Original Article

Hormone receptor expression in breast carcinoma at our hospital: An experience

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ABSTRACT

Background: Breast carcinoma is the most common cancer among women in the urban Indian population and second only to cervical cancer in the rural population based on cancer registry data. Prognosis and management of breast cancer are influenced by classic variables such as histologic type, grade, tumor size and lymph node status. More recently hormone receptor (HR) status of estrogen receptor (ER), progesterone receptor (PR), and HER-2/neu expression have opened a new gateway in the field of adjuvant hormonal and/or chemotherapeutic regimen. **Objective:** The objective of this study was to assess the ER, PR, and HER-2/neu reactivity pattern in breast carcinomas at our hospital. **Materials and Methods:** A study of 100 patient samples of breast carcinoma was carried out from June 2011 to June 2014 in the Department of Pathology, ESIC Medical College and PGIMSR, ESIC Model Hospital, Rajaji Nagar, Bengaluru. Brief demographic and clinical data were obtained. Immunohistochemistry (IHC) was done by peroxidase antiperoxidase technique for detection of ER, PR, and HER-2/neu receptor status. Details regarding histopathological diagnosis, pathological grading, staging, and HR status of breast carcinoma were collected. Obtained parameters were evaluated using descriptive statistical analysis and presented in terms of percentage. **Results:** The age of the patients ranged from 24 to 75 years. Majority of tumors were infiltrating ductal carcinomas-not otherwise specified and predominantly histological grade 2. By IHC 52% were ER+/PR+, 25% were HER-2/neu positive and 20% of triple negatives. **Conclusion:** Detection of hormone expression is of paramount importance since these are one among the classic variables needed for providing suitable adjuvant hormonal and/or chemotherapeutic options, targeted treatment, and predicting prognosis.

Key words: Breast carcinoma, hormone receptor analysis, immunohistochemistry

INTRODUCTION

Breast carcinoma is the most common cancer among women in the urban Indian population and second only to cervical cancer in the rural population based on cancer registry data.[1-3] Survival of the breast carcinoma patients is dependent on early detection and timely appropriate treatment.[1-7] Prognosis and management of breast cancer are influenced by classic variables such as histologic type, grade, tumor size, and lymph node status.[4-7] On the contemporary hormone receptor (HR) status of estrogen receptor (ER), progesterone receptor (PR) and HER-2/neu expression have opened a new gateway in the field of adjuvant hormonal and/or chemotherapeutic regimen. Receptor status is a critical assessment in all breast carcinomas as it determines the suitability of using targeted treatment like tamoxifen and trastuzumab.[2-7] Carcinomas with ER+/PR+ have a good prognosis as compared to carcinomas with ER−/PR− and still worse with triple negatives (TNs).[2-7] In this regard, the study was undertaken to know the HR expression in patients with breast carcinoma among insured patients.

Objective

The objective of this study was to assess the ER, PR, and HER-2/neu reactivity pattern in breast carcinomas at our hospital.

MATERIALS AND METHODS

A prospective study conducted from June 2011 to June 2014 in the Department of Pathology, ESIC Medical College and PGIMSR, ESIC Model Hospital, Rajaji Nagar, Bengaluru.

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Hundred patients with breast carcinoma were subjected to the study wherein their demographic and clinical details collected. Modified radical mastectomy specimens were subjected for routine histopathological examination and immunohistochemical analysis. Specimens were routinely fixed for 24–48 h in 10% neutral buffer formalin. They were examined grossly and representative tissue bits were taken according to standard guidelines and then processed. Sections were stained with routine hematoxylin and eosin stain. Histopathological features were determined.

Representative sections with tumor and adjacent normal breast tissue (internal control) were further processed for immunohistochemistry (IHC) using peroxidase-antiperoxidase technique. Sections were taken on silane coated slides. Antigen retrieval was done by pressure cooker using ethylenediaminetetraacetic acid buffer solution. Slides were stained with monoclonal antibodies obtained from "Scytec" company of the following clones ER (mouse monoclonal clone 1D5), PR (mouse monoclonal clone PR 88) HER-2/neu (rabbit monoclonal clone EP1045Y). 500 cells on tissue sections were counted for positivity. ER+, PR+ was denoted by nuclear staining using Allred scoring system which takes into account both intensity of staining and proportion of positive tumor cells. American Society of Clinical Oncology guidelines 2007 denoting cytoplasmic membrane staining was used for HER-2/neu grading.

Statistical analysis

- The data were analyzed using SPSS software version 18.0 (SPSS Inc, Chicago)
- Obtained parameters were evaluated using descriptive statistical analysis and presented in terms of percentage.

RESULTS

In the present study, female patients with breast carcinoma were aged between third and seventh decade of life. The youngest was 24 years and oldest 75 years of age. Majority (76%) were in third and fourth decade of life [Table 1]. Left breast (50%) was marginally more affected than right sides (49%) of breast and in a single case both breasts (1%) were affected.

Variants of breast carcinoma of which the most common histologic subtype was infiltrating ductal carcinoma-not otherwise specified (IDC-NOS) (87%) followed by lobular carcinoma (5%) [Table 2].

In the present study, the most common histologic grade encountered was grade 1 accounting to 54% followed by grades 2 and 3 with 27% and 19% respectively.

Hormone receptor status analysis revealed ER+/PR+ (52%) being the most common HR expressed followed by HER-2/neu (25%) and TNs (20%) [Table 3].

Most of the breast carcinomas encountered were in stage 2 (57%) followed by stage 1 (28%) and stage 3 (15%).

DISCUSSION

Incidence of breast carcinoma rises throughout a woman's lifetime. Age range among Indian breast cancer patients is found to be lower when compared to the Western countries with an average difference of one decade. This is likely to be due to the different age distribution of the Indian population, where only 7% of the population is above the age of 60 years.[5-8]

In the present study, 49% of women were in the age group of 41–50 years, in contrast a study by Pakseresht *et al*.[9] had

Table 1: Age distribution among patients with breast carcinoma

Age range	*n* (%)
<30	4 (4.0)
31–40	27 (27.0)
41–50	49 (49.0)
51–60	16 (16.0)
61–70	2 (2.0)
>71	2 (2.0)
Total	100 (100)

Table 2: Various histopathological subtype of breast carcinoma

Histopathological subtype	Frequency (*n*=100) (%)
IDC-NOS	87 (87)
Lobular carcinoma	5 (5)
Mucoepidermoid carcinoma	1 (1)
Mucinous carcinoma	1 (1)
Papillary carcinoma	1 (1)
Neuroendocrine carcinoma	1 (1)
IDC-comedo carcinoma	1 (1)
IDC-both breast	1 (1)
IDC-pagets	1 (1)
Metaplastic carcinoma	1 (1)
Total	100 (100)

IDC-NOS: Infiltrating ductal carcinoma-not otherwise specified

Table 3: Frequency of various IHC hormone receptor status of breast carcinoma

IHC hormone receptor status	Frequency (%)
ER+/PR+	52 (52)
ER+/PR−	2 (2)
ER−/PR+	0 (0)
HER2/neu+	25 (25)
Triple positive	1 (1)
Triple negative	20 (20)
Total	100 (100)

IHC: Immunohistochemistry, ER+: Estrogen receptor positive, ER−: Estrogen receptor negative, PR+: Progesterone receptor positive, PR−: Progesterone receptor negative, HER2: Human epidermal growth factor receptor 2

a lower age range from 31 to 40 years (34.5%), whereas Suvarchala and Nageshwararao[8] (45.31%), Ambroise *et al*.[6] (46.4%), and Rhodes *et al*.[10] (36.42%) had higher age range between 51 and 60 years.

Literature search reveals breast carcinomas are more common in the left breast than the right. The possible explanations are that, the left breast being more bulky and having a larger volume of breast tissue comparatively. However, side of breast involved has no clinical significance.[6,11] In the present study, also left breast were marginally more affected than right with a single case of bilateral breast carcinoma.

In the present study, histologic subtype IDC-NOS comprises the majority accounting to 87% followed by lobular carcinoma 5% and rest one case each of other variants. This was in comparison with other Indian and Western studies wherein IDC-NOS are the commonly encountered breast carcinoma variant.[5,7,8,12-14]

In the present study, majority of breast tumors were grade 2 (54%) followed by grade 3 (27%) and grade 1 (19%) which is in concordance with all studies except for one study by Ghosh *et al*. having more of grade 3 (75.4%).[5-8,12]

In the present study, 52% were ER+/PR+, 25% were HER-2/neu positivity, and 20% of TNs [Figures 1-4]. These results were in concordance with other Indian studies having lowered positive receptors and higher HER-2/neu expression and TNs.[4,6,8] However, the Western literature showed higher positive receptor status and lower TNs and HER-2/neu,[7,10,12,15] [Table 4].

Our study showed that 55% of cases had positive ER expression while 53% expressed PR. This is lower when compared to some Western studies which have reported 73% ER+ and 58% PR+[10] and 68.9% ER/PR+.[12] A study from Mumbai also showed that HR expression in India is lower compared to the West.[4] The percentage of tumors expressing ER but not PR was 2% in our study. The study from Mumbai has revealed it to be 10.6%.[4] A Western study has also reported a higher incidence 19.8 ER+/PR− phenotype.[10] In our study, 1% triple positive breast carcinoma was encountered in contrast Western study has reported a higher incidence 10.2 for this phenotype.[12]

The presence of HRs (ER and PR) in the tumor tissue correlates well with the response to hormone therapy and chemotherapy. Studies have shown that ER+ tumors respond to additive or ablative hormone therapy, compared with ER− tumors. Tumors that are better differentiated are more likely to be ER+ and PR+ and have a relatively better prognosis. PR is a surrogate marker of a functional ER and is valuable in predicting the behavior of breast carcinoma. Loss of PR by tumor cells is associated with a worse prognosis. Patients with larger tumors, poorly differentiated morphology and higher stage tumors have more chance of an ER− and PR− status.[6-8,12,15]

The significance of the single HR+ phenotype that includes ER+/PR− and ER−/PR+ is still poorly understood. These single HR+ phenotypes are often of higher histology grade, larger in size, aneuploidy, and higher expression of proliferation-related genes than ER+/PR+. Both single HR+ groups are similar and they both have same biological characteristics in terms of disease-free survival and response to treatment is in between ER+/PR+ and ER−/PR−.[16,17]

HER-2/neu positivity was present in 25% of our cases. In the Western studies, the values ranged from 17% to 27%.[12,18-20] A study from Malaysia showed that 31.5% of breast cancers were HER-2/neu positive.[21] The frequency of HER-2/neu positivity varies among Indian studies. In a study from South India by Vaidyanathan *et al*., found a figure of 43.2% positivity by IHC and 25.5% by genomic polymerase chain reaction.[22] Another study from the same region has documented 29% HER-2/neu positivity by IHC.[23] Another study from Varanasi, North India revealed it to be 46.3%.[24] The frequency of HER-2 positivity may change if we take into account cases detected by fluorescence *in situ* hybridization (FISH) analysis.[6] However, FISH was not performed in our study neither in the other recent studies from India.

The TN breast cancers are characterized by a lack of expression of ER, PR and HER-2/neu receptors which

Table 4: Comparison of various studies showing hormone receptor status

IHC hormone receptor status	Onitilo *et al.* 2009[12]	Sharif *et al.* 2010[15]	Suvarchala and Nageshwararao 2011[8]	Ambroise *et al.* 2011[6]	Ghosh *et al.* 2011[5]	Present study 2014
ER+/PR+	68.9	62.8	32.8	47	51.2	52
ER+/PR−	-	11.8	14.0	1		2
ER−/PR+	-	4.1	10.94	0		0
HER2/neu+	7.5	28.1	-	27	24.8	25
Triple positive	10.2	-	-	-		1
Triple negative	13.4	-	42.19 (ER−/PR−)	25	29.8	20

IHC: Immunohistochemistry, ER+: Estrogen receptor positive, ER−: Estrogen receptor negative, PR+: Progesterone receptor positive, PR−: Progesterone receptor negative, HER2: Human epidermal growth factor receptor 2

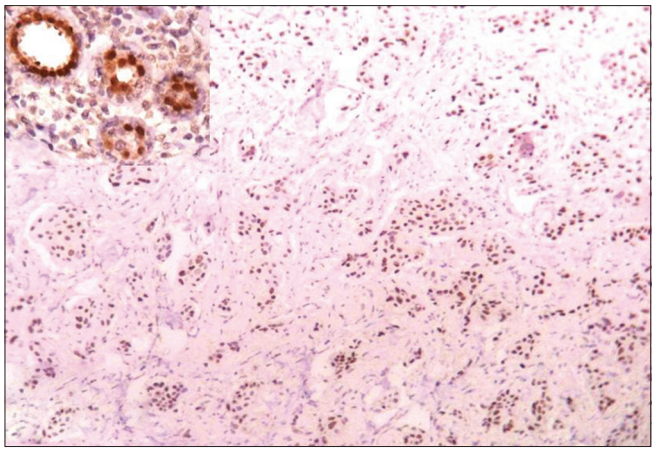

Figure 1: Immunohistochemistry nuclear stain positivity for estrogen receptor-Allred score-8 (×10). Inset showing internal control

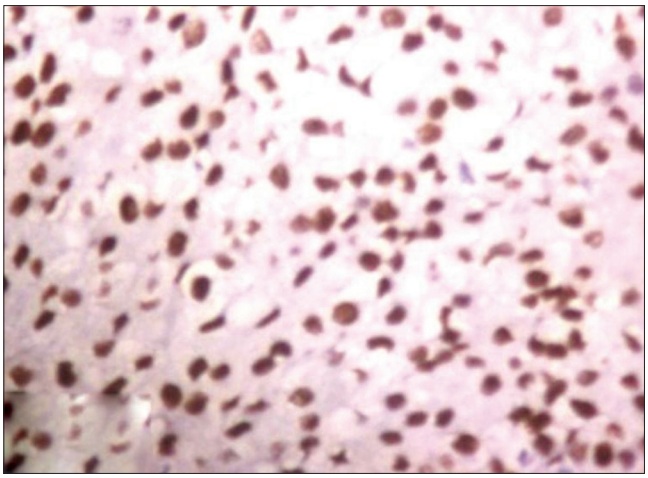

Figure 2: Immunohistochemistry nuclear stain positivity for estrogen receptor-Allred score-8 (×40)

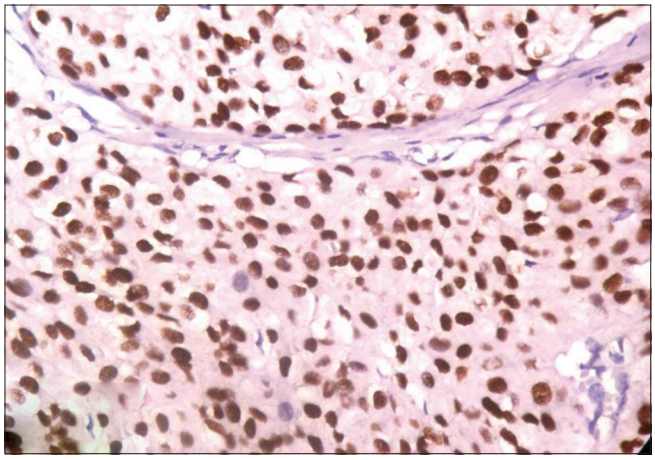

Figure 3: Immunohistochemistry nuclear stain positivity for progesterone receptor-Allred score-8 (×40)

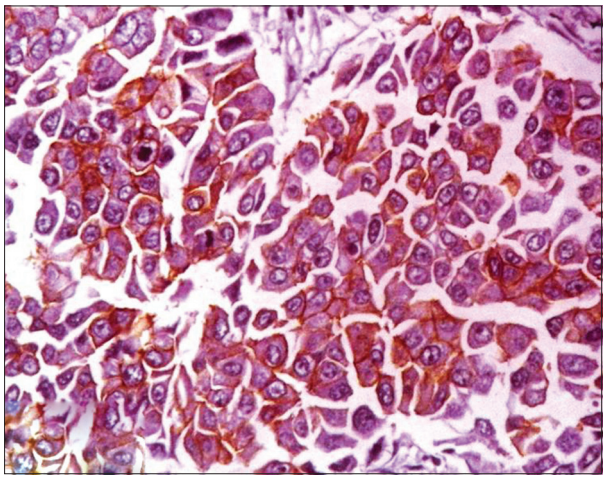

Figure 4: Immunohistochemistry nuclear stain positivity for HER-2/neu receptor-score-3+ (×40)

constituted 20% of our cases. Studies among Asian women have reported more than 30% of breast cancer with the TN phenotype.[6,25,26] Western countries have showed that TN tumors are of 14–29.5% of breast carcinomas.[12,27-32] Studies have also shown that TN tumors vary markedly with ethnicity and documented a higher incidence in African women compared to White women.[6,12,25-32]

In the present study, stage 2 were the most common breast carcinomas accounting to 57% followed by stage 1 (28%) and stage 3 (15%) in concordance with other Indian studies.[14,33] In Western countries, stage 1 (56.4%) are the majority followed by stages 2 and 3 possibly due to increased awareness and rampant breast cancer screening programs.[12,34]

CONCLUSION

The HR expression in the present study is in the concordance and comparable to other published Indian studies having lowered ER, PR+ receptors and higher HER-2/neu expression and TNs. Detection of hormone expression is of paramount importance since these are one among the classic variables needed for providing suitable adjuvant hormonal and/or chemotherapeutic options, targeted treatment, and predicting prognosis.

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