Hormone Receptor Status of Breast Cancer in Young Women in Northern Region of India- A Study.

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ABSTRACT

Background: The aim of this study is to compare the expression of prognostically meaningful immunohistochemical markers such as Oestrogen receptor (ER), progesterone receptor (PR), expression pattern in young (<35 years) female breast cancer patients as compared to > 35 years of age . In most studies published so far, this patients group has not being analyzed separately particularly with such large data from this part of India. **Methods:** This study is an observational study, which includes 1691 cases of breast cancer of which 269 were young females. In this study, patients were analysed on the basis hormone receptor expression, evaluated immunohistochemically. **Results:** In our study, young (<35 years) female breast cancer patients constituted 15.90 % of the total female breast cancer population. Overall Oestrogen Receptor (ER) positivity in female breast cancer cases is found to be higher in the age group above 35 years, however ER and PR positive set of expression is found to be equal in both group of population of breast cancer below and above 35 years of age. **Conclusion:** We conclude that female breast cancer cases from this northern region of India do show relatively higher percentage of young females of breast cancer as compared to world literature.

Keywords: Breast Cancer, Oestrogen Receptor, Progesterone Receptor, young patients, immunohistochemical markers.

INTRODUCTION

Breast cancer is one of the most common malignant tumors and a main cause of death from oncological diseases in women worldwide. As per the statistics of 2015, the number of breast cancer cases were found to be 1,00,061 as against 94,208 cases of cervical cancer in India. Thus, breast cancer is now the most common malignancy among Indian women.[1,2] Trend for occurrence of breast cancer in younger population is becoming more and more. Now it has become a well acknowledged fact that the incidence of breast cancer in younger women differs according to race. Studies from across the world have defined 'young patients' in case of breast cancer (BC), as women diagnosed with breast cancer before the age of 35 to 40 years.[3,4] Studies from western world have shown that young patients account from 2 to 5% of all breast cancer population.[5, 6,7]

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Breast cancer in young patients in western world is rare as typically older women are affected, over the age of 50 years and up to 40% of all cases of breast cancer is diagnosed in female patients older than 65 years.[8] Identification of young patients is clinically valid as BC in that age group presents with certain biological differ¬ences and often requires special management. Breast cancer in young patients is often characterized by the presence of a low histological differentiation, high mitotic activity, and frequent vascular wall invasion. Typically, BC in young women has a more aggressive course, less favorable prognosis, and worse survival rates as compared to older sub¬jects.[9]

MATERIALS AND METHODS

Study Design
The study is retrospective and prospective observational study. The study was carried out on retrospective and prospective cases of breast cancer in women younger 36 years of age in Mahavir Cancer Sansthan and Research Centre which is a tertiary care cancer hospital of Bihar. A total of 1691 cases of epithelial malignancy of female breast cancer were included, of which 269 were females of lesser than 35 years of age. Rare malignancies presenting in breast like sarcomas and lymphomas were not included. The cases were selected randomly, who presented in our hospital from

October 2012 to March 2017. The identity of the cases was kept secret and ethical permission was taken from Institutional Ethical Committee, Mahavir Cancer Sansthan and Research Centre.

Methodology for Immunohistochemistry

All the cases were immunohistochemically evaluated for oestrogen and progesterone hormone receptor status, (ER and PR), expression using standard HRP Detection system method. Pressure cooking/microwave method was used for antigen retrieval. Adequate tissue fixation in 10% neutral buffered formalin for 6-48 hours was ensured. Paraffin sections (3-4 μm thick) with maximum invasive tumour component were selected for IHC. The antibodies used for ER and PR were monoclonal rabbit anti-Human Oestrogen Receptor, BIOGENEX (Clone ID5 and EP1; prediluted) and monoclonal, mouse anti-Human Progesterone Receptor, BIOGENEX (Clone PR 88; prediluted) respectively. The scores for ER and PR were calculated using the Allred Scoring method. All the tests were interpreted with negative and positive controls. Staining of the nuclei of the normal ductal epithelium was used as the internal control for ER and PR staining while interpreting the slides. ER and PR positivity is interpreted by seeing immunohistochmical expression in nuclei [Figure 3-5].

ER, PR scoring was done as per the Allred scoring system.

Allred scoring

Proportion score:

0 - No cells are ER positive

1 - ≤ 1% of cells are ER positive

2 - 1-10% of cells are ER positive

3 - 11-33% of cells are ER positive

4 - 34-66% of cells are ER positive

5 - 67-100% of cells are ER positive

Intensity score:

0 - Negative

1 - Weak

2 - Intermediate

3 - Strong

ER/ PR status is considered negative when proportion score +

intensity score is ≤ 2 and positive when ≥ 2.

Statistical Analysis

Analysis was done by using statistical software Graphpad Prism version 5.0. Data of Continuous variables are depicted as mean ± standard deviation; or median (range).

RESULTS

Out of the 1691 cases of female breast cancer that presented to our Department of Pathology, for hormone receptor analysis after histopathological confirmation of duct carcinoma, 269 cases were found to be either below or of 35 years of age. It

constituted 15.90 % of the total female breast cancer population. The median age is 32 years for this population. Mean ± Standard Error of Mean (SEM) age is 31.72 ± 3.78 years. Patients ≤ 35 years of age had predominantly unfavourable hormone receptor status accounting for 59.1%, while patients >35 years of age had little lesser unfavourable hormone receptor status which accounted for 51.89% patients of above 35 years of age of female breast cancer patients.

Dual hormone receptor negative tumours constitute 47% of the cases of female breast cancer in less than 35 years of age group [Figure 1], whereas in the same age group ER negative PR positive tumors constituted 5% of all cases of breast carcinoma. ER negative PR positive tumors were 12% in female breast cancer patients of above 35 years of age [Figure 2] which is 7% higher as compared to patient population of below 35 yrs. Contrary to other studies a peculiar finding is present in our study that both ER and PR positive tumors have constituted the same percentage (47%) of tumors in both age groups, however overall positivity for ER is higher (56%) in patients of above 35 years of age.

Table 1: Table summarising patient age group with favourable/unfavourable hormone receptor status.
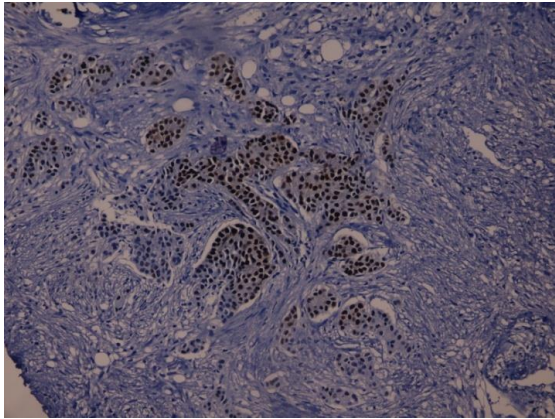
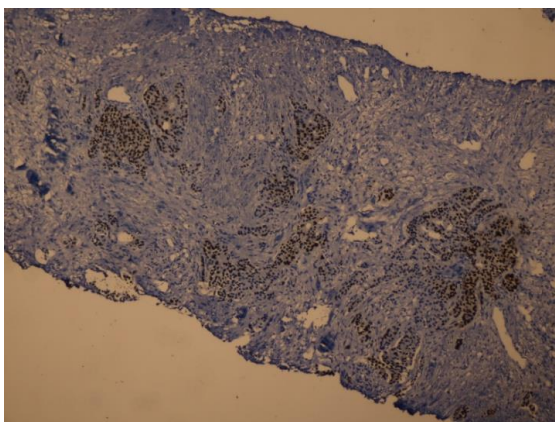|	Unfavourable (ER-PR-,ER-PR+)	Favourable (ER+PR-,ER+PR+)
Age ≤35 years (n=269)	159	110
Age ≥35 years (n=1422)	738	684
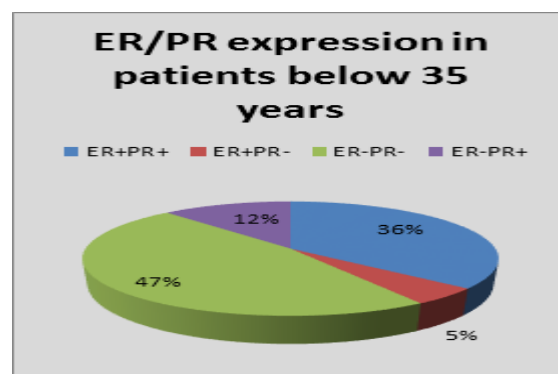
**Figure 1: ER/PR expression in patients below 35 years.**
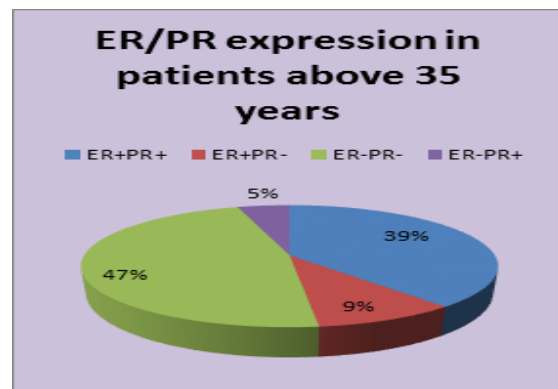
Figure 2: ER/PR expression in patients above 35 years.

Figure 3: Oestrogen receptor expression by breast tumor cells. Oestrogen receptor has a nuclear expression in the majority of the tumor cells.

Figure 4: Estrogen receptor expression by breast tumor cells. Estrogen receptor has a nuclear expression in the majority of the tumor cells chromogene DAB, X 400.
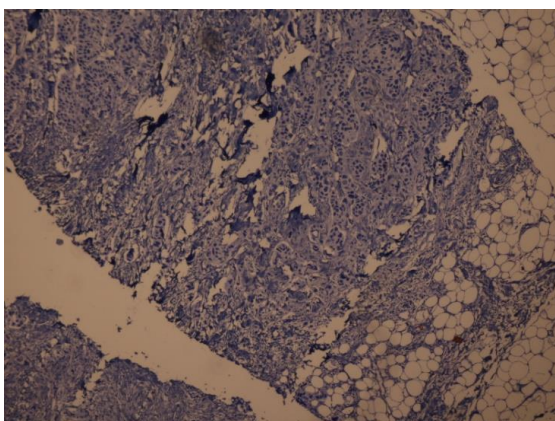
Figure 5: Case with negative Oestrogen receptor expression. Immunohistochemistry staining, chromogene DAB, X 400.

DISCUSSION

Overall, breast cancer is more common in Caucasian women than in African Americans; however, in women under the age of 35, breast cancer is more than twice as common in African American women. In Caucasian women of less than 35 years of age only 2.4% of all breast cancer cases are diagnosed in this age group, whereas in our study 15.90% of all breast cancer cases are below 35 years of age. Younger age has been generally accepted as an independent adverse prognostic indicator of survival in breast cancer.[10-13]

Adjuvant therapy, which helps in prolonging survival, is determined by the expression of Estrogen Receptor (ER), Progesterone Receptor (PR) and Human Epidermal Receptor (HER-2/neu) on the cancer cells. Statistics show that ER + PR+/HER2/neu +/- tumors have a good five year survival rate (about 94%). As these tumors have good prognosis, these tumors are considered to have favourable hormone receptor expression.[14-16]

Assi et al., highlighted in their study that breast cancer in young women is associated with high grade tumors, hormone receptor negativity and HER-2 neu overexpression. Many studies across the globe have demonstrated that most of the breast cancers in young women are estrogen receptor (ER) and progesterone receptor (PR) negative indicating a poorer prognosis.[17-19]

CONCLUSION

This study, is done on a large sample size, has been able to draw important inferences. The study shows that breast cancer has a higher incidence in older women, but cancers in younger women of ≤35 years of age is relatively higher in this part of India constituting 15.90% of all female breast cancer patients. These patients have more unfavourable hormone receptor expression though ER and PR positive set of expression is found to be equal in both group of population of breast cancer below and above 35 years of age.

Identification of these patterns will eventually help in better prognostication and development of personalised treatment of breast cancers and improve patient survival.

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