Khalij Libya Journal of Dental and Medical Research. 2026;10(2):161-167
https://doi.org/10.47705/kjdmr.26213
eISSN:2708-888X

Original article

The study of Estrogen Receptor Expression in Breast Cancer in the Oncology Center of Imam Hussein Hospital in Karbala

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Abstract
The most prevalent malignancy in women worldwide, and one of the main reasons why women die from cancer, is breast cancer (BC). Estrogen receptors, which are known to stimulate tumor cell growth and proliferation, are biologically expressed in the tumors of most women with BC. The study results show the relationship of receptor (ER) expression with age group. This study showed that the highest expression of ER was in the third group, with 36.36%, compared to the other groups. There was also a high incidence of estrogen receptor (ER) expression in the invasive ductal carcinoma, invasive lobular carcinoma, and LABC stages of breast cancer; the score 3 (positive expression) group had the highest expression of ER (32.72%, 58.33%, and 56.25%, respectively) compared to the other groups. Furthermore, there was a high incidence of estrogen receptor (ER) expression in the metastatic and multifocal breast cancer stages; the negative expression (score 1) group had the highest expression of ER (75%) compared to the other groups. Statistical analysis revealed that a higher incidence of non-expression (negative) count in the thrid age group was about 12 (30%) patients compared to the other groups, while negative expression 1 was the highest incidence in the third and fifth groups, about 10 (45.45%) patients in each group compared to the other groups, while low positive expression was the highest incidence in the third group, about 24 (57.14%) patients compared to the other groups. Also, the positive expression was the highest rate in the third group, about 26 (44.82%) patients, compared to the other groups.
Keywords. *Estrogen Receptor (ER), Estrogen Receptor Positive (ER+).*

Received*: 12/04/26*
Accepted*: 11/06/26*
Published*: 20/06/26*

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Introduction

The most prevalent malignancy in women worldwide, and one of the main reasons why women die from cancer, is breast cancer (BC). Estrogen receptors, which are known to stimulate tumor cell growth and proliferation, are biologically expressed in the tumors of most women with BC [1]. The great majority of people with estrogen receptor (ER) positive BC now have a far higher chance of survival thanks to medications that have been discovered over the past 50 years to alter the way estrogen binds to its receptor. It was shown that a significant percentage of individuals with BC had better survival rates after having their ovaries removed.

It was believed that the disruption of nerve connections between the ovaries and the breast was the cause of this improvement, but the exact mechanism was still unknown [2]. Breast epithelial cells react to the hormonal influences of progesterone and estrogen by a traditional ligand receptor pathway, which was supported by the finding of estrogen and progesterone receptors in breast tissue in the 1960s [3]. The study of the relationship between receptors (ER) expression and non-expression in types of breast cancer.

Materials and methods

This study, which was conducted from February to September 2023 at the Oncology Center of Imam Hussein Hospital in Karbala, included samples from 198 female patients who had breast cancer. Samples were collected after the consulting physician's diagnosis. The disease has been classified into several types according to its nature, invasion, and etiology.

The data that has been collected includes age and type of breast cancer, as well as expression of hormone receptors (ERs) for each woman.

- score 1 for (ER) considered a negative expression
- score 2 for (ER) considered low positive expression
- score 3 to 8 for (ER) considered positive expression

Statistical analysis

The Statistical analysis was performed by using the SPSS program. Analysis of variance (Crosstabs) was used to evaluate changes between groups.

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Results

Receptor expression

(Table 1) shows the relationship between receptor (ER) expression and age group. This analysis showed that the third group had the highest expression of ER (36.36%) when compared to the other groups.

Table 1. Correlation between estrogen receptor (ER) expression and age group.

Age group (years)	Frequency (n=198)	Percentage
<30	10	5.05 %
31-40	24	12.12 %
41-50	72	36.36 %
51-60	44	22.22 %
61-70	36	18.18 %
> 70	12	6.06 %

Comparison between biomarkers of estrogen receptor expression according to the invasive ductal carcinoma stage of breast cancer

The correlation between receptor (ER) expression and the stage of invasive ductal carcinoma in breast cancer is depicted in (Figure 1). According to this study, the score 3 (positive expression) group had the highest expression of ER (32.72%) compared to the other groups.

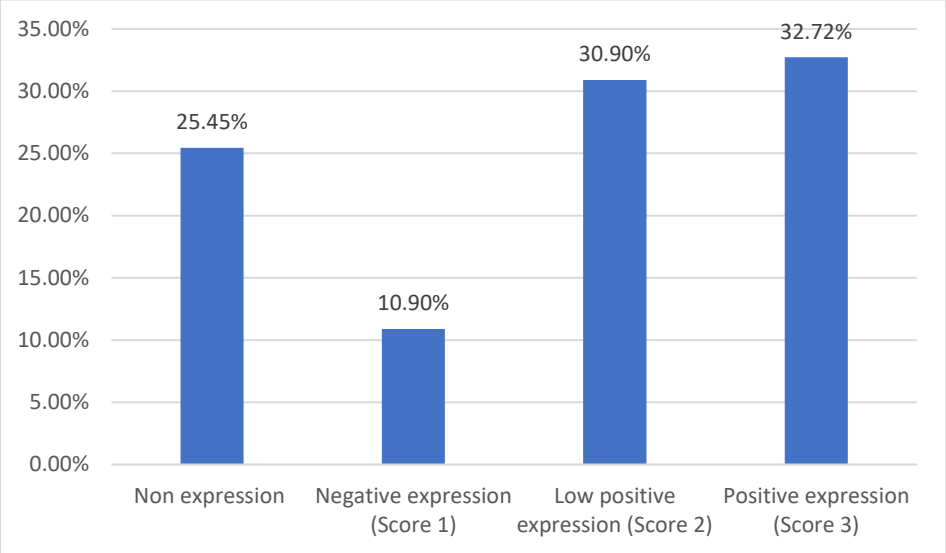

Figure 1. Estrogen receptor expression according to the invasive ductal carcinoma stage of breast cancer.

Comparison between biomarkers *of estrogen receptor expression according to the invasive lobular carcinoma stage of breast cancer*

(Figure 2) shows the relationship of receptor (ER) expression with the invasive lobular carcinoma stage of breast cancer. This study showed that the highest expression of ER was in the positive expression (score 3) group 58.33% compared to the other groups.

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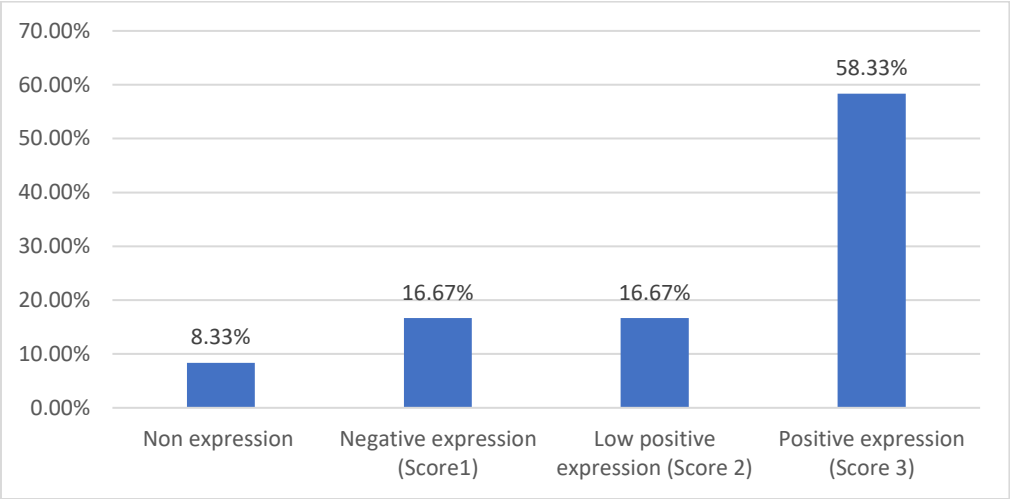

Figure 2. Estrogen receptor expression according to the invasive lobular carcinoma stage of breast cancer

Comparison between biomarkers of estrogen receptor expression according to the locally advanced breast cancer (LABC) stage of breast cancer.

(Figure 3). shows the relationship of receptor (ER) expression with locally advanced breast cancer (LABC) stage of breast cancer. This study showed that the highest expression of ER was in the positive expression (score 3) group 56.25 % compared to the other groups.

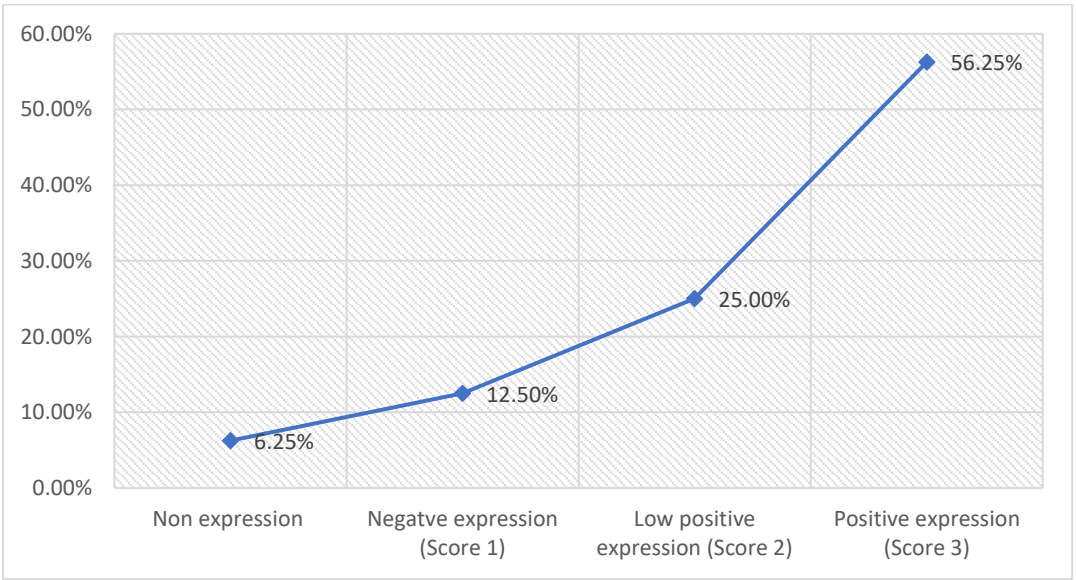

Figure 3. The relationship of receptor (ER) expression with the locally advanced breast cancer (LABC) stage of breast cancer.

Comparison between biomarkers of estrogen receptor expression according to the metastatic stage of breast cancer.

(Figure 4) shows the relationship of receptor (ER) expression with the metastatic stage of breast cancer. This study showed that the highest expression of ER was in the negative expression (score 1) group 75.00 % compared to the other groups.

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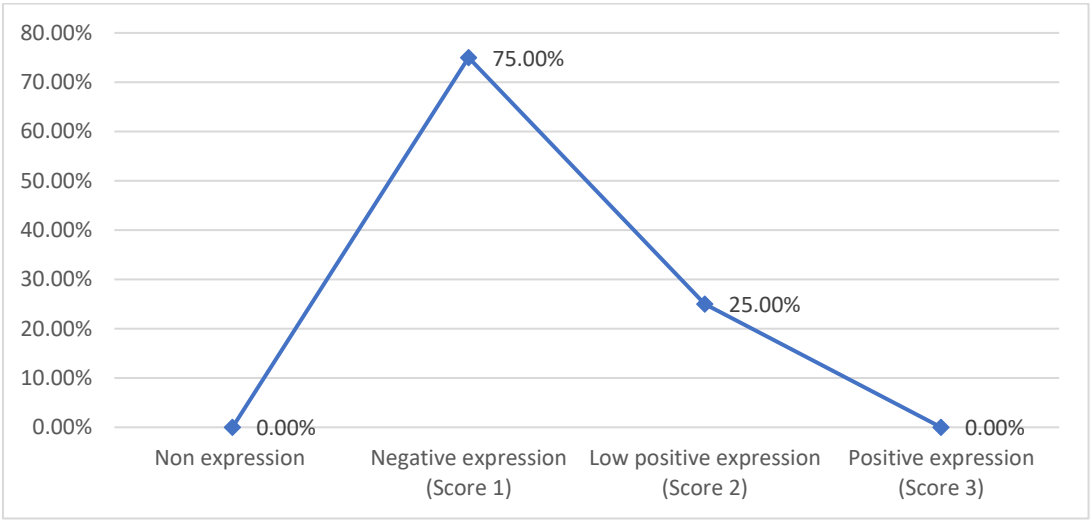

Figure 4. Estrogen receptor expression according to the metastatic stage of breast cancer

Comparison between biomarkers of estrogen receptor expression according to the multifocal breast cancer stage

(Figure 5) shows the relationship of receptor (ER) expression with multifocal breast cancer stage. This study showed that the highest expression of ER was in the negative expression (score 1) group 75.00 % compared to the other groups.

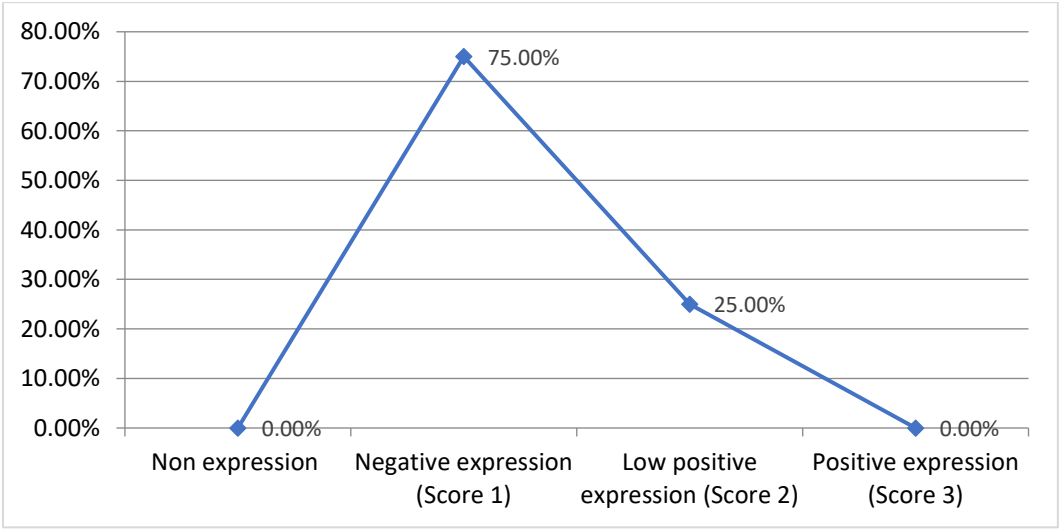

Figure 5. Estrogen receptor expression according to the multifocal breast cancer stage

Estrogen Receptor expression

(Table 2) shows the association between receptor expression(ER) and age groups. There was a higher incidence of non expression (negative) count in the third group a rate of 12n (30.0 %) patients compared to the other groups, while negative expression (score1) was the highest incidence in the third and fifth groups about 10 each group (45.45%) patients compared to the other groups, and low positive expression (score2) was highest rate in thrid group about 24 (57.14%) patients, also positive expression (score3) was the highest rate in third group about 26 (44.82%) patients.

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Table 2. Correlation between estrogen receptor (ER) expression according to age groups.

Group R. expression	AGE GROUPS						Total
	Age Group <30	Age Group 31-40	Age Group 41-50	Age Group 51-60	Age Group 61-70	Age Group >70	
Non-expression (Negative) Count % within ER	n:4 10.0%	n:8 20.0%	n:12 30.0%	n:10 25.0%	n:8 20.0%	n:6 15.0%	n:48 100.0%
Expression1 (Negative) Count % within ER	n:2 9.09%	n:4 18.18%	n:10 45.45%	n:6 27.27%	n:10 45.45%	n:0 0.00%	n:32 100.0%
Expression2 (Low positive) Count % within ER	n:2 4.76%	n:8 19.05%	n:24 57.14%	n:8 19.05%	n:8 19.05%	n:0 0.00%	n:50 100.0%
Expression3 (positive) Count % within ER	n:2 3.45%	n:4 6.90%	n:26 44.82%	n:20 34.48%	n:10 17.24%	n:6 10.35%	n:68 100.0%
Total Count % within ER	n:10 5.05%	n:24 12.12%	n:72 36.36%	n:44 22.22 %	n:36 18.18%	n:12 6.06%	n:198 100.0%

Discussion

Receptor expression

In the present study, the most common age group with the highest frequency of estrogen receptor (ER) expression was 41-50 year-old patients (36.36%), and the positive expression of ER (score 3) was the most common in the same age group (44.82%). The results showed that middle-aged women (particularly those in the perimenopausal age group) were more likely to have ER-positive breast cancer, suggesting that hormonal changes at this time may affect tumour growth and receptor activity. This outcome is in line with the conclusions of recent studies which have also reported a significant relationship between age-related hormonal exposure and increased ER positivity in breast cancer patients, as well as improved endocrine responsiveness and favorable prognosis in ER-positive breast cancer [4]. Furthermore, the tumors in middle-aged females are more likely to be ER-positive and have less proliferation and better treatment responses than ER-negativ]e tumors [5].

The present study also confirmed that invasive ductal carcinoma and invasive lobular carcinoma had high positive ER expressions, and the percentage of score 3 was 32.72% in IDC and 58.33% in ILC, respectively. More than 90% of invasive lobular carcinoma cells are ER positive, which indicates that this type is more hormone dependent and endocrine sensitive than invasive ductal carcinoma. The results of these studies correspond with recent molecular research that suggests that IDC has preserved hormone receptor expression, different molecular signatures, and a decreased proliferative nature, making it more responsive to endocrine therapy [6]. Moreover, recent studies have determined that histological subtype is also an independent predictor of disease free survival and treatment response among women with hormone receptor-positive breast cancer.

By contrast, the cases of breast cancers in the present study with negative ER expression were predominantly metastatic and multifocal breast cancers, with 75% of the cases being score 1 expression in both these groups of breast cancers. This reduction in ER expression may be due to tumor dedifferentiation and progression towards a more aggressive biological type. The loss of ER positivity has been linked to endocrine resistance and increased metastatic potential and clinical resistance. In recent studies, it has been found that metastatic breast tumors are often positive for ESR1 mutations and negative for ER expression, both of which help to make endocrine therapy less effective and lead to less survival [7-8]. This is why in this study, ER-negative expression predominated in advanced and multifocal tumors and why these have an aggressive clinical course and are hormone-insensitive.

Estrogen Receptor expression

The present study has revealed that the third age group showed non-expression of ER most commonly. This result is similar to that reported by Shah [9] and AlZaman [10] who found ER-negative predominant in relatively younger patients. This observation could be due to the aggressive biological characteristics often seen in ER-negative breast carcinomas such as increased proliferative activity and decreased differentiation. The results however contrast with the study conducted by Makhlouf [11] that showed higher rate of ER positivity in older age groups, which could be attributed to ethnic, genetic and environmental differences between the study population.

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The score 1 of negative ER expression was the highest in the third and fifth age group. The same has been reported by Shah [9] who saw that weak or absent ER expression correlated with biologically aggressive tumors and poor prognostic characteristics. Low ER activity tumors are now known to be a sub-group that can be either partially responsive to endocrine therapy and/or have some molecular characteristics of hormone-positive disease.

Low positive ER expression score 2 was mostly seen in the third age group, which is consistent with the study conducted by Adel [12]. There is a clinical importance for low ER-positive tumors because they are often intermediate between strongly positive and completely negative tumors. Several studies reported increased proliferative indices and decreased sensitivity to hormone therapy in these tumours as compared with strongly ER-positive carcinomas.

Positive ER expression score 3 was the highest frequency. Similar results were also reported by Adel [12] with some differences noted between the 2nd and 4th age groups. The same was reported by Zheng [13] who stated that a high ER percentage usually corresponds to high tumor differentiation and good response to endocrine therapy. The predominance of ER-positive tumors in middle aged women may suggest some association with hormonal factors during the perimenopause, when they may be involved in the pathogenesis of hormone-dependent breast carcinoma.

Conclusion

This institutional study of 198 cases of breast cancer patients from Kerbala City, Iraq, suggests that the mean age of breast cancer patients was between 41 and 50 years old, with ER expression positivity of 36.36% compared to other age groups. An increment of biomarker of the estrogen receptor expression according to the invasive ductal carcinoma, invasive lobular carcinoma and LABC stages of breast cancer; the score 3 (positive expression) group had the highest expression of ER (32.72%, 58.33% and 56.25%, respectively) compared to the other groups, while the estrogen receptor expression according to the metastatic and multifocal breast cancer stages; the negative expression (score 1) group had the highest expression of ER (75%) compared to the other groups. Statistical analysis revealed that a higher incidence of non-expression (negative) count in the third age group was about 12n (30.0 %) patients compared to the other groups, while negative expression 1 was the highest incidence in the third and fifth groups, about 10 (45.45%) patients in each group compared to the other groups, while low positive expression was the highest incidence in the third group, about 24 (57.14%) patients compared to the other groups. Also, the positive expression was the highest rate in the third group, about 26 (44.82%) patients, compared to the other groups.

Acknowledgment

The author is thankful to the Department of Oncology at the Center of Imam Hussein Hospital in Karbala, Iraq.

Conflict of interest. Nil

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