

RELATION OF AGE, PARITY AND SIZE OF THE LESION TO OESTROGEN AND PROGESTERONE RECEPTOR STATUS IN PATIENTS OF BREAST CANCER

Garima Sharma* Harish matta**

*associate professor, dept of physiology, dmc&h, Ludhiana. **hod, dept of surgery, fortis hospital, Ludhiana.

Abstract: Background: Breast cancer is one of the most common cancers among women in India and abroad. Tumor markers are becoming increasingly important in breast cancer research because of their impact on prognosis, treatment and survival, and because of their relation to breast cancer subtypes. According to the American cancer society, about two out of every three cases of breast cancer are hormone receptor positive. Most of these cases are ER+ or receptive to both estrogen and progesterone. The aim of the study is to study the relationship of ER and PR receptors with the age, parity and size of the lesion in patients of breast cancer. **Method:** Estrogen receptor(ER) and Progesterone receptor (PR) levels have been measured in 50 patients of primary breast cancer and compared with size of the lesion and other variables to determine their relationship. They were measured by immunohistochemistry. **Result:** This study showed a significant relation of age, parity and size of the lesion to the ER and PR receptors in patients of breast cancer. **Conclusion:** When both receptor measurements were used in combination, a group of receptor-negative (ER and PR negative), patients were seen to be having worse disease .Younger age group and decreased parity contributed to increased incidence.

Key Words: Breast cancer,Oestrogen, Progesterone.

Author for correspondence Dr Garima Sharma, Associate Professor, Department of Physiology, Dayanand medical college and hospital, Ludhiana, Punjab, India. Phone no. 9872210369, E-mail :drgarimamatta@gmail.com

Introduction:

A Tremendous increase in breast cancer awareness and research has helped improve the screening and diagnosis as well as advances in the treatment of breast cancer. Cancer survival rates have increased, and the number of deaths steadily has been declining, which is largely due to a number of factors such as earlier detection, a new personalized approach to treatment and a better understanding of the disease. The breast cancer cells may have receptors for the hormones estrogen and progesterone.¹ Hormone receptors are proteins found in and on breast cells that pick up hormone signals telling the cells to grow.

A cancer is called estrogen-receptor-positive (or ER+) if it has receptors for estrogen.² This suggests that the cancer cells, like normal breast cells, may receive signals from estrogen that could promote their growth. The cancer is progesterone-receptor-positive (PR+) if it has progesterone receptors.³ Again, this means that the cancer cells may receive signals from progesterone that could promote their growth. Roughly two out of every three breast cancers test positive for hormone receptors.

Testing for hormone receptors helpsto decide whether the cancer is likely to respond to hormonal therapy or other treatments. Hormonal therapy includes medications that either lower the amount of estrogen in your body or block estrogen from supporting the growth and function of breast cells.⁴ If the breast cancer cells have hormone receptors, then these medications could help to slow or even stop their growth. If the cancer is hormone-receptor-negative (no receptors are present), then hormonal therapy is unlikely to work. Then other kinds of treatment are chosen.

Cell receptors, including hormone receptors, are special proteins found within and on the surface of certain cells throughout the body, including breast cells. These receptor proteins are the “eyes” and “ears” of the cells, receiving messages from substances in the bloodstream and then telling the cells what to do. In other words, the receptors act like an on-off switch for a particular activity in the cell. If the right substance comes along that fits into the receptor — like a key fitting into a lock — the switch is turned on and a particular activity in the cell begins.

One type of receptor found in normal breast cells is the hormone receptor. By attaching to hormone receptors, estrogen and/or progesterone contribute to the growth and function of breast cells. Estrogen and progesterone are often called “female hormones” because they play an important role in women’s menstrual cycle, sexual development, pregnancy, and childbirth. Even after menopause, however, women continue to have these hormones in their bodies.⁵ Men have them, too, although in much smaller amounts than women.

Like healthy breast cells, most breast cancer cells — but not all — have hormone receptors and respond to the signals coming from these hormones. For hormone-receptor-positive breast cancer cells, hormonal therapy can be used to interrupt the influence of hormones on the cells’ growth and overall functioning.⁶ If you take the hormone away or block it, as these medications do, the cancer cells are less likely to survive. It’s also worth noting that some breast cancers that are hormone-receptor-positive can lose their receptors over time. The opposite is also true: hormone-receptor-negative cancers can gain receptors⁷. If the breast cancer recurs in the future as advanced disease, doctors should order a repeat biopsy and retest the cancer for hormone receptors. If the cancer cells no longer have receptors, hormonal therapy is unlikely to help treat the cancer. If the cells have gained hormone receptors, however, then hormonal therapy may be helpful.

Most breast cancers are hormone-receptor-positive.

- **ER+:** About 80% of breast cancers are estrogen-receptor positive.
- **ER+/PR+:** About 65% of estrogen-receptor-positive breast cancers are also progesterone-receptor-positive. This means that the cells have receptors for both hormones, which could be supporting the growth of the breast cancer.
- **ER+/PR-:** About 13% of breast cancers are estrogen-receptor-positive and progesterone-receptor-negative. This means that estrogen, but not

progesterone, may be supporting the growth and spread of the cancer cells.

- **ER-/PR+:** About 2% of breast cancers are estrogen-receptor-negative and progesterone-receptor-positive. This means that the hormone progesterone is likely to support the growth of this cancer. Only a small number of breast cancers test negative for estrogen receptors but positive for progesterone receptors.
- **ER-/PR-:** If the breast cancer cells do not have receptors for either hormone, the cancer is considered estrogen-receptor-negative and progesterone-receptor-negative (or “hormone-receptor-negative”). About 25% of breast cancers fit into this category. Any positive test result — whether just for estrogen receptors, just for progesterone receptors, or both — means that the breast cancer is considered “hormone-receptor-positive.”

Hormonal therapy may help to slow or stop the growth of hormone-receptor-positive breast cancers by lowering your body’s estrogen levels or blocking the effects of estrogen. These medications also may reduce the risk of recurrence.⁸

Whether a tumor has estrogen and/or progesterone receptors also helps to determine a patient’s risk of recurrence (return of the cancer after treatment) and whether the cancer can be treated with hormone therapy. Hormone therapy blocks the tumour from using oestrogen and/or progesterone for cancers that are ER and/or PR positive, slowing or stopping tumour growth. Two types of drugs may be used; one type called tamoxifen can be used for women of all ages, while other types of drugs called aromatase inhibitors (AIs) stop tissues and organs other than the ovaries from producing estrogen.⁹ Aromatase inhibitors must never be used alone for women who have not gone through menopause.

For women who have not gone through menopause, hormone therapy for ER and/or PR positive tumors may include stopping the production of estrogen and progesterone in the ovaries with surgery or injections.¹⁰

Materials and Methods:

50 subjects were taken for this study from breast clinic opd from a local hospital in Ludhiana. Subjects were put to a detailed questionnaire in the form of a proforma. Informed consent was sought for the study. Subjects belonged to all socioeconomic strata, both educated and uneducated, both married and unmarried. Only histopathologically confirmed carcinoma cases were included. Modified radical mastectomies, quadrectomy and wide local excision specimens were included. The mastectomy specimens were fixed in by keeping them overnight in 10% formalin. After fixation, macroscopic examination was done. Size, quadrant and focality is assessed. Lymph nodes are retrieved meticulously, number noted and sections of grossly involved nodes were taken. 3 micron thick sections are cut. ER and PR immunohistochemistry was performed. Grading of tumours was done using WHO guidelines. The tumor is tested for both estrogen and progesterone receptors. Because the results are used to guide treatment, it's important that the results be accurate. The method which was used to test the tumor for estrogen and progesterone using Allred scoring system is called immunohistochemistry or IHC.¹¹ IHC testing can detect estrogen and progesterone receptors in cancer cells from a sample of tissue in the primary tumour. IHC was performed by using the streptavidin- peroxidase detection system. Scoring of ER and PR reactivity was done. The ER and PR status should be tested on the primary tumor and/or areas of spread (called metastases) for each patient newly diagnosed with invasive breast cancer or a breast cancer recurrence. A tumor is ER and/or PR positive if at least 1% of the cells examined have estrogen and/or progesterone receptors, and for such a tumour, hormone therapy should be considered. Testing was done on larger tissue

samples. If the cancer had spread, testing on those areas was done as well.

Statistical methods: Simple statistical methods were used like percentages, qualitative tests (Chi-square) and quantitative (paired t-test) were done.

Results:

A total of 50 cases were included in the study which include radical mastectomies, local wide excisions and quadrectomies. The mean age of the patients was 54.5 years. Youngest patient was 30 years old and oldest was 80 years old. Incidence of breast cancer was seen to be highest in the age group 50-59 years. From table 1, it was seen that in younger age group 30-39 years, 67% patients were ER PR negative which carries a bad prognosis where as in the age group 60-69 years, 61.5% are ER PR positive making the prognosis better.¹² In nulliparous females the ER PR status was found to be negative, where as in parity 2, the %age of ERPR positive/ER positive PR negative is about 66.6% which is statistically significant.¹³ Given below in table 2.

It is also seen that the size of the lesion is larger in ER PR negative patients than ER PR positive ones.¹³ Out of 39 patients who were having size of tumour in the range of 21-60mm or ≥ 60 , 23(60%) were ER PR negative, which is statistically significant as given in table 3.

Table 1 ER PR status in relation to age

Age at diagnosis (YRS)	No. of cases	ER+/PR+	ER+/PR-	ER-/PR+	ER-/PR-
30-39	6(12%)	1	1	—	4
40-49	9(18%)	2	1	—	6
50-59	20(40%)	7	2	—	11
60-69	13(26%)	8	2	—	3
≥ 70	3(6%)	1	1	—	1

Table 2- ER PR status in relation to parity

Parity	No.of cases	ER+/PR+	ER+ /PR-	ER- /PR+	ER- /PR-
0	3(6%)			–	3
1	4(8%)	1		–	3
2	22(44%)	7	5	–	10
3	17(34%)	6	2	–	9
>3	5(10%)	1	1	–	3

Table 3- ER PR Status in relation to size of the tumour

Size of tumour in mm	No. of cases	ER+/PR+	ER+ /PR-	ER- /PR+	ER- /PR-
0-20	11(22%)	6	2	–	03
21-40	25(50%)	7	3	–	15
41-60	13(26%)	5	1	–	07
>60	01(2%)	–	–	–	01

Discussion:

The breast cancer remains the second largest killer in women after cervical cancer.¹⁴ Positive ER/PR status has been associated with decreased breast cancer morbidity and mortality independently of various demographic factors.¹⁵ It was seen in the present study that younger patients were less likely to be ER+/PR+ as compared to older patients. Similarly when receptor positivity was compared with size of the tumour, it was found that patients with smaller sized lesions were more likely to be ER+/PR+ as compared to larger lesions. These results are in concordance with study by Dunnwald LK et al.

In the present study, it was also seen that positive ER+/PR+ is associated with increase in parity and the nulliparous women¹⁶ usually have ER-/PR- status and hence a bad disease. Due to smaller sample size in our study, not much correlation was seen.

Conclusion: There was seen a significant association of age, parity and size of the tumour with the ER/PR receptor status of the patient. These findings are consistent with other studies

showing the relationship between ER/PR receptors and these parameters.

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