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A Clinicopathological Study of Pre and Post Menopausal Breast Cancer Patients in North Bengal Population & Their Correlation with Estrogen and Progesterone Receptor Status

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Abstract
Breast cancer is the commonest cancer among Indian females. Tumour size, lymph node, grade, vascular invasion, Estrogen receptor Progesterone receptor (ER PR) and HER2neu receptor expression are important both prognostically and in deciding therapy.
Materials and Methods: *52 operated breast cancer patients of North Bengal region with complete history and staging were studied. Clinical profile (menopausal status, tumour size, stage, lymph nodes), pathologic findings (histological type, grade, skin/nipple areola involvement, LVI, perineural spread, lymph node status) and ER PR status were correlated.*
Results: *Most patients presented at late stage with more than 5 cm tumour often with lymph node metastasis. Commonest age group was 45-54 years, majority were postmenopausal and most tumours were histological grade 2. Positive ER/PR status was observed in 57.69% cases and ER/PR status correlated significantly with clinicopathological parameters.*
Keywords: *Breast cancer, Clinicopathological parameters, ER PR status.*

Introduction

Breast cancer is the commonest cancer among Indian females with age adjusted rate as high as 25.8 per 100,000 women and mortality 12.7 per 100,000 women[1].A statistically significant increase in age adjusted rate over time (1982-2014) in all the PBCRs[1].

Breast cancer is considered a heterogenous disease comprising of distinct biological subtypes with diverse natural history presenting a varied spectrum of clinical, pathological and molecular features with different prognostic and therapeutic implications. Apart from histological grade, tumour size, lymph status and vascular invasion, hormone receptor status (ER PR profile) and Human Epidermal Growth Factor Receptor-2 (HER2neu receptor) status are very important both prognostically and in therapeutic approach[2,3]. They help decide adjuvant systemic chemotherapy, hormonal therapy and HER2neu directed therapy. Proliferation index marker (Ki-67)[3] is the new tool for prognostication & therapeutic decision making along with histopathology, ER/PR and HER2 neu status.

Estrogen receptor (ER) status is regarded as the most powerful predictive marker in breast cancer management[4], progesterone receptor (PR) status is a weaker predictor of response to endocrine therapy[5]. About 70% of breast cancers are hormone receptor positive across the globe while only about 50% are hormone positive in Indian studies[6].

Materials and Methods

This descriptive study was conducted in the departments of Pathology and Radiotherapy in North Bengal Medical College Hospital, a tertiary care unit catering to people from six North Bengal districts, state of Sikkim, part of Assam, part of Bihar, Nepal and Bangladesh too. All female breast cancer patients operated in the Institution and registered in Radiotherapy Department from February 2011 to January 2012 were included after proper informed consent and institutional ethics committee clearance. Relevant history, clinical staging and investigations were collected. Detailed macroscopic findings- tumour size, colour, consistency, margin, skin, nipple areola involvement and number of lymph nodes were noted. Microscopic parameters studied were histological type, grade (Nottingham modification of Bloom Richardson method), surgical margin, skin, nipple areola involvement, DCIS and Extensive intraductal component, lympho-vascular invasion (LVI), perineural spread and lymph node status. ER-PR receptor status was evaluated by immunohistochemical study. ER-PR status was correlated with age, menopausal status, histological type, grade, stage, lymph node status, LVI, skin and nipple areola involvement.

Results and Analysis

52 patients operated in the institution with complete history and staging were enrolled. Out of them 20 cases were in the age group 45-54 years (38.5%) followed by age group 35-44 years (30.8%). Mean age of the study population was 43.9 years with standard deviation (SD) of 9.34. 32 patients (61.54%) were post-menopausal whereas 20 patients (38.46%) were premenopausal. Breast cancer in first degree relative was found in only 2 patients (3.85%).30 patients (57.69%) had >5cm tumour, 19 patients (36.54%) had T2 tumours (2-5cm). 48 patients (92.31%) had single tumour mass. Upper and outer quadrant was the commonest location (32 patients, 61.53%). Infiltrating duct carcinoma, NOS constituted the largest group (46 patients, 88.46%) followed by medullary (3 patients, 5.77%) and lobular carcinoma (2 patients, 3.85%. 27 patients (51.9% were Grade 2 while 20 patients (38.5%) were Grade 3 and 5 patients (9.6%) were Grade 1. 23 patients (44.23%) had lymph node metastasis and 29 patients (55.77%) were node negative. 16 patients (30.77%) had 4-10 positive nodes, 4 patients (7.69%) had more than 10 positive nodes and 3 patients (5.77%) had 1-3 positive nodes. LVI was present in 15 patients (28.8%) and absent in 37 patients (71.2%). Only 5 patients (9.62%) had skin/nipple areola involvement.

ER PR positivity was expressed by 30 cases (57.69%) among which 18 patients (34.62%) were both ER+ve and PR+ve while 22 patients (42.31%) were both ER-ve PR-ve.

Table 1: Study population ER PR status

ER, PR STATUS	**No.**(out of 52)	%
ER +VE PR +VE	18	34.62
ER +VE PR -VE	8	15.38
ER -VE PR +VE	4	7.69%
ER -VE PR -VE	22	42.31

Tumours are considered ER/PR +ve when they express both ER& PR positivity or single positivity (ER +ve or PR +ve). Most of the cases in age group 45-67 years expressed ER PR positive status (22 cases out of 26, 84.62%) while majority of the cases in 25-44 age were ER-/PR- (18 out of 26, 69.23%). ER PR positivity increased with age and this was statistically significant (p=0.00127).

Amongst 32 post-menopausal women 26 (81.25%) were ER/PR +ve and 6 (18.75%) were ER/PR -ve. In contrast, amongst 20 premenopausal women 16 (80%) were ER/PR

negative and only 4 (20%) were ER/PR +ve. The difference is statistically significant (p <0.05).

Majority of the tumours with size <5cm were ER/PR +ve (81.82%) whereas larger tumours >5cm were ER/PR -ve more commonly (60%) and the difference is statistically significant.58.7% of IDC, NOS showed ER/PR positivity. In other histological types 50% of tumours showed ER/PR positivity (statistically insignificant).ER/PR positivity was found in 20 out of 27 (74%) of Grade 2 tumours whereas in Grade 3 tumours most (15, 75%) were ER/PR -ve. Majority of the patients with Lymph node metastasis were ER/PR -ve (15 cases, 65.22%). On the other hand, 75.86% of those without lymph node metastasis showed ER/PR positivity (statistically significant). 60% of tumours with Lymphovascular invasion were ER/PR negative. 60% of those who had skin/nipple areola involvement were ER/PR negative (not significant statistically).

Table 2: ER/PR status correlation with Age, Menopause, Grade, Lymph Node, LVI and skin/nipple areola involvement

	ER PR +ve	ER PR -ve	Total
Age			
< or = 44 years	8 (26.6%)	18 (81.82%)	26
>44 years	22 (73%)	4 (18.18%)	26
Menopausal status			
Pre-menopausal	4 (20%)	16 (80%)	20
Post-menopausal	26 (81.25%)	6 (18.75%	32
Tumour Size			
<or = 5 cm	18 (81.82%)	4 (18.18%)	22
>5 cm	12 (40%)	18 (60%)	30
Histological Grade			
Grade 1	5 (100%)	0	5
Grade 2	20 (74.07%)	7 (25.93%)	27
Grade 3	5 (25%)	15 (75%)	20
Lymph node			
Present	8 (34.78%)	15 (65.22%)	23
Absent	22 (75.86%)	7 (24.14%)	29
Lympho-vascular invasion			
Present	6 (40%)	9 (60%)	15
Absent	24 (64.86%)	13 (35.14%)	37
Skin/Nipple Areola +			
Present	2 (40%)	3 (60%)	5
Absent	28 (59.57%)	19 (40.43%)	47

Discussion

The present study was undertaken to assess various clinicopathological parameters in breast cancers in women, to study ER PR status and to correlate the ER/PR status with clinicopathologic features. The age distribution, menopausal status, parity, breast cancer history in first degree relative, tumour location, size, histologic type, grade, LVI, Lymph nodal involvement and skin/nipple areola involvement were comparable to other similar studies.

Dunnwald L.K. et al studied a cohort of 155,175 women with known joint ER/PR receptor status, 98,463 cases had ER+/PR+ tumours (63%). Of the remaining, 19,886 cases had ER+/PR- tumours (13%), 4,896 cases had ER-/PR+ tumours (3%), and 31,930 cases had ER-/PR- tumours (21%). Older women were more likely to be diagnosed with ER+/PR+ tumours, whereas more than one third of women 30 to 39 years old presented with ER-/PR- tumours[7].

Tanuja Shet et al studied 798 cases of breast cancer hormone receptors over the last 8 years in a tertiary cancer centre in India. Sixty percent of the patients were in the age group of 31-50 years. Seventy percent of the tumours were grade III tumours. The percentage of hormone receptor expression in breast cancer in the last 8 years

varied from 52 to 57%. The overall receptor expression in the last 8 years shifted within a 5% range, confirming that the hormone receptor expression in Indian patients with breast cancer is low[8].

In this study, 30 out of 52 cases (57.69%) were ER/PR positive and 22 out of 52 cases (42.3%) were ER/PR negative comparable to other Indian studies.

Dunnwald L K et al[7] had observed that older patients were more likely to be ER/PR +ve while more than third of patients in the age group 30-39 years presented with ER -ve PR -ve tumours. They found that compared to ER/PR positive tumours, ER/PR negative tumours tend to have larger size, more advanced disease and higher tumour grade.

In general, breast cancer has been reported to occur a decade earlier in Indian patients compared to their western counterparts. More than 80% of Indian patients are under 60 years. The average age in six population-based cancer registries in India ranged from 44.2 years to 49.6 years[9].

E. Ur Rahman et al. studied 289 breast cancer patients in Mayo Hospital, Lahore and found ER PR positivity was 46.02% (133 cases), 30.4% (88 patients) were triple negative (ER -ve, PR -ve Her2neu -ve). Most triple negative patients were premenopausal while 60.29% of cases were ER PR -ve and Her2neu+ve[10].

In our study the mean age of the patients was 43.9 years. There was significant association of ER/PR positivity with advanced age and more ERPR negativity was expressed in younger age. Majority of postmenopausal women (81.25%) were ER PR positive and 80% of premenopausal women were ER/PR negative. These results are comparable to other Indian studies.

Kakarala M. et al[11] in a study of Asian Indian/Pakistani women in US found that frequency of invasive ductal carcinoma was much higher and invasive lobular carcinoma was much lower compared to Caucasians (69.1% vs 65.6%, $p<0.001$).

In our study, 88.46% presented with IDC, NOS type and only 3.85% had invasive lobular carcinoma. 51.9% (27 cases) were grade 2 followed by grade 3 tumours (38.5%).

In the study of Dunnwald et al hormone positivity was higher (80.2%) in patients without lymph node metastasis in comparison to patients with metastatic lymph node (77%). Shrigondekar P et al[12] in a study of 222 breast cancer patients did not find any correlation of Er/PR with lymph nodal status. In our study majority of patients with lymph node metastasis expressed ER/PR negativity (65.22%).

In our study lympho-vascular invasion was found in 15 out of 52 cases (28.8%). Majority of patients with LVI expressed ER/PR negativity (60%) while most patients without LVI were ER/PR +ve (64.86%). The result was not statistically significant. Desai et al[13] and Dutta et al[14] also showed inverse relationship of LVI with hormone receptor positivity.

Conclusion

Breast carcinoma is a heterogenous disease. Invasive ductal carcinoma, not otherwise specified (IDC, NOS) type is the most common histological type in North Bengal region. Most of the patients present late with more than 5 cm tumour often with lymph node metastasis. Commonest age group is 45-54 years, majority are postmenopausal. Most tumours are histological grade 2. Positive ER/PR status is observed in 57.69% cases and ER/PR status correlates significantly with clinicopathological prognostic parameters.

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