A CLINICAL STUDY OF HORMONE RECEPTOR STATUS IN CARCINOMA BREAST

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ABSTRACT

BACKGROUND
The world's most common cancer and the second main cause of cancer death among women in the United States is breast cancer. Breast cancer is the second most common cancer among women in India after carcinoma cervix. A single parameter with the strongest prognostic significance is hormone receptor status. Intracellular steroid-hormone receptor proteins, primarily Oestrogen Receptor (ER) and Progesterone Receptor (PR) have received intensive study both as indicator of prognosis and as guide to hormone therapy. Recently, importance of HER2/neu in breast cancer has been a topic of considerable interest, both in its role as a prognostic indicator and as a predictor of response to therapy.

The aim of the study is to assess the incidence of hormone receptor positivity in females with carcinoma breast and to compare hormonal receptor status with clinicopathological grading of the tumour.

MATERIALS AND METHODS
A study of cases of carcinoma breast in females were done. Sample included 75 patients. Patients for clinical study were selected from the general surgical wards of Tirunelveli Medical College Hospital for a period of 18 months.

RESULTS
Out of 75 patients, 52 patients (69.33%) were positive for oestrogen receptor and 23 (30.66%) were negative. 39 patients (52%) were progesterone receptor positive and 36 (48%) were progesterone receptor negative. 28 (37.33%) patients had Her2 receptor positive and 47 (62.66%) were negative.

CONCLUSION
These results were comparable with the previous studies and thus reinforce the usefulness of estimation of the receptor status for treatment purpose in breast carcinoma.

KEYWORDS
Oestrogen Receptor (ER), Progesterone Receptor (PR), HER2/Neu.

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BACKGROUND
Breast cancer is the most common cancer among women. Worldwide over 1.1 million women are diagnosed with this disease each year and incidence rates are still on the increase in several countries. The world's most common cancer and the second main cause of cancer death among women in the United States is breast cancer. Breast cancer is the second most common cancer among women in India after carcinoma cervix.¹ Breast cancer is more common in elderly women. Since breast cancer in older women is more common, they have usually been the centre of attention, so the most breast cancer studies have focused on older women.² According to literature, breast cancer occurring in younger women are of more aggressive type.³,⁴ They are usually high-grade, poorly-differentiated, high tumour invasive potential, greater chances of early lymphatic spread and ER, PR negative and Her2 positive. Studies show that the breast cancer in younger women is unique and needs a different treatment strategy than what might be used for older women with breast cancer.⁵-⁸

Recurrence of the tumour is more common in younger women compared to elderly women.⁹ Clinically, in young age, breast tumours are of large size with greater lymphatic spread.

Commonest neoplasm of breast is the tumour arising from epithelial component of glandular element of breast. Infiltrating ductal carcinoma being the most common type of carcinoma (70%), lobular carcinoma is the second most common followed by smaller groups such as medullary, mucinous, comedocarcinoma, papillary, tubular and inflammatory carcinoma. In recent years, interest in prognostic factors has been stimulated by the success of systemic adjuvant therapy for early stage of breast carcinoma. The important pathological prognostic factors in invasive breast carcinoma include patient's age, tumour size,
lymph node metastasis, nuclear grade, histological grade, histological type, hormone receptor status and Her2/neu. The most important prognostic factor is lymph node status (N) and next to it is the tumour size (T).\textsuperscript{10-12} A single parameter with the strongest prognostic significance is hormone receptor status.\textsuperscript{13} The final outcome in breast cancer management depends upon the initial stage of the tumour at diagnosis and associated prognostic factors such as status of the lymph nodes, size of the tumour and grading of the tumour.

Therefore, it is essential to find the markers that have predictive and prognostic values. It predicts the chances of recurrence of cancer and also identifies, which patients do and which do not benefit from adjuvant treatment. So, patients with low risk are avoided of unnecessary adjuvant treatment and also the patients with high risk could be identified and given appropriate, early and aggressive treatment.

Oestrogen and Progesterone Receptors (ER, PR) and more recently, HER2/neu have with increasing importance influenced the management of the malignancy. Beaton’s showed the role of oestrogen in breast cancer by showing regression of breast cancer following oophorectomy over 100 years ago.\textsuperscript{14} Intracellular steroid hormone receptor proteins, primarily Oestrogen Receptor (ER) and Progesterone Receptor (PR) have received intensive study both as indicator of prognosis and as guide to hormone therapy.\textsuperscript{15} Oestrogen plays a central role in the growth and differentiation of normal breast epithelium, stimulating cell proliferation and regulating the expression of genes, including the progesterone receptor.\textsuperscript{16} Hormone receptor status in breast cancer helps to determine patient suitability for hormone therapy. Tumours that express both ER and PR have the greatest benefit from hormonal therapy and those containing only ER or only PR still have significant response.\textsuperscript{17}

HER2/neu is an oncogene. The amplification and overexpression is seen with breast cancer. Recently, importance of HER2/neu in breast cancer has been a topic of considerable interest, both in its role as a prognostic indicator and as a predictor of response to therapy. With the advent of the drug trastuzumab (Herceptin), a humanised monoclonal antibody directed against cells that express HER2/neu, assessment of HER2/neu status in patients with metastatic breast carcinoma has become an even more important clinical consideration.\textsuperscript{18}

Immunohistochemical (IHC) detection has become essential to many malignancies and plays a key role in tumour diagnosis, treatment and prognostic assessment.

In this study, we studied 75 cases of breast cancer patients to detect the expression of Oestrogen Receptor (ER), Progesterone Receptor (PR) and human epidermal growth factor receptor-2 (HER2) by IHC and analysed the associations between these indicators and the clinicopathological characteristics.

\textbf{Aim of Study} - To assess the incidence of hormone receptor positivity in females with carcinoma breast.

\textbf{Objectives of the Study}
1. To identify hormonal receptor status in female patients with breast malignancies.
2. To predict the tumour response to endocrine therapy.
3. To compare hormonal receptor status with clinicopathological grading of the tumour.
4. To formulate the adjuvant treatment modality.

\textbf{MATERIALS AND METHODS}
A study of cases of carcinoma breast in females were done. Sample included 75 patients. Patients for clinical study were selected from the general surgical wards of Tirunelveli Medical College Hospital for a period of 18 months. The study subjects were selected when they presented with the following inclusion and exclusion criteria.

\textbf{Inclusion Criteria}
1. Clinically diagnosed breast malignancy in females of all age groups.
2. Age of patient, tumour size, histological subtype and grading of the tumour.
3. TruCut biopsy and mastectomy specimens.

\textbf{Exclusion Criteria}
1. Patients already treated for contralateral breast carcinoma.
2. Male breast carcinoma.

\textbf{Method Used} - Biopsy samples (either TruCut biopsy or postop mastectomy specimens) were sent to pathology lab where they were processed and analysed for the histological subtype of the tumour, its pathological grading and the clearance of resected margins of the tumour. Hormonal receptor assay was done using immunohistochemistry technique in our college pathology department and results were interpreted.

\textbf{OBSERVATION AND RESULTS}
In this study, a total of 75 patients were studied starting from the age groups above 30. Most of them were between 40 and 50 years. Second most common was in younger age less than 40 years. Most of the patients came under the age group 40-50 years about 29.33%.

The least was in the 50-60 years age of about 21.33%.

**Figure 2. Size of the Tumour**

In our study group, 42 patients had a tumour of size less than 5 cm, which is about 56% of the whole group. 33 patients had a tumour greater than or equal to 5 cm in size, which constitutes 44% of the study sample.

**Figure 3. Pathological Grading**

In this study, which included breast cancers of different histological types and grade.

- IDC I- 26 patients.
- IDC II- 28 patients.
- IDC III- 12 patients.
- Medullary carcinoma- 4.
- Invasive lobular carcinoma- 3
- Ductal carcinoma in situ- 2.

**Figure 4. ER Status**

**ER Status** - Out of 75 patients, 52 patients (69.33%) were positive for oestrogen receptor and 23 (30.66%) were negative.

**Figure 5. PR Status**

**PR Status** - 39 patients (52%) were progesterone receptor positive and 36 (48%) were progesterone receptor negative.

**Figure 6. HER2 Status**

In this study, which included breast cancers of different histological types and grade.
**HER2 Status** - Here 28 (37.33%) patients had Her2 receptor positive and 47 (62.66%) were negative.

<45 years- 12 patients (39%) positive; 19 (61%) negative. >45 years- 15 patients (34%) positive; 29 (66%) negative.

In patients under 45 years of age (total 31), 23 patients (74.19%) were ER positive and 8 (25.81%) were negative. Above 45 years of age (total 44), 28 patients (63.63%) were ER positive and 16 (36.36%) were negative.

In estimation of PR receptors under 45 years, 23 patients (74.19%) were PR positive and 8 (25.81%) were negative. Above 45 years of age, 28 (63.63%) patients were PR positive and 16 (36.36%) were negative.

In tumours less than 5 cm in size:
- ER positive- 34 patients.
- ER negative- 8 patients.
- PR positive- 26 patients.
- PR negative- 17 patients.
- Her2 positive- 14 patients.
- Her2 negative- 27 patients.

In tumours more than or equal to 5 cm in size:
- ER positive- 18 patients.
- ER negative- 15 patients.
- PR positive- 12 patients.
- PR negative- 20 patients.
- Her2 positive- 15 patients.
- Her2 negative- 19 patients.

**DISCUSSION**

In my study, a total of 75 female patients with breast cancer in my institute were studied. The incidence of ER, PR,
Her2/neu receptors among them correlating with age, tumour size, histological type and the pathological grading was evaluated. 52 patients (69.33%) were positive for oestrogen receptor and 23 (30.66%) were negative. 39 patients (52%) were progesterone receptor positive and 36 (48%) were progesterone receptor negative. 28 (37.33%) patients had Her2 receptor positive and 47 (62.66%) were negative.

Most of the tumours in women above 45 years of age were hormone receptor positive. In women younger than 45 years, both positive and negative were nearly equal. Similar results were observed in tumours less than 5 cm where positivity predominated and more than 5 cm where both positive and negative were utmost equal. Her2 was more negative in most of the patients of our study irrespective of age and tumour size.

These results were comparable with the previous studies and thus reinforce the usefulness of estimation of the receptor status for treatment purpose in breast carcinoma.

All patients with hormone receptor positivity were started with tamoxifen 10 mg b.i.d. for a total duration of 5 years and their compliance is good till date with minimal side effects.

CONCLUSION
Breast cancer is one of the most common cancers among women of all age groups. In recent years, there is an increase in the incidence of breast cancer due to the lifestyle modifications and increase in screening programs, which help to detect them at an early stage. Breast cancer treatment involves a multidisciplinary approach. Hormone therapy is one among the treatment modality. Oestrogen, progesterone and Her2/neu receptor status estimation is very crucial at present in order to predict the tumour response to the hormonal therapy and also to assess the prognosis of the cancer.

REFERENCES