Evaluation Of Some Biochemical Parameters In Patients With Breast Cancer In Basrah Governorate

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Abstract

Breast cancer is the most frequently diagnosed life-threatening cancer in women and the leading cause of cancer death among women. Breast cancer is the second leading cause of cancer deaths among women . In Iraq, breast cancer is the commonest type of female malignancy, ac-counting for approximately one-third of the registered female cancers according to the latest Iraqi Cancer Registry. In this study, patients and volunteers from Basrah Governorate (southern Iraq) participated. A total of fifty five participants were subdivided into two groups, breast cancer patients 35 aged (20-60) years, and 20 healthy individuals (control group) aged (20-60) years. Serum levels of Estrogen , Progesterone , glutathione peroxidase, superoxide dismutase , immunoglobulinG , immunoglobulinM and cancer antigen 15-3 were measured by standard methods. The study reported that Progesterone and IgG were statistically significant ($p<0.05$) in patients with breast cancer compared to healthy control . Estrogen, glutathione peroxidase and superoxide dismutase were statistically very high significant ($p \leq 0.0001$) in patients with breast cancer compared to healthy control .There was very high significant positive correlation between estrogen and IgM ($p \leq 0.0001$) .

Key words : Steroid hormones(progesterone and estrogen), Enzymatic antioxidants(GPX and SOD), Immunoglobulins(IgG and IgM), Cancer antigen15-3(CA15-3) .

Introduction

Breast cancer comprises 10.4% of all cancer incidences among women, making it the second most common type of non-skin cancer (after lung cancer) and the fifth most common cause of cancer death(1). In Iraq, breast cancer is the

main cause of mortality among Iraqi women, accounting for about one-third of all cancer cases recorded in the country in 2019 (2). In Iraq, breast cancer is the commonest type of female malignancy, ac-counting for approximately one-third of the registered female cancers according to the latest Iraqi Cancer Registry . This shows that the breast is the leading cancer site among the Iraqi population in general, surpassing even bronchogenic cancer. As proposed by the World Health Organization, early detection and screening, especially when combined with adequate therapy, offers the most immediate hope for a reduction in breast cancer mortality. This was the basis of the Iraqi national program for early detection of breast cancer, which was initiated in 2001, in an attempt to down-stage this disease at the time of presentation. Since then, specialized centers and clinics for early detection of breast tumors have been established in the major hospitals in all Iraqi provinces. Studies on patients from the three governorates of the north of Iraq, showed that the average age of breast cancer patients was 47.4 ± 11.0 years. Breast Cancer in Kurdish women of Sulaymanyia Iraq is currently diagnosed at advanced clinical stages with 60% of patients being under 50 years of age. The middle zone of Iraq, more informative data on incidence and clinic-pathological features of breast cancer in Iraq came from reports on patients from Baghdad , Ramadi-Falluja , Mosul , and middle Euphrates area. Reports from Basrah, showed that breast cancer is the most frequent cancer in females. Its incidence is higher in developed countries than in developing ones partly due to variation in risk exposure and partly due to better detection methods. Scattered evidence in Basrah, Iraq, suggests that breast cancer has been increasing at a significant pace in recent years (3). Breast cancer is one of the most common cancers among women worldwide and the leading cause of death among Iraqi women (4). Campaigns are frequently launched by health organizations to raise public awareness of a specific disease. Some health campaigns aim to increase public awareness of a specific health threat. The results of National Breast Cancer Awareness Month (NBCAM), one of the most well-known and persistent detection efforts, which was founded in 1985. The major objective of NBCAM is to promote routine breast examinations in order to enable early illness detection. Higher survival rates for breast cancer are linked to early detection

and treatment (5). Age, family history, reproductive factor, estrogen and life style are five important risk factors of breast cancer. Due to the strong correlation between the prevalence of breast cancer and advancing age, ageing is one of the most significant risk factors for breast cancer. Family history is a factor in close to 25% of occurrences of breast cancer. Women are more likely to contract this illness if their mother or sister has the sickness. The risk of breast cancer can be increased by reproductive factors such early menarche, delayed menopause, late age at first pregnancy, and low parity. Estrogens, both endogenous and exogenous, are linked to an increased risk of breast cancer. Ovariectomy can lower the risk of breast cancer in premenopausal women since the ovary often produces endogenous estrogen. Oral contraceptives and hormone replacement therapy (HRT) are the main sources of exogenous estrogen. Breast cancer risk can be raised by contemporary lifestyle factors such excessive alcohol use and dietary fat consumption (6). Breast cancer may be classified into four main stages (stages I–IV) (7) . The diagnostic process for breast cancer: self or clinical breast exam, mammogram, MRI (Magnetic Resonance Imaging), breast biopsy and ultrasound imaging(8,9,10). The types of breast cancer: non – invasive breast cancer, ductal carcinoma in situ, invasive breast cancer, Paget diseases, triple negative breast cancer (TNBC) and inflammatory breast cancer (IBC)(8,11). Progesterone is necessary for controlling typical mammalian female reproductive physiology(12),several exogenous synthetic progestogens (progestins) used in conjunction with estrogen during menopausal hormone therapy or as a form of contraception raise the risk of breast cancer(13),estrogen is a key sex steroid hormone that regulates many biological processes(14), Lower estrogen exposure lowers breast cancer recurrence and new diagnoses in high-risk women, according to experimental and clinical studies. Estrogens are thought to have a role in the growth and development of breast cancer. with the main theory being that estrogens' interactions with receptors lead to higher rates of cell proliferation . Among women who are at high risk of developing breast cancer, the rate of initial diagnoses is decreased by lowering endogenous estrogen levels through bilateral oopherectomy or by inhibiting estrogen effects with specific estrogen receptor modulators such tamoxifen and raloxifene . Breast cancer rate has been linked to early menarche, a delayed first full-term pregnancy, and a delayed

menopause, all of which increase lifelong estrogen exposure. However, there is conflicting epidemiologic proof that premenopausal endogenous estrogens increase the risk of breast cancer (15). IgG, a kind of immunoglobulin, has been discovered to be produced by neoplasms and to stimulate tumor growth in cancer cell lines(16).The immune system's IgM molecule is used to detect antigens linked to tumors(17). Superoxide dismutase (SOD) and glutathione peroxidase (GPX) are the main antioxidants used in first line defence, and their efficacy(18), breast cancer begins, progresses, and invades as a result of oxidative stress, which is an imbalance between oxygen free-radical production and antioxidant scavenging . Excessive oxygen free radical production can oxidatively damage biomolecules, which then leads to mutagenesis . Oxidative stress is known to raise the risk of breast cancer, according to several studies. Compared to healthy persons, SOD activity was markedly higher in breast cancer patients. Additionally, reports of elevated GPX activity in breast cancers (19).A mucinous glycoprotein called CA15-3 is one of Mucin1 (MUC-1) gene's products(20), CA-15-3 detection plays a significant role in both breast cancer screening and diagnosis(21), Untreated breast cancer patients had significantly higher serum levels of CA15-3(22).

Aims of the Study: measuring levels of sex hormones (Estrogen and Progesterone) , antioxidants (GPX and SOD) , some immunoglobulins (IgG and IgM) and cancer antigen15-3 (CA15-3) in breast cancer patients and comparing them with healthy controls as indicators of breast cancer .

Materials & Methods

Sample collection :

Study patients samples collected from breast cancer patients in Basrah province . About 5ml of the blood was drawn from a forearm vein patient. Healthy control was collected from friends and relatives . Venous blood samples were dispensed into gel tubes. After clotting, it was then centrifuged at 2500 rpm for 10 min. The serum is transferred to Eppendorf tubes and frozen at a temperature -20 ^{0}C for later assayed.

In this study, patients and volunteers from Basrah Governorate (southern Iraq) participated. For the period from October 2022 to February 2023, a total of fifty five participants were subdivided into two groups, breast cancer patients 35 aged (20-60) years, and 20 healthy individuals (control group) aged (20-60) years.

Evaluation of Cancer Antigen :

For monitoring response to therapy in metastatic breast cancer patients The electrochemiluminescence immunoassay "ECLIA" is intended for use on Elecsys and COBAS E411 immunoassay analyzers. Sandwich principle. Total duration of assay: 18 minutes.

Evaluation of Progesterone hormone :

The electrochemiluminescence immunoassay "ECLIA" is intended for use on Elecsys and COBAS E411 immunoassay analyzers. Competition principle. Total duration of assay: 18 minutes.

Evaluation of Estrogen hormone :

Serum of estradiol level was measured by using a fully automated COBAS E411 analyzer which was using the Electrochemiluminescence immunoassay "ECLIA" method in analysis. competition principle .

Evaluation of Glutathione peroxidases :

This ELISA kit uses Sandwich-ELISA as the method. The Micro-ELISA stripplate provided in this kit has been pre-coated with an antibody specific to GPX Standards or samples are added to the appropriate Micro-ELISA stripplate wells and combined to the specific antibody.

Evaluation of superoxide dismutase :

This ELISA kit uses Sandwich-ELISA as the method. The Micro-ELISA stripplate provided in this kit has been pre-coated with an antibody specific to SOD. Standards or samples are added to the appropriate Micro-ELISA stripplate wells and combined to the specific antibody.

Evaluation of ImmunoglobulinG :

The COBAS C 311 analyzer is a stand-alone system that offers consolidated testing from a broad menu of clinical chemistry applications. This analyzer has the capacity for ion-selective electrode (ISE) determination of IgG levels in serum, plasma, and urine. Immunoturbidimetric assay.

Evaluation of ImmunoglobulinM :

The COBAS C 311 analyzer is a stand-alone system that offers consolidated testing from a broad menu of clinical chemistry applications. This analyzer has the capacity for ion-selective electrode (ISE) determination of IgM levels in serum, plasma, and urine. Immunoturbidimetric assay.

Statistical Analysis :

Analysis Of Variance (One-way ANOVA) was applied by Minitab ver.16 software was calculated to identify significant differences . Mean and standard deviation (SD) was used to represent the data . The relationship between the parameters was tested using the Pearson's Correlation Coefficients .

Results & Discussion

The statistical analysis in this study, table (1) and figure (1) show the concentration of CA15-3 in patients with breast cancer (25.18± 54.76) U/ml that is higher than healthy controls (10.49± 2.38) U/ml with no statistically significant (P > 0.05) .

Table (1): CA15-3 Level in Patients and Control

Variables	Patients NO=35			Control NO=20			*P* value
	Mean± SD	Median	Min-Max	Mean ± SD	Median	Min-Max	
CA15-3 (U/ml)	25.18 ± 54.76	15.01	1-300	10.49 ± 2.38	10.10	7.25-16.14	0.189

One-way ANOVA

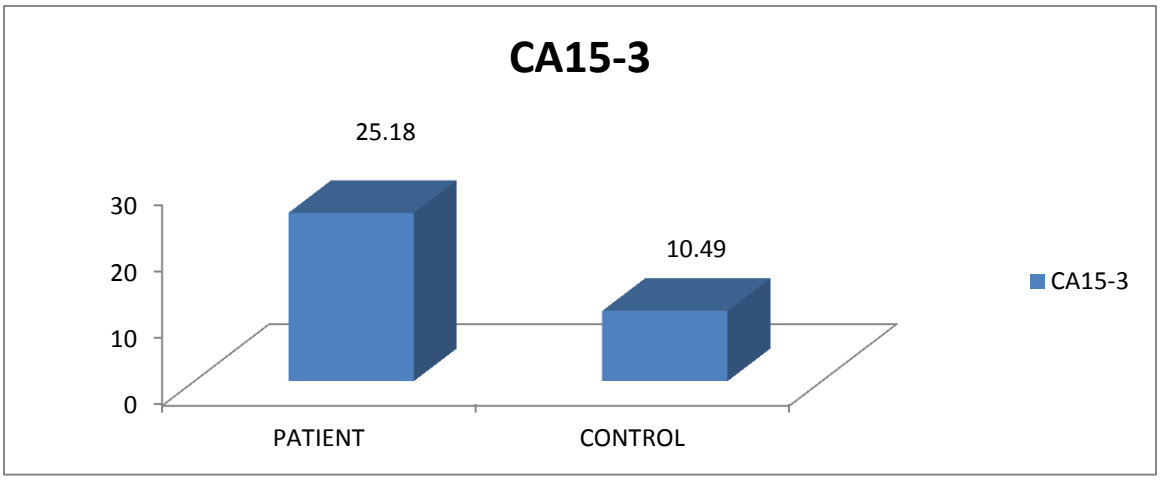

Figure (1): Mean ±SD Level of CA15-3 in Serum of Patients and Healthy Control .

Results of this study were in accordance with the results reported by other authors (Khorrami, *et al* .2019) (23), revealed that breast cancer patients have higher CA15-3 levels in their serum, which supports its use as a non-invasive and easy biomarker for the diagnosis, monitoring, and prognosis of breast cancer. This results agree with that of (Hashim, *et al*. 2014) (24), both healthy and malignant breast ductal epithelium express cancer antigen 15-3. It is a mucin that is a member of a sizable family of glycoproteins that are heterogeneously expressed on the apical surface of several types of healthy epithelial cells, including those found in the breast. When monitoring patients with metastatic breast cancer receiving treatment and for the early diagnosis of tumor recurrence, serum CA 15-3 is employed as a substitute marker of disease mass. Some patients with breast cancer who have distant metastases have increased CA 15-3 levels. Elevated CA 15-3 is used to predict the discovery of recurrences in patients, despite the fact that the National Comprehensive Cancer Network and American Society of Clinical Oncology's most recent guidelines do not advise its use for surveillance. This results agree with that of (Zhao, *et al*. 2021) (25), that revealed additionally, it was found that breast cancer patients had higher serum CA15-3 concentrations. Whose discovery that prior research has already demonstrated the connection between tumor size which is a representation of tumor burden and an elevated level of CA15-3. In the current investigation, we also found a correlation between tumor size and an increase in CA15-3 levels. Additionally, the tumor's size was determined. The results in this study agree with the studies held by (Li, *et al*. 2018) (26) , having a reasonably high level of CA15-3 was a reliable indicator of the patients' prognosis.

The statistical analysis in this study, table (2) and figure (2) show the concentration of Progesterone in patients with breast cancer (0.25±0.81)ng/ml that is lower than healthy controls (1.83±3.13)ng/ml with statistically significant ($p<0.05$) .

Table (2): Progesterone Level in Patients and Control :

Variables	Patients NO=35			Control NO=20			*P* value
	Mean± SD	Median	Min-Max	Mean ± SD	Median	Min-Max	
Progesterone (ng/ml)	**0.25 ± 0.81**	**0.11**	**0.05-4.4**	**1.83 ± 3.13**	**0.19**	**0.05-9.21**	**0.006**

One-way ANOVA

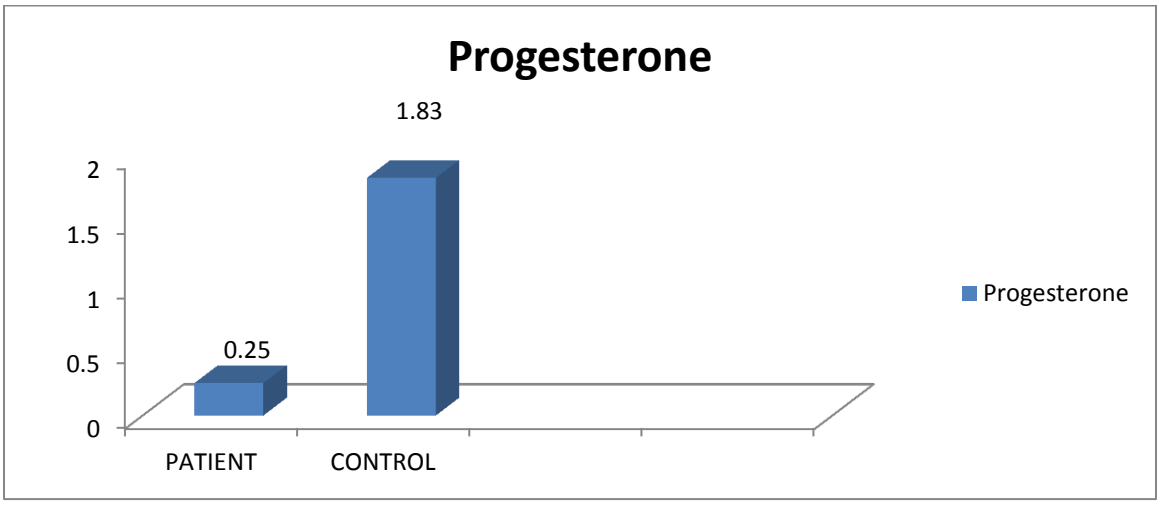

Figure (2): Mean ±SD Level of Progesterone in Serum of Patients and Healthy Control .

Steroid hormones such as estrogen and progesterone are essential in controlling mammalian reproduction, with one of their main functions being to control uterine development and function. Breast cell proliferation is decreased by progesterone. It helps breast cells mature and slows down their rate of multiplication. Additionally, it encourages healthy breast cell death, which is crucial for cancer prevention (27),(28). Menopause and premature menopause are connected to low levels of estrogen and progesterone. The hormones (estrogen & progesterone) in the body can be thought of as "talking to each

other." Consequently, significant conditions, such as breast cancer and uterine cancer are associated with higher levels of estrogen compared to progesterone (estrogen Dominance) (29) , the results of our study do not agree with them .

The results in this study agree with the studies held by (Rosal, *et al*, 2011)(30) , the mean percentage of stained nuclei for estrogen and progesterone receptors decreased significantly and similarly after exposure to tamoxifen or raloxifene ($P < 0.0001$).Progesterone and estrogen receptor alpha expression is dramatically decreased by tamoxifen and raloxifene. Also agrees with (Sathyamoorthy *et al.*, 2020)(31), who concluded that Progesterone levels' role in the development of disease is still debatable. And agrees with (Kaaks, *et al.*, 2014)(32)**,** who finds that There was no evidence linking premenopausal estrogen and progesterone levels to a higher risk of breast cancer. Also agrees with (Trabert, *et al.* , 2020) (33) , showed that circulating progesterone levels and breast cancer risk have been examined in a small number of population-based studies. Prediagnostic circulating progesterone levels and breast cancer risk were not linked in one research of postmenopausal women that included 322 breast cancer cases and 643 matched controls.

The statistical analysis in this study, table (3) and figure (3) show the concentration of Estrogen in patients with breast cancer (53.08±28.69)pg/ml that is lower than healthy controls (114.75±85.43)pg/ml with statistically very high significant ($p \leq 0.0001$) .

Table (3): Estrogen Level in Patients and Control :

Variables	Patients NO=35			Control NO=20			*P* value
	Mean± SD	Median	Min-Max	Mean± SD	Median	Min-Max	
Estrogen (pg/ml)	**53.08 ± 28.69**	**44.4**	**35.28-140.1**	**114.75 ± 85.43**	**86.16**	**42.4-321.9**	**0.000**

One-way ANOVA

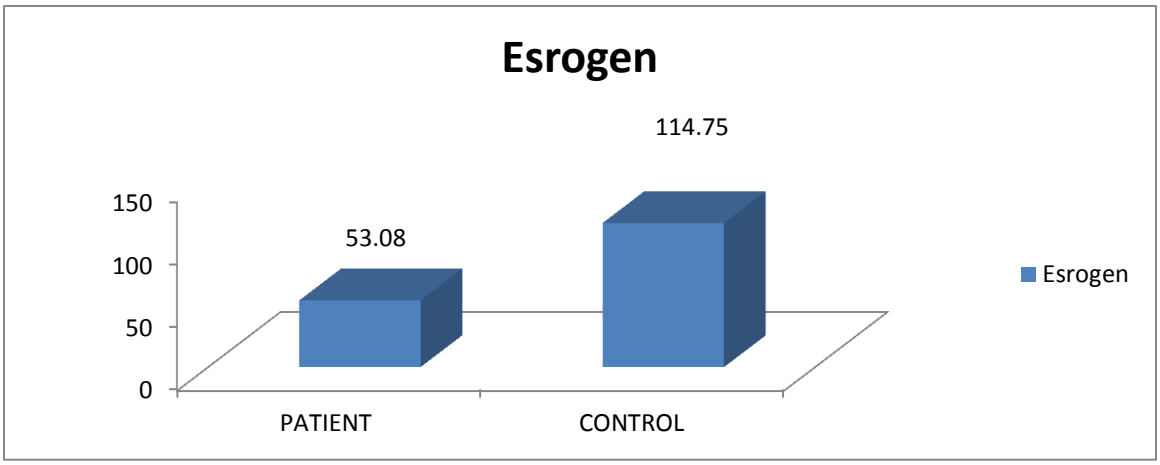

Figure (3): Mean ±SD Level of Estrogen in Serum of Patients and Healthy Control .

Lower estrogen exposure lowers breast cancer recurrence and new diagnoses in high-risk women, according to experimental and clinical studies. Estrogens are thought to have a role in the growth and development of breast cancer. with the main theory being that estrogens' interactions with receptors lead to higher rates of cell proliferation . Among women who are at high risk of developing breast cancer, the rate of initial diagnoses is decreased by lowering endogenous estrogen levels through bilateral oopherectomy or by inhibiting estrogen effects with specific estrogen receptor modulators such tamoxifen and raloxifene . Breast cancer rate has been linked to early menarche, a delayed first full-term pregnancy, and a delayed menopause, all of which increase lifelong estrogen exposure. However, there is conflicting epidemiologic proof that premenopausal endogenous estrogens increase the risk of breast cancer(15) .

This results not agree with that of (Heidi *et al* . 2018) (34) , that revealed high estrogen levels are linked to an increased risk of several malignancies, including uterine and breast cancer. High levels of progesterone have been associated with an increased risk of breast cancer. In addition to that not agree with that of (Wang, *et al* . 2017) (35) , that revealed in addition to circulating estrogen levels, local estrogen levels also contribute to the development of breast cancer. Results of this study were in accordance with the results reported by other authors (Savolainen-Peltonen, *et al.*, 2014)(36), Although postmenopausal estrogen levels in the blood are low, they have been positively linked to a higher risk of breast cancer in postmenopausal women.

Similar results were obtained by (Kaaks, *et al.*, 2014)(32)**,** who finds that there was no evidence linking premenopausal estrogen and progesterone levels to a higher risk of breast cancer. (Al-Abassi, *et al*., 2018)(37) who suggested that the mean of progesterone concentration in serum showed a significant increasing in patients (6.319±0.75) ng/ml compared to control (3.206±1.08) ng/ml (P<0.05), As well as the estradiol observed a higher significant decreasing difference level in patient (540.88±17.97) pg/ml compared to control (635.79±36.03) pg/ml (P<0.01), present results agree with them about estrogen but not agree about progesterone.

The statistical analysis in this study, table (4) and figure (4) show the concentration of IgG in patients with breast cancer (1639.11±486.90)mg/dL that is higher than healthy controls (1348.25±221.23) mg/dL with statistically significant (p<0.05) .

Table (4): IgG Level in Patients and Control :

Variables	Patients NO=35			Control NO=20			*P* value
	Mean± SD	Median	Min-Max	Mean± SD	Median	Min-Max	
IgG (mg/dL)	1639.11 ± 486.90	1510	1013-2681	1348.25 ± 221.23	1329	977-1800	0.011

One-way ANOVA

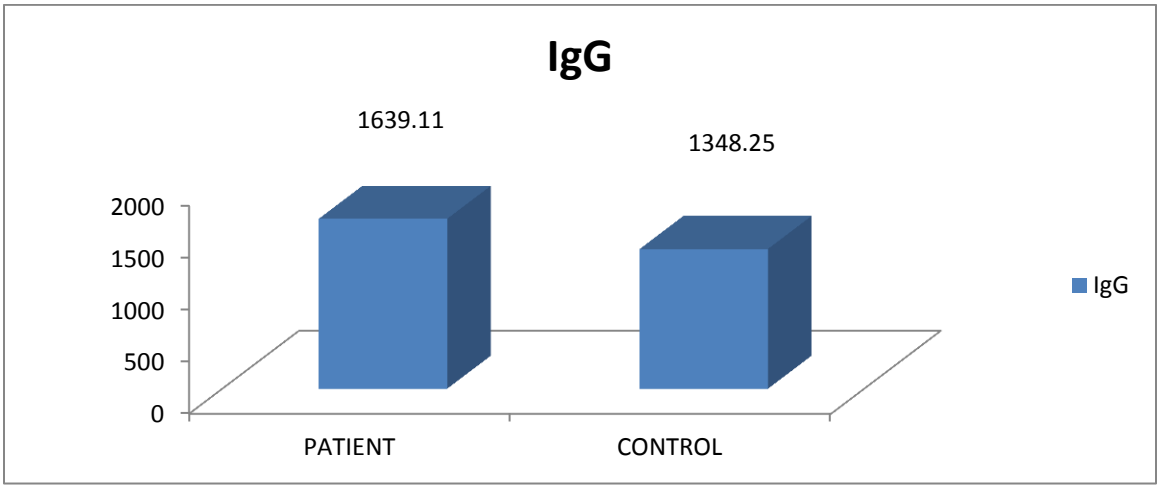

Figure (4): Mean ±SD Level of IgG in Serum of Patients and Healthy Control.

This results matched with some researchers (Ma, *et al*,2013)(38), it was shown that immunoglobulin G (IgG) is produced by neoplasms and stimulates tumor growth in cancer cell lines. Additionally, we discovered that the number of IgG-expressing cancer cells was greater and they were distributed more widely in the metastatic cancer cells than in the main lesion. According to these findings, IgG-expressing breast cancer cells behave biologically more aggressively than IgG-negative cancer cells, which may be a sign of disease progression and metastasis. These immune complexes may help cancer cells escape the immune system. IgG is a significant player in breast cancer and might be a good target for treatment. IgG, a kind of immunoglobulin, has recently been discovered to be produced by neoplasms and to stimulate tumor growth in cancer cell lines. Additionally, we discovered that the metastatic cancer cells contained a greater number and a more even distribution of IgG-expressing cancer cells than the cancer cells in the initial lesion . According to these findings, IgG-expressing breast cancer cells behave biologically more aggressively than IgG-negative cancer cells, which may be a sign of disease progression and metastasis. These immune complexes may help cancer cells escape the immune system. IgG is a key player in breast cancer and may be a promising therapeutic target. Also the study agrees with (Saku, *et al.*, 2021)(39)**,** who finds that in summary, according to this research, patients with metastatic recurrent breast cancer (mrBC) had higher plasma IgG antibodies.

The statistical analysis in this study, table (5) and figure (5) show the concentration of IgM in patients with breast cancer (112.57±219.24)mg/dL that is lower than healthy controls (136.3±60.06)mg/dL with no statistically significant ($P > 0.05$) .

Table (5): IgM Level in Patients and Control :

Variables	Patients NO=35			Control NO=20			*P* value
	Mean ± SD	Median	Min-Max	Mean ± SD	Median	Min-Max	
IgM (mg/dL)	**112.57 ± 219.24**	**82**	**16-1207**	**136.3 ± 60.06**	**139.5**	**23-285**	**0.602**

One-way ANOVA

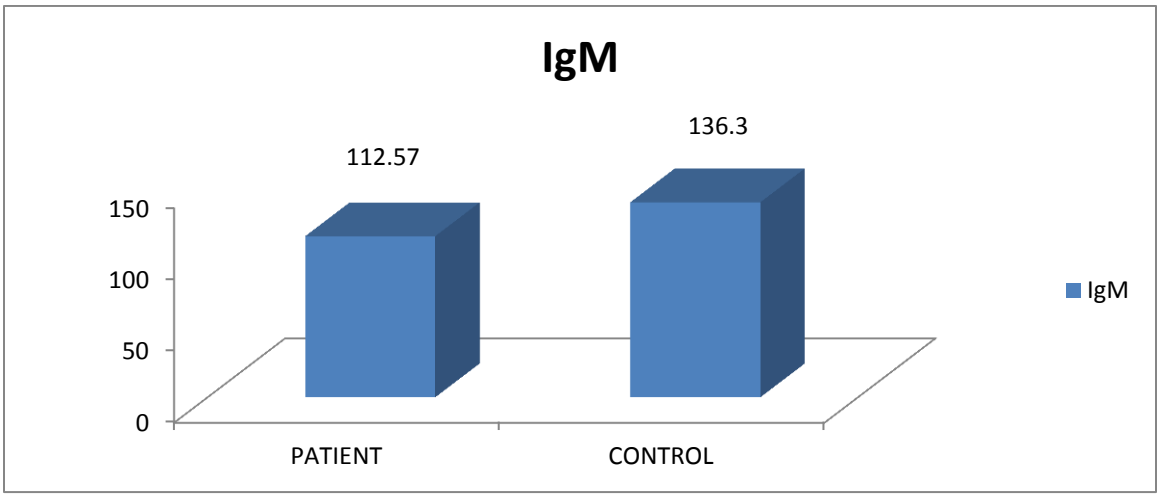

Figure (5): Mean ±SD Level of IgM in Serum of Patients and Healthy Control.

The function of natural and adaptive IgM in reducing cancer cells in the early stages of disease and their importance as early diagnostic tools are described in the current review. The immune system's IgM molecule is used to detect antigens linked to tumors (40) .

As mentioned by a researchers (Fremd, *et al*, 2016)(41), previous studies have revealed that mucin1 (MUC1) IgG antibody levels are considerably greater in breast cancer patients than in the whole control population, whereas no significant difference was identified for IgM antibody levels, present study agrees with the above researcher. (Ali *et al*., 2014)(42), who suggested that in comparison to the control group, the findings showed that immunoglobulins IgA, IgG, and IgM were significantly higher in breast cancer, present results agree with them about IgG but not agree about IgM . This study agrees with a study held by (Roberts *et al*., 1975)(43), who showed that (table 6):

Table (6): Serum Immunoglobulin M Levels in Patients and Controls

Controls & patients		**IgM (mg / 100ml) (mean± SD)**
Control		**196±12**
Breast cancer	**Stages I & II**	**164±14**

	Stage III	**161±11**
	Stage IV	**173±18**

The statistical analysis in this study, table (7) and figure (6) show the concentration of GPX in patients with breast cancer (62.99±40.73)ng/ml that is higher than healthy controls (24.05±16.92)ng/ml with statistically very high significant ($p \leq 0.0001$) .

Table (7): GPX Level in Patients and Control :

Variables	**Patients NO=35**			**Control NO=20**			***P* value**
	Mean± SD	**Median**	**Min-Max**	**Mean ± SD**	**Media**	**Min-Max**	
GPX (ng/ml)	**62.99 ± 40.73**	**59.8**	**0.2-155.2**	**24.05 ± 16.92**	**21.3**	**1.12-57.99**	**0.000**

One-way ANOVA

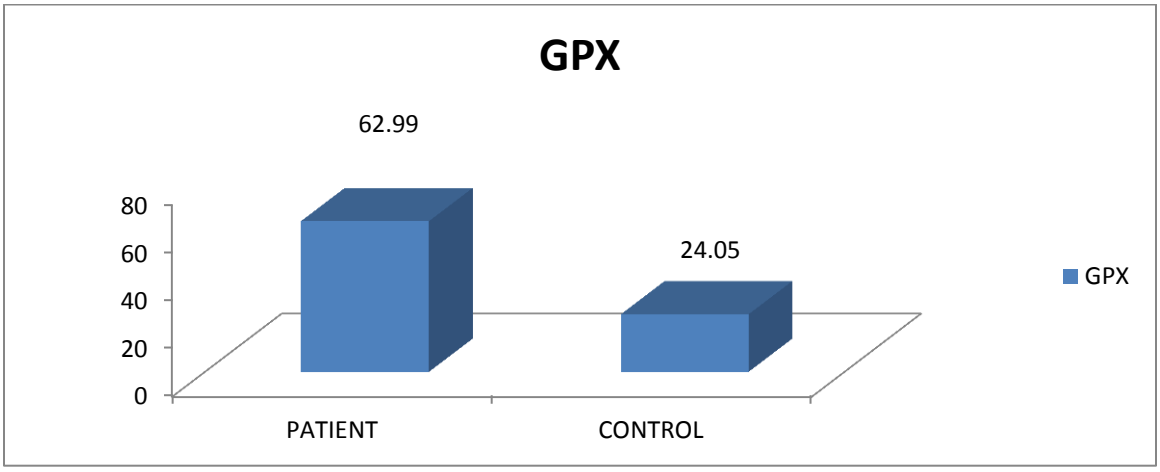

Figure (6): Mean ±SD Level of GPX in Serum of Patients and Healthy Control.

Superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPX) are the main antioxidants used in first line defence, and their efficacy (44). Peroxidases (POX) act in the extracellular space to scavenge H2O2 and SOD catalyses the elimination of •O2− by dismutating it into O2 and H2O2. CAT transforms the H2O2 into water and molecular oxygen

(O2) (45) . Breast cancer begins, progresses, and invades as a result of oxidative stress, which is an imbalance between oxygen free-radical production and antioxidant scavenging . Excessive oxygen free radical production can oxidatively damage biomolecules, which then leads to mutagenesis . Oxidative stress is known to raise the risk of breast cancer, according to several studies. Compared to healthy persons, SOD activity was markedly higher in breast cancer patients. Additionally, reports of elevated GPX activity in breast cancers (19)

Similar results were obtained by (Jardim, et al.,2013)(46), that revealed their findings imply that high levels of GPX may be associated with treatment response, clinical outcome, and an increase of chemotherapy resistance in these tumors. This results agree with that of (Jablonska, *et al.*, 2015)(47)**,** Who finds that in their study, the increased GPX activity was accompanied by an increase in plasma lipid peroxidation in cancer patients. But this study not agree with that of (Danesh *et al* . 2022) (48) , that revealed breast cancer patients had considerably lower levels of malondialdehyde (MDA) and glutathione peroxidase (GPX) compared to the control group.

The statistical analysis in this study, table (8) and figure (7) show the concentration of SOD in patients with breast cancer (24.33±15.51)ng/ml that is higher than healthy controls (5.31±2.70)ng/ml with statistically very high significant ($p \leq 0.0001$).

Table (8): SOD Level in Patients and Control :

Variables	Patients NO=35			Control NO=20			*P* value
	Mean± SD	Median	Min-Max	Mean± SD	Median	Min-Max	
SOD (ng/ml)	24.33 ± 15.51	21.1	2.76-57.52	5.31 ± 2.70	4.83	1.1-9.96	0.000

One-way ANOVA

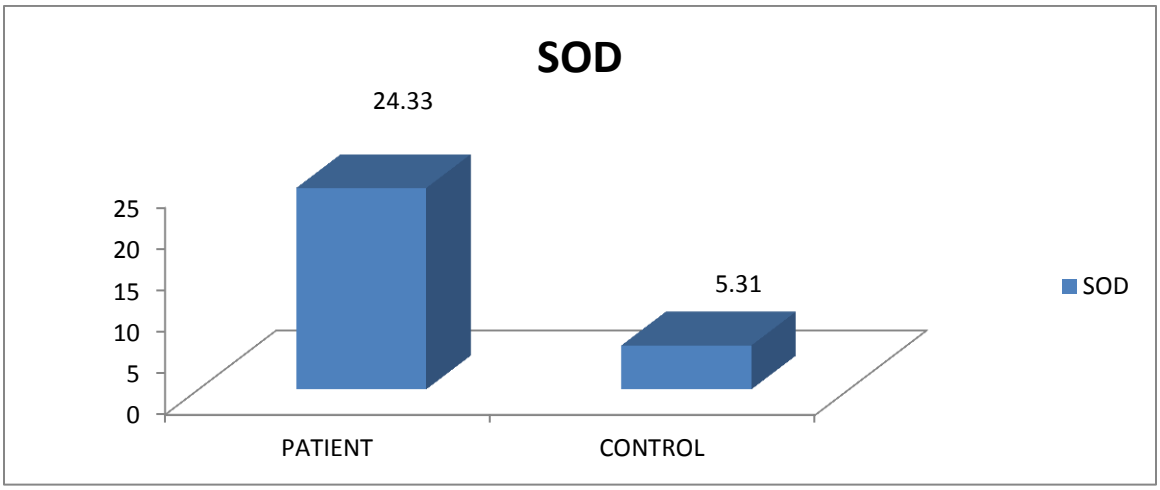

Figure (7): Mean ±SD Level of SOD in Serum of Patients and Healthy Control.

This results agree with that of (Danesh *et al* . 2022) (47) , that revealed superoxide dismutase (SOD) and catalase (CAT), two indicators of oxidative stress, were markedly increased in cancer patients. In addition, (Kangari, et al, 2018)(19), When compared to controls, SOD activity was significantly higher in the breast cancer patients. However, GPX activity was significantly lower in breast cancer patients compared to controls, while this results agree with them about SOD but not agree about GPX .

Table (9) shows the correlation coefficient (r) of biochemical Variables in the patient females :

Table (9): correlation coefficient (r) of biochemical Variables in the patient females.

Patients		
Parameters	**r**	**P-value**
CA15-3 & progesterone	**-0.036**	**0.836**
CA15-3 & estrogen	**-0.073**	**0.679**
CA15-3 & IgG	**-0.028**	**0.872**
CA15-3& IgM	**0.009**	**0.958**
CA15-3& GPX	**-0.039**	**0.825**
CA15-3& SOD	**-0.134**	**0.444**
Estrogen& IgG	**-0.006**	**0.973**
Estrogen& IgM	**0.608**	**0.000**
Estrogen& GPX	**-0.077**	**0.662**

Estrogen& SOD	**-0.061**	**0.727**
IgG& GPX	**-0.262**	**0.128**
IgG& SOD	**0.003**	**0.986**

And table (10) shows the correlation coefficient (r) of biochemical Variables in the control females:

Table (10): correlation coefficient (r) of biochemical Variables in the control females

Control		
Parameters	**r**	**P-value**
CA15-3 & progesterone	**0.11**	**0.645**
CA15-3 & estrogen	**0.001**	**0.998**
CA15-3 & IgG	**-0.084**	**0.724**
CA15-3& IgM	**-0.198**	**0.403**
CA15-3& GPX	**-0.099**	**0.679**
CA15-3& SOD	**0.428**	**0.060**
Estrogen& IgG	**0.179**	**0.449**
Estrogen& IgM	**-0.191**	**0.419**
Estrogen& GPX	**-0.398**	**0.082**
Estrogen& SOD	**0.264**	**0.262**
IgG& GPX	**0.202**	**0.394**
IgG& SOD	**-0.131**	**0.582**

In patients group, the statistical analysis in this study was very high significant positive correlation between estrogen and IgM ($p \leq 0.0001$),(r: 0.608) .

Conclusions

The results obtained in this study are a decrease in the level of progesterone and estrogen in breast cancer patients compared to the control group. It was also concluded that the level of IgG increased in patients with

breast cancer compared to the control group, while the level of IgM decreased in patients with breast cancer. Also, high levels of enzymatic antioxidants (GPX & SOD) were obtained in breast cancer patients compared to the healthy group. Finally, a high level of tumor marker (CA15-3) was obtained in breast cancer patients compared to the control group. The statistical analysis in this study was very high significant positive correlation between estrogen and IgM ($p \leq 0.0001$),(r: 0.608) .

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