

The study of correlation of estrogen receptor, progesterone receptor, and HER2 receptor status in breast cancer and its incidence in a tertiary center hospital in south India



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ABSTRACT

Background: Breast cancer is the most common cancer in female representing approximately 25% of all cancer. It is also ranked number one cancer among Indian females with age-adjusted incidence rate of 25.8 per 100,000 women and mortality 12.7 per 100,000 women. Hormone receptors are the receptor protein found in normal breast cells. **Aims and Objectives:** The aims of this study were to assess the histologic type, estrogen receptor (ER), progesterone receptor (PR), and HER2/neu of all breast carcinoma patients coming to the inpatient department of general surgery of a tertiary care hospital. This study was conducted to assess the histologic type, ER, PR, and HER2/neu of all breast carcinoma patients coming to the outpatient department of general surgery of a tertiary care hospital. **Materials and Methods:** The present study is a prospective observational study conducted in the department of general surgery at KR Hospital for 1 year from December 2020 to November 2021. All patients who underwent modified radical mastectomy for breast carcinoma or core biopsy to start chemotherapy and hormone therapy before surgery were included in the study. They were subjected to histopathological examination and immunochemistry. **Results:** The most common age group, in which breast carcinoma was diagnosed, was 51–55 years. The most common type of breast carcinoma is invasive ductal carcinoma seen in 66% of the patients. Among the 100 patients IHC, ER positive was seen in 54% of the patients, PR positive was seen in 39% of the patients, and HER2neu-positive was seen in 31% of the patients. Most common was ER/PR + HER2neu – in 28% of the patients. Triple-negative hormonal status was seen in 23% of the patients. **Conclusion:** This single institutional study of 100 cases of breast cancer patients from South India suggest that mean age of breast cancer patient was between 51 and 55 years, with invasive ductal carcinoma being the most common histological type with ER positivity of 54% and PR positivity of 39% and triple-negative cancers of 23%, not grossly different from rest of the country but significantly lower than Western studies.

Key words: Breast cancer; Receptor status; Estrogen; Progesterone; HER2 receptor

INTRODUCTION

Breast cancer which is considered universal worldwide is the most common cancer in female, representing approximately 25% of all cancers. It is also ranked number one cancer among Indian females with age-adjusted

incidence rate of 25.8 per 100,000 women and mortality 12.7 per 100,000 women.¹ Hormone receptors are the receptor protein found in normal breast cells. By attaching to the hormone receptors, estrogen and progesterone contribute to the growth and function of breast cell. A cancer is called estrogen receptor (ER) positive (ER+)

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if it has receptor for estrogen. This suggest that the cancer cell, like normal breast cells, may receive signals from estrogen that could promote their growth. The cancer is progesterone receptor positive (PR+VE) if it has PRs. This means that the cancer cells may receive signals from progesterone that could promote their growth. Hormonal therapy includes medications that either (i) lower the amount of estrogen in body or (ii) block estrogen from supporting the growth and function of breast cells. If the breast cancer cells have hormonal receptors, then these medications could help to slow or even stop their growth. If tumour is hormone receptor negative, hormone therapy is unlikely to work.² Among these biomarkers, ER, PR, and HER2/neu are mostly used for assessment of breast cancer. Her2/neu proto-oncogen (erbB-2) encodes a 185kDa transmembrane phosphoglycoprotein with tyrosine kinase activity. It is standard practice to determine both estrogen and PR status at the time of diagnosis for definitive surgical therapy.³

Evaluation of hormone receptor on surgically resected specimen or core biopsy material is essential to assess the utility of hormone therapy and thus the College of American Pathologists and American Society of Clinical Oncology recommend ER and PR testing for all newly diagnosed cases of invasive breast cancer and breast cancer recurrences.⁴ The determination of ER, PR, and Her2 receptor activity in breast cancer is standard medical practice now a days.⁵

Testing for hormone receptors in breast tumor tissue is important tool for because the results help to decide whether the cancer is likely to respond to hormonal therapy or other treatments. Hence, this study was carried out to find out the number of breast cancers presenting to a tertiary care center and the histological type and to determine the hormonal status of these breast cancers.

Aims and objectives

The aims of this study were to assess the histologic type, estrogen receptor (ER), progesterone receptor (PR), and HER2/neu of all breast carcinoma patients coming to the inpatient department of general surgery of a tertiary care hospital. This study was conducted to assess the histologic type, ER, PR, and HER2/neu of all breast carcinoma patients coming to the outpatient department of general surgery of a tertiary care hospital.

MATERIALS AND METHODS

This study was carried out for a duration of 1 year from December 2020 to November 2021 at Mysore Medical College, a tertiary care hospital, Mysore, Karnataka.

The inclusion criteria were: Patients who

1. Had undergone mastectomy o breast conservation
2. Core biopsy to start chemotherapy and hormone therapy before surgery
3. Had complete immunohistochemistry data for ER, PR, and HER2.

Data included age, histopathological typing, and receptor status of all the breast cancer patients. All cases are subjected to immunohistochemistry for ER, PR, and HER2 on formalin fixed, paraffin-embedded breast tumor section using ready use monoclonal antibody, and HRP polymer detection system with 3'-3' (PAB) as the chromogen. Adequate tissue fixation in 10% buffered formalin for 6-24hrs was ensured and thin paraffin (3-4h thickness) sections with maximum invasive tumor component were selected for IHC. Both H and E and IHC slides were reviewed by two independent pathologist and results were interpreted with positive and negative controls. For ER and PR, results were integrated as positive when more or equal to 1% of tumor cells showed positive nuclear staining as per the ASCO/CAP interpretation guidelines 2010.

Initial immunohistochemistry for HER2 was carried out in all cases and HER2 was carried out in all cases and HER2 scoring was categorized as positive as 0, 1+, 2+, and 3+. The result was considered as positive for HER (score 3+) if uniform intense membrane staining of >30% of invasive tumor cells was seen. Test was considered negative if there was no staining (score) incomplete membrane staining that is faint/barely perceptible and within >10% of invasive tumor cells (Score 1+). Equivocal results (Score 2) were labeled when circumferential membrane staining that is incomplete and or weak/moderate and within >10% of the invasive tumor cells; or complete and circumferential membrane staining that is intense and within ≤10% of the invasive tumor cells which were noticed as per ASCO–CAP HER2 Test Guideline 2013 Recommendations.

Statistical analysis

Quantitative value of the data was presented as mean ±SD. Statistical analysis is done by using SPSS software version 26 for window.

RESULTS

For 1 year, 100 patients presented to the department of surgery of KR hospital with lump in the breast and were diagnosed as breast carcinoma.

A total of 100 patients were studied, of which 56 underwent modified radical mastectomy and 44 patients underwent core needle biopsy.

All cases were subjected to immunohistochemistry for knowing ER, PR, and HER2 neu in the carcinoma of breast and histopathological examination.

The most common age group in which breast carcinoma diagnosed in our was 51–55 year.

The most common type of breast carcinoma seen on histopathological examination was invasive ductal carcinoma seen in 66% of the patients.

The most common age group in which breast carcinoma diagnosed in our was 51–55 years (23%) followed by 41–45 years and 56–60 years (20%) each. The least number of breast carcinoma was seen below the age of 35 years (Table 1).

All the samples were sent for histopathological examination. The most common type of breast carcinoma found on histopathological examination that was invasive ductal carcinoma which was seen in 66% of the patients followed by invasive lobular carcinoma which was found in 10% of the patients. The least common type of carcinoma was papillary and mixed infiltrating carcinoma which constituted 1% each (Table 2).

ER, PR, and HER2 receptor were evaluated by immunohistochemistry in all the cases. Out of the 100 breast cancer cases, ER+ was seen in 54%, PR+ was seen in 39%, and HER2 + was seen in 31% of the patients (Table 3).

Among the 100 patients, ER/PR + status was seen in 34% of the patients, ER+/PR – in 20%, and ER–/PR+ in 5% of the patients. ER/PR – was seen in 41% of the patients (Table 4).

On correlating ER/PR and HER2 receptors together, 23% of the cases were ER/PR + and HER2 – which was the most common type seen followed by triple-negative cases which constitute 23% of the cases, while triple-positive cases were only 6% (Table 5).

DISCUSSION

Breast cancer is the most common cancer in women worldwide and is a major health concern especially in developing countries, where majority of cases are being diagnosed in late stages. In India, it is also the most common cancer among women and affects them one decade earlier than women in Western countries suggesting that breast cancer occurs at a younger premenopausal age in India.⁶

Table 1: Age distribution of the study participants

Age categories (years)	Frequency (n=100)	Percentage
≤35	3	3
36–40	8	8
41–45	20	20
46–50	16	16
51–55	23	23
56–60	20	20
>60	10	10

Table 2: Pathological spectrum/types of breast cancer among study participants

Type of tumor	Frequency (n=100)	Percentage
Invasive lobular carcinoma	10	10
Invasive ductal carcinoma	66	66
Invasive carcinoma of no special type	7	7
Lobular carcinoma	3	3
Lobular ductal carcinoma	2	2
Tubular carcinoma	3	3
Mucinous carcinoma	5	5
Medullary carcinoma	2	2
Papillary carcinoma	1	1
Mixed infiltrating carcinoma	1	1

Table 3: Hormone receptor positivity status of breast cancer patients

Hormone receptor	Positivity status	Frequency	Percentage
ER	Positive	54	54
	Negative	46	46
PR	Positive	39	39
	Negative	61	61
HER2 Neu	Positive	31	31
	Negative	69	69

Table 4: Results of ER/PR receptor status among breast cancer patients

Hormone receptor positivity status	Frequency	Percentage
ER positive and PR positive	34	34
ER positive and PR negative	20	20
ER negative and PR positive	5	5
ER negative and PR negative	41	41

The prognosis of breast cancer depends on several factors including ER/PR/HER2 status. It is now well-established that ER positive tumors are associated with better overall survival compared to ER negative tumors.⁷ Hence, there is a necessity that the hormone receptor status must be evaluated in every breast cancer case. In our study, the most common histological type was invasive ductal carcinoma (66%). The most common age group, in which breast carcinoma was diagnosed, was 51–55 years. In breast cancer, the average incidence of ER and PR positivity is

Table 5: Correlation of ER, PR, and HER2-neu Receptor among breast cancer patients

Hormone receptor positivity status	Frequency	Percentage
HER positive, ER positive, and PR positive	6	6
HER positive, ER positive, and PR negative	3	3
HER positive, ER negative, and PR positive	4	4
HER positive, ER negative, and PR negative	18	18
HER negative, ER positive, and PR positive	28	28
HER negative, ER positive, and PR negative	17	17
HER negative, ER negative, and PR positive	1	1
HER negative, ER negative, and PR negative	23	23

77% and 55%, respectively, as shown in the studies.⁸ The Western literature showed that by immunohistochemistry, about 70–80% of invasive breast carcinoma express nuclear ER in a proportion ranging from $\geq 1\%$ to 100% positive cells and such as ER and PR which are expressed in the nuclei of 60–70% of invasive breast cancers, with expression that varies in continuum ranging from 1% to 100% positive cells.^{9,10} However, lower rates of positive estrogen and PR breast cancers are found in Indian population from the Western literature.

In our study, only 54% of cases showed that ER positivity and 39% showed PR positivity. Studies from other regions of India have also documented lower positivity for both the receptors. Desai et al., from India have documented low ER positivity of 32.6% only, while PR positivity was seen in 46.1% of their breast cancer cases.¹¹ Another study from South India showed 46.87% ER positivity and 43.75% PR positivity.¹² The frequency of negative ER and PR is much more common in India (46.5%) than in the West (10%).¹³ In our study, ER/PR – was seen 41% which is similar to the previous studies conducted. In a study from Kerala, the overall ER positivity was found to be 52%.¹⁴ Overall ER positivity in the present study was 54%. The average ER positivity for white women in the US is 77%.¹⁵

In Kerala, study showed that 41.5% of patients were PR positive, while 55% of Caucasian women in the US are PR positive.¹⁵ In our study, PR positive was seen in 39% of the population. One study from North East India comprised 972 cases of invasive breast carcinoma and triple-negative breast cancer (ER, PR, and HER2/neu) constituted 31.9% (310 cases) of total cases.¹⁶ Percentage of triple-negative breast cancers in our study was 23%, while triple-positive breast cancers constitute only 6%. This percentage is

considerably higher compared with that seen in Western populations. Another study from one tertiary care center in India revealed 22.7% triple-negative cases.¹⁷ Moreover, one large study by Sandhu et al., by combining the data from 17 studies from India involving 7237 breast cancer patients found 31% incidence of triple-negative breast cancer.¹⁸ Thus, the prevalence of hormone receptor-positive breast cancer in Asian countries has been found to be lower than the Western world.

Limitations of the study

Our study did not include detection of Ki-67. So we could not comment on the Ki-67 status of the breast cancer in the study group and sample size is small

CONCLUSION

This single institutional study of 100 cases of breast cancer patients from South India suggest that mean age of breast cancer patient was between 51 and 55 years, with invasive ductal carcinoma being the most common histological type with ER positivity of 54% and PR positivity of 39% and triple-negative cancers of 23%, not grossly different from rest of the country but significantly lower than western studies.

Further studies are also required in larger group taking into account various clinical parameters, along with molecular study and survival pattern analysis to substantiate these immunohistochemical findings.

Similarly with high incidence of triple-negative breast cancers, an additional research is needed to understand the determinants of TNBC in India for future better outcome in these patients.

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Ethical approval

The study approved by our Institutional Ethical Committee.

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