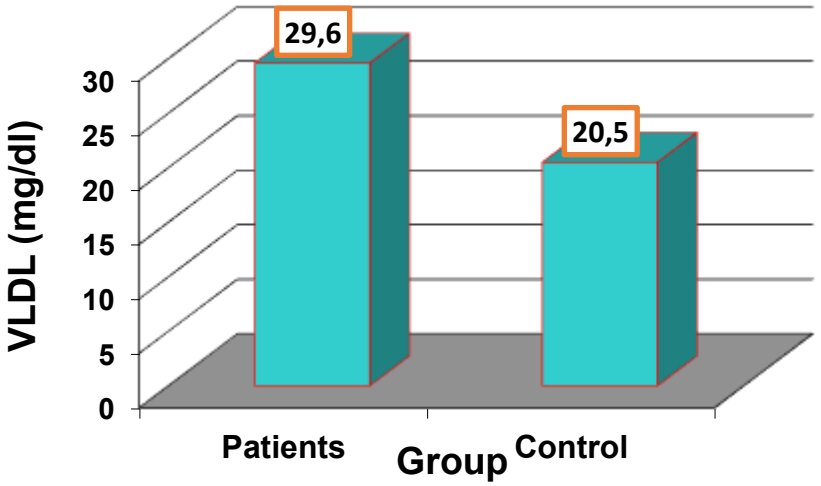


Figure 10. vLDL level in patients and control groups

The differences observed in the lipid parameters were found to be statically significant ($P \leq 0.05$), which highlights the extent to which breast cancer influences lipid metabolism. The augmented cholesterol, triglycerides, LDL, and VLDL along with the reduction in HDL demonstrate changes in the lipid profile in favor of cancer growth and inflammation. These results show the importance of lipid metabolism in the pathology of breast cancer and the potential of monitoring the lipid profile as a possible indicator of disease progression and response to treatment [32].

Conclusion

The study indicates profound alterations in metabolism and hormone levels in women diagnosed with breast cancer, such as increased concentrations of estradiol, progesterone, prolactin, and indicators of dyslipidemia, including cholesterol, triglycerides, LDL, and VLDL, and a decrease in HDL and antioxidant defense (GSH). These alterations suggest a scenario involving oxidative stress, hormonal imbalances, and

modified lipid metabolism, and might contribute to tumor progression and can be a potential indicators of the severity of the disease and of the response to treatment in breast cancer patients.

Ethical approval: This study protocol was approved by the Institutional Ethical Committee and written informed consent was obtained, explicitly, from all the subjects involved in the study.

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