

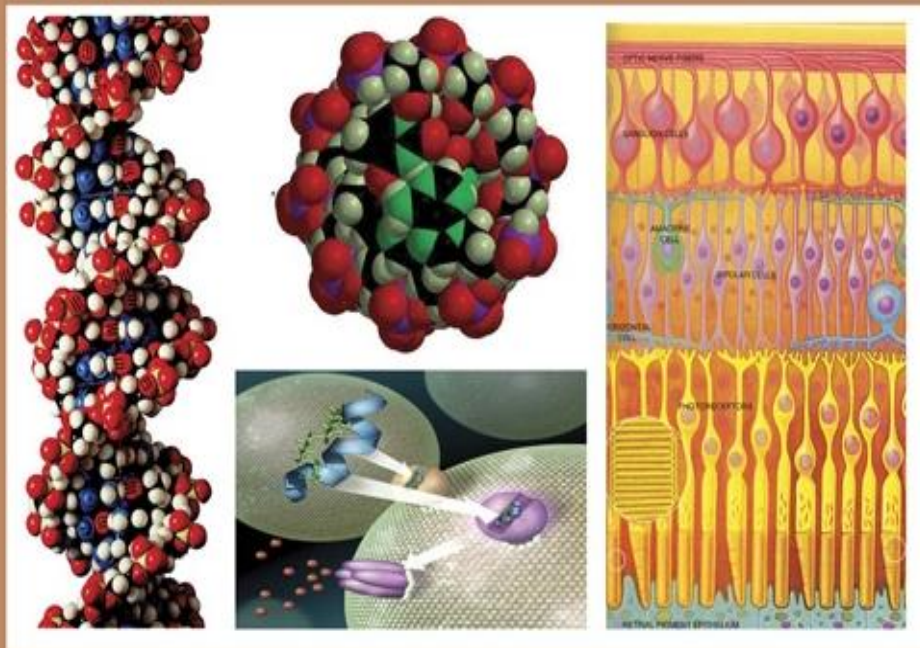


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EGYPTIAN ACADEMIC JOURNAL OF

# BIOLOGICAL SCIENCES

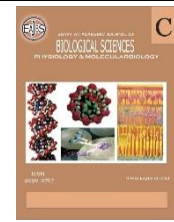
PHYSIOLOGY & MOLECULAR BIOLOGY



ISSN  
2090-0767

WWW.EAJBS.EG.NET

Vol. 15 No. 2 (2023)



## Effect of Invasive Ductal Carcinoma on Some Physiological and Immunological Parameters in Women with Breast Cancer

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### ARTICLE INFO

#### Article History

Received:15/7/2023

Accepted:29/8/2023

Available:3/9/2023

#### Keywords:

Breast Cancer,  
Invasive Ductal  
Carcinoma, Body  
Mass Index,  
Carcinoembryonic  
antigen.

### ABSTRACT

**Background:** Breast cancer is the most common type of cancer in women, with one to eight women developing breast cancer in their lifetime. This study aims to investigate the effect of invasive ductal carcinoma on some physiological and immunological parameters in women with breast cancer. **The methods:** The current study at the National Cancer Centre in Al-Najaf province for the period between 8/15/2022 to 1/20/2023. this study included 60 women with breast cancer considered as the patients and 30 healthy women free of diseases considered a control group, both groups, their ages ranged between (30-68) years old, body mass index, erythrocyte sedimentation rate, C-reactive protein, iron stores (ferritin) and fetal carcinoembryonic antigen were estimated. **Results:** The results showed that invasive ductal carcinoma is the most prevalent type of breast cancer with a rate of 68.7% within the studied sample. As for metastasis, it was noted that stage 0 was the highest with a rate of 96.7%. The results of the disease stage also showed that stage 2 was the highest with a rate of 73.3%. The results showed an increase in body mass index (BMI) in the control group compared to the patients' group. A significant increase in the erythrocyte sedimentation rate (ESR) was also observed in women with breast cancer compared with the group of healthy women. The results of the statistical analysis also showed a significant increase in iron stores (Ferritin), CRP and CEA among the affected women compared with the healthy women.

The results showed that there were no significant differences in the type of invasive ductal carcinoma compared to the invasive lobular carcinoma for the criteria represented by body mass index, and erythrocyte sedimentation rate. As for the levels of ferritin, C-reactive protein and CEA, the results of the statistical analysis showed that there was a significant increase in their levels in patients with invasive lobular carcinoma compared with the other group with invasive ductal carcinoma.

The results also showed that there is an effect of the type of disease ((invasive ductal carcinoma)) on each of the erythrocyte sedimentation rate and CEA. **Conclusions:** the results obtained through the current study, we conclude that invasive ductal carcinoma is the most common type of breast cancer with an increase of ESR, CRP, ferritin and CEA in women with breast cancer. The effect of invasive ductal carcinoma on CEA and ESR criteria was more than invasive lobular carcinoma.

## INTRODUCTION

Cancer is a deadly disease and one of the main issues facing societies today. Cancer occurs when the cell divides irregularly and out of control, and this will lead to irregular growth. This growth results in a mass of excess tissue known as a tumor. Cancer is given a name for the part with which it begins, and on this basis, breast cancer is defined as irregular growth, spread and multiplication of cells that are found in breast tissue (Cao *et al.*, 2021).

There are many types of breast cancer that differ histologically, as breast tumors arise from the epithelial cells of the ductal epithelial tissue or the lobular epithelial tissue and are divided into two main types:

1 Carcinoma in situ

2- Invasive carcinoma (Lips *et al.*, 2022).

The invasive ductal breast cancer is one of the most common types and it begins in the milk ducts, penetrating the wall of the ducts as it grows in the fatty tissue of the breast. This type is capable of metastasis to other parts of the body through the lymphatic system or the bloodstream of metastatic breast cancer (Yao *et al.*, 2023).

The study aims to know the relationship between invasive ductal carcinoma and its effect on some physiological and immunological parameters in women with breast cancer, represented by body mass index, erythrocyte sedimentation rate, C-reactive protein, iron stores (ferritin), and fetal carcinoembryonic antigen.

## MATERIALS AND METHODS

### Study Samples:

The current study was conducted at the National Cancer Center in Al-Najaf Governorate for the period from 8/15/2022 to 1/20/2023. The study included 90 blood samples, including 60 blood samples from women with breast cancer, and their ages ranged from 30\_68 years, in addition to selecting a random group. It included 30 blood samples from healthy women of the same age group.

### Collect Blood Samples:

Blood samples were collected 5ml of venous blood using medical syringes; 3 ml placed in a gel tube, and then separated using a centrifuge at a speed of 3000 rpm, for 5 minutes for the purpose of immunological examinations. And 2 ml was transferred to tubes containing EDTA to measure the Erythrocyte sedimentation rate.

### BMI Calculator:

Weight and height were measured for the group of breast cancer patients, as well as the case for the control group, using a digital balance and a measuring tape. Body mass index was calculated by applying the following equation (Cleary *et al.*, 1997):

$BMI (kg/m^2) = \text{body weight (kg)} / \text{height squared (m}^2\text{)}$ .

### Erythrocyte Sedimentation Rate (ESR):

The common method for conducting the ESR test is called the Westergren method, and a special pipette of 300 mm long and graduated from zero to 200 mm is used for it. (Ramadan M. Suleiman. 2015).

### Estimation of C-reactive Protein (CRP)

#### Level:

The latex agglutination slip assay for the qualitative and semi-quantitative determination of C-reactive protein in undiluted serum was provided by Human, Germany.

### Estimation of the Carcinoembryonic Antigen (CEA) Level:

The concentration of CEA in blood serum was measured by a carcinoembryonic antigen measurement kit (CEA-kit) prepared by bioMerieux according to the method (Eboreime and Idemudia, 2015).

### Estimation of Ferritin Level:

The concentration of ferritin in blood serum was measured by a ferritin kit prepared by bioMerieux according to the method (Imbert *et al.*, 1987).

### Statistical Analysis:

The analysis was performed using SPSS v.28 and Microsoft software Excel 2019 for graphs. The distribution of continuous variables was analyzed using the Kolmogorov–Smirnov test, in order to assess significant departures from normality.

Normal distribution statistical analysis for the differences between groups and Data are expressed as mean ± SE (standard error). Using, Independent T-tests to compare continuous variables between groups. Whenever the multiple comparisons between groups were performed by one-way ANOVA with Tukey`s post hoc. Categorical variables were analyzed by the chi-square test. For detecting the value of predicted biomarkers by Binary and Nominal Regression analyses, obtained on Odds ratio (OR) and 95%CI. The significance of differences was detected at p<0.05. (Sullivan, 2017).

**RESULTS**

The results of the current study shown in Table (1) indicated that invasive

ductal carcinoma is the most common type of breast cancer with a rate of 86.7%, followed by invasive lobular carcinoma with a rate of 13.3%. As for the size of the tumor, the second degree was more predictable with a rate of 45.0%, followed by the third degree with a rate of 28.3%, then the first degree with a rate of 26.7%. The results of the study also showed a spread of cancer cells to the lymph nodes within the studied sample.

As for metastasis, it was noted that stage 0 was the highest with a rate of 96.7% compared to stage 2. The results of the disease stage also showed that stage 2 was the highest with a rate of 73.3% compared to the third stage, which was 26.7%.

**Table (1):** Distribution of disease characteristics in breast cancer patients.

Variables	Categories	N	%	Chi-square	p-value
Types of breast cancer	Invasive ductal carcinoma	52	86.7%	32.267	0.0001
	Invasive lobular carcinoma	8	13.3%		
Tumor Size (T)	1	16	26.7%	3.7	0.157
	2	27	45.0%		
	3	17	28.3%		
Lymph node (N)	0	16	26.7%	6.00	0.112
	1	19	31.7%		
	2	18	30.0%		
	3	7	11.7%		
Metastasis (M)	0	58	96.7%	52.267	0.0001
	1	2	3.3%		
Cell grade	2	44	73.3%	13.067	0.0001
	3	16	26.7%		

The results shown in Table (2) showed a significant increase (p<0.05) in the body mass index (BMI) in the control group compared to the patients' group. A significant (p<0.0001) increase in the erythrocyte sedimentation rate (ESR) was also observed

in women with breast cancer compared to a group of healthy women, and the results of the statistical analysis showed a significant increase (p<0.0001) in the ferritin iron store. CRP and CEA in affected women compared with healthy women.

**Table (2):** Comparison of some vital indicators between women with Brest cancer and healthy women.

Variables	Patients n=60	Controls n=30	p-value
Age (Year)	50.1±1.56	52.07±2.35	0.477
BMI (kg/m <sup>2</sup> )	27.54±0.61*	29.7±0.99	0.052
ESR (mm/hr)	48.13±2.45 *	20.67±1.21	0.0001
Ferritin (mg/l)	247.41±17.94 *	101.68±7.09	0.0001
CRP (mg/dL)	16.65±2.23 *	2.98±0.38	0.0001
Cea (ng/mL)	4.88±0.44 *	1.51±0.14	0.0001

Significant differences at p-value <0.05.

The results of the current study showed in Table (3) that there were no significant differences (p>0.05) for the type of invasive ductal carcinoma compared to the invasive lobular carcinoma for the criteria represented by BMI, and erythrocyte sedimentation rate. As for the levels of

ferritin, C-reactive protein and CEA, the results of the statistical analysis showed a significant increase (p<0.05) in their levels in patients with invasive lobular carcinoma compared with the other group with invasive ductal carcinoma.

**Table (3):** The effect of Type of cancer on all the studied criteria in the women with breast cancer group

Variables	Type of cancer		p-value
	Invasive ductal carcinoma n=52	Invasive lobular carcinoma n=8	
Age (Year)	49.38±1.69	54.75±3.88	0.245
BMI (kg/m <sup>2</sup> )	27.41±0.67	28.38±1.47	0.596
ESR (mm/hr)	48.6±2.77	45.13±3.96	0.635
Ferritin (mg/l)	235.59±18.3	324.25±59.38*	0.053
CRP (mg/dL)	15.44±2.18	24.49±8.9*	0.050
Cea (ng/mL)	4.75±0.45	5.67±1.55*	0.054

Significant differences at p-value <0.05.

The results also showed that there is an effect of the type of disease ((invasive ductal carcinoma)) on all the studied criteria

represented by the erythrocyte sedimentation rate and CEA with a probability level (p < 0.0001) Table (4).

**Table (4):** Nominal Regression for predicting the independent factors of Biochemical parameters in types breast cancer patients.

Invasive ductal carcinoma <sup>a</sup>	B	SE	p-value	OR	95% CI
ESR (mm/hr)	0.039	0.009	0.0001*	1.040	1.022 - 1.057
Cea (ng/mL)	0.292	0.080	0.0001*	1.339	1.145 - 1.565

a. The reference category is Invasive lobular carcinoma. B: side effects. SE: standard error. OR: odds ratio. 95% CI: Confidence Interval for OR.

## DISCUSSION

The results of the current study indicated that invasive ductal carcinoma is the most prevalent type of breast cancer with a rate of 86.7%, followed by invasive lobular carcinoma with a rate of 13.3% within the sample studied, and this is proven by the majority of studies, as it indicated that the percentage of invasive ductal carcinoma ranges from approximately 50% to 80%. While it indicated that the percentage of invasive lobular carcinoma is approximately 20% of cancer cases (Al-Ishaq *et al.*, 2023), Invasive ductal carcinoma which is the most common type of breast cancer, refers to the uncontrolled growth of cancer cells, which originate from the milk ducts present in the breast tissue.

The most common cause of invasive ductal carcinoma is DNA damage to breast tissue cells. DNA damage can cause changes in various genes, such as BRCA1 and BRCA2, which normally control cell growth, prolong cell survival, manage cell division, and prevent cell death. Unwanted if such changes occur, they can gradually lead to uncontrolled cell growth, become cancerous and potentially infiltrate the stroma. A variety of genetic and environmental risk factors can lead to DNA damage and the consequent development of invasive ductal carcinoma. This can be the result of a wide range of triggers including age, gender, medical history, and hormonal exposure.

While lobular breast cancer is slow in growth compared to other breast cancers, as well as difficult of detecting in mammograms, because it is characterized by small round tumor cells that grow in the form of a single incoherent band, and it is detected in older patients (Tasli *et al.*, 2022; Arpino *et al.*, 2004; Du *et al.*, 2018). As for the size of the tumor, the second degree was more prevalent with a rate of 45.0%, which means that the size of the tumor is greater than 20 mm and smaller than 50 mm, followed by the third degree with a rate of 28.3%, meaning that the size of the tumor is greater than 50 mm, then

the first degree with a rate of 26.7%. The tumor is less than 20 mm.

The results of the study also showed that the spread of cancer cells to the lymph nodes within the sample studied, n1 was the largest category with a rate of 31.7%, and this means that the spread of cancer cells to one or three axillary lymph nodes in the lower or middle part under the arm. As for metastasis, it was noted that stage 0 was the highest with a rate of 96.7%, and this indicates that there are no cancer cells spread far from the breast tissue, and this was diagnosed by x-rays or other imaging tests. The results of the disease degree also showed that the second degree was the highest with a rate of 73.3%, meaning that cancer cells appear less similar to normal cells and grow faster. Through this classification of TNM and Cell grade, it can be judged that most patients did not exceed the size of the tumor five centimetres, and the cancer cells did not move away from the breast tissue and surrounding tissues, i.e. did not spread to other parts of the body, and the degree of malignancy of the cells was medium.

With regard to the body mass index, a significant decrease was observed in the group of patients, and this could be explained by the fact that cancer and its treatment cause weight loss. The rapid and irregular growth of cancer, this growth leads to taking food from normal cells and depriving them of nutrients, and is not usually affected by the number of calories or the type of food that is eaten (Yao *et al.*, 2023).

A significant increase in the level of erythrocyte sedimentation rate was observed in women with breast cancer, compared with a group of healthy women. The results also showed an increase in the levels of C-reactive protein (CRP) for the group patients compared to the control group, and the reason for this is that this protein rises in cases of severe infections that affect the body as well as in the case of cancer (Saha *et al.*, 2019), and also its rise in breast cancer patients is due to the high plasma concentration of interleukin-6, which is It is produced

predominantly by phagocytic cells during the presence of inflammation (Eboreime *et al.*, 2015), Chronic inflammation has been shown to be closely associated with an increased risk of cancer and its progression, by promoting excessive cell proliferation and activating a cascade of cellular events, which promotes the growth of cancer cells. Moreover, tumor development itself may also trigger immune response and inflammation.

In many cases, the analysis of CRP, Ferritin and ESR is elevated in cancer patients, but the result depends particularly on the type of cancer, its stage and duration, and the method and severity of antitumor therapy.

A high level of ESR analysis has also been identified as a predictive factor that negatively affects the duration of survival in patients with various malignancies, such as colorectal cancer, head and neck cancer, breast cancer, glioma, and prostate cancer.

As for the high level of carcinoembryonic antigen (CEA), many pathological conditions and cases of tumors can lead to an increase in the level of CEA protein, but the most common type of cancer that leads to its elevation is colorectal cancer, and other types of cancer that lead to its elevation include: pancreas, Stomach cancer, Breast cancer and ovarian cancer. This test is also useful in monitoring treatment and detecting disease recurrence.

When comparing the type of disease to the studied criteria, it was observed that the ferritin was elevated, and this result agrees with (Neelam *et al.*, 2020), An increase in iron stores is also associated with inflammatory diseases and the presence of malignant tumors in the body, and an increase in ferritin in the serum of women is considered an additional biological marker in the diagnosis and staging of breast cancer (Ćujić *et al.*, 2011).

It was also observed that invasive ductal carcinoma affects physiological and immunological parameters by increasing its concentrations in patients' serum. Higher levels of CRP and ESR are associated with breast cancer prognosis (Holm *et al.*, 2023).

## Conclusion

In light of the results obtained through the current study, we conclude that invasive ductal carcinoma is the most common type of breast cancer and that in each of ESR, CRP, and ferritin, their increased concentrations are associated with the presence of malignant tumours, including breast cancer.

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