Original Article

Expression of Estrogen and Progesterone Receptor Status in Breast Carcinoma Using Quick Score: A Study at a Tertiary Care Centre in Kerala

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ABSTRACT

Background: Breast carcinoma is the most common malignant tumour and the leading cause of carcinoma death in women. The hormone receptor status is important nowadays due to its prognostic and therapeutic significance. The objective of this study was to correlate estrogen (ER) and progesterone receptor (PR) status with clinicopathological parameters like age, lymphnode status, size of the tumour and tumour grade of breast carcinoma.

Methods: This study was conducted in the Department of Pathology, Government Medical College, Thrissur from January 2012- June 2013. 100 mastectomy specimens were received and analysed for both histological grading and immunohistochemically by quick score for ER and PR markers.

Results: Majority of the cases were between 50-60 years of age with invasive ductal carcinoma grade 2. ER, PR positivity in this study was 67% and 62% respectively with both receptors positive for 61% of cases. In this study 55% showed no axillary lymphnode involvement and 45% showed lymphnode involvement with majority cases had size between 2 and 5 cm.

Keywords: Breast cancer, Immunohistochemistry, Estrogen receptor, Progesterone receptor, Bloom Richardson Grading , Quick score

Introduction

Breast carcinoma is the most common malignant tumor and the leading cause of carcinoma death in women, with more than 1,000,000 cases occurring worldwide annually.[1] The importance of steroid hormone receptors to the biology of breast cancer was recognized over 40 years ago, when it was observed that radiolabelled estrogens concentrated preferentially in the estrogen-influenced target organs of both animal and human breast cancers. These findings gave rise to the concept of an estrogen receptor (ER). It has since become clear that human breast cancers are dependent upon estrogen and/or progesterone for growth and that this effect is mediated through estrogen receptors (ERs) and progesterone receptors (PRs).

The assessment of estrogen receptor (ER) status of breast carcinoma has become the routine practice nowadays. The assessment of progesterone receptor (PR) status along with ER gives a stronger predictive power.[2] The presence of ER is related to a favourable response to endocrine therapy and improved overall survival.[3]

Aims of study is to asses estrogen and progesterone receptor (ER,PR) status in breast malignancies and correlate the immunohistochemistry results with clinicopathological parameters like age, size of the tumor, lymph node involvement and modified Bloom Richardson grading system.

Materials and Methods

This was a hospital based cross sectional study of 100 patients with invasive carcinoma breast who had undergone mastectomy. This study was conducted in the Department of Pathology, Government Medical College, Thrissur for a period of one and a half years from January 2012 to June 2013.

Inclusion Criteria: All mastectomy cases proven to be invasive breast carcinomas referred to the Department of Pathology, Government Medical College, Thrissur for immunohistochemical assessment of hormone receptor is included in the study.

Exclusion Criteria: Excision and incision biopsies proven to be malignant histologically were not included in the study.

100 mastectomy specimens were included in the study. All the mastectomy specimens recieved fixed in 10% formalin and cut into 5mm slices. Each paraffin-embedded block were cut into 4-micro meter sections. Paraffin embedded

sections were stained using Hematoxylin & Eosin to verify the presence of invasive breast cancer. All tumors were graded according to a modified version of the Bloom-Richardson histologic grading criteria.

From the selected blocks, sections were stained immunohistochemically for estrogen and progesterone receptors. Mouse monoclonal antibody is used for immunohistochemical staining. Scoring for ER, PR was done by Quick score system which takes the proportion and intensity of nuclear staining into account. NPI was calculated using the formula NPI = (0.2XS) +N+G where S is the size of tumor in cm, N is the number of lymph nodes involved: 0 =1, 1-3 = 2, >3 = 3, G is the grade of tumour: Grade I =1, Grade II =2, Grade III =3 . Data was collected and entered in Microsoft office excel 2007 sheet. This was then analysed using SPSS software 17.0.

Results

In this study of 100 patients, estrogen receptor positivity was found to be 67% and progesterone receptor positivity was 62%. Age of the patients ranges between 32 to 81 with mean age 52 years. (Table1) Maximum number of cases were obtained in the age group of 51-60 years. (36%). (Table 1) According to the histologic grading more cases were observed in Grade II category (75%) followed by Grade III category (16%) and least number were in the Grade I category (9%). (Table 3) 52/67(77.6%) cases with ER positive had a grade 2 and 47/62 (75.8%) cases with PR positivity also had a grade 2 according to modified Bloom Richardson grading system. (Table 4) Eight patients (Table 2) had a tumor size of < 2 cm, of which 50% were ER positive and 82 patients had size between 2 and 5 cm of which 70.7% were ER positive. In our study 55% showed no axillary lymphnode involvement and 45% showed lymphnode involvement.

Discussion

Worldwide, breast cancer is the most common invasive cancer in women. Breast cancer comprises 22.9% of invasive cancers in women[4] and 16% of all female cancers.[5] Breast cancer is related to age with only 5% of all breast cancers occur in women under 40 years old.

Table 1: Size of the tumor, Lymphnode involvement and NPI.

Size	Frequency	Percent	No of lymphnodes involved	Frequency	Percent	NPI	Frequency	Percent
< 2 cm	8	8.0	0	55	55.0	0	12	12.0
2-5 cm	82	82.0	≤ 5	30	30.0	≤ 5	68	68.0
> 5 cm	10	10.0	Above 5	15	15.0	Above 5	20	20.0
Total	**100**	**100.0**	**Total**	**100**	**100.0**	**Total**	**100**	**100.0**

Table 2: Age wise distribution with ER positive, ER negative and PR positive and PR negative status.

Age group	ER Positive		ER Negative		Total	Age group	PR Positive		PR Negative		Total
	Frequency	Percent	Frequency	Percent			Frequency	Percent	Frequency	Percent	
31-40	6	60.0	4	40.0	10	31-40	6	60.0	4	40.0	10
41-50	23	69.7	10	30.3	33	41-50	22	66.7	11	33.3	33
51-60	22	61.1	14	38.9	36	51-60	20	55.6	16	44.4	36
Above 60	16	76.2	5	23.8	21	Above 60	14	66.7	7	33.3	21
Total	**67**	**67.0**	**33**	**33.0**	**100**	**Total**	**62**	**62.0**	**38**	**38.0**	**100**

Table 3: Distribution based on Lymphnode invovement with ER positive, ER negative, PR positive and PR negative.

No of lymphnode involved	ER Positive		ER Negative		Total	No of lymphnode involved	PR positive		PR negative		Total
	Frequency	Percent	Frequency	Percent			Frequency	Percent	Frequency	Percent	
No metastasis	30	54.5	25	45.5	55	0	29	52.7	26	47.3	55
≤ 5	25	83.3	5	16.7	30	≤ 5	23	76.7	7	23.3	30
Above 5	12	80.0	3	20.0	15	Above 5	10	66.7	5	33.3	15
Total	**67**	**67.0**	**33**	**33.0**	**100**	**Total**	**62**	**62.0**	**38**	**38.0**	**100**

Table 4: Distribution based on ER with PR positivity.

ER	PR positive	PR Negative
Positive	61	6
Negative	1	32
PR Total	62	38.0

Table 5: Relationship Between Er and Pr With Clinicopathological Parameters in 100 Cases of Ductal Carcinoma of Breast.

PARAMETERS	ER + (n=67)	ER − (n=33)	P value	PR + (n=62)	PR- (n=38)	P value
Lymph node metastasis Present Absent	37 30	8 25	0.013*	33 29	12 26	0.087
SIZE <2 cm 2-5 cm >5 cm	4 58 5	4 24 5	0.238	4 55 3	4 27 7	0.057
GRADE 1 2 3	9 52 6	0 23 10	0.004*	8 47 7	1 28 9	0.081
AGE 31-40 41-50 51-60 Above 60	6 23 22 16	4 10 14 5	0.638	6 22 20 14	4 11 16 7	0.765

* - *Statistically significan*

Table 6: Comparison of Data Between This Study and Other Similar Studies.

| Parameters	Mudduwa et al's study	Sofi et al's study	Present study
Estrogen receptor Positive Negative	45.7% 54.3%	66.3% 33.7%	67% 33%
Progesterone receptor Positive Negative	48.3% 51.7%	64.3% 35.7%	62% 38%
Histologic grade Grade 1 Grade 2 Grade 3	14.6% 36.4% 49%	7.6% 52.1% 40.3%	9%(9/100) 75%(75/100) 16%(16/100)
Mean age (in years)	52.5+/- 11.95	48.21	52.72+/-10.05
Tumor size (in cm)	3.52+/- 2.34	3.56	3.65+/-2.52
Lymph nodemetastasis Present Absent	57.6% 42.4%	61.2% 34.8%	45% 55%
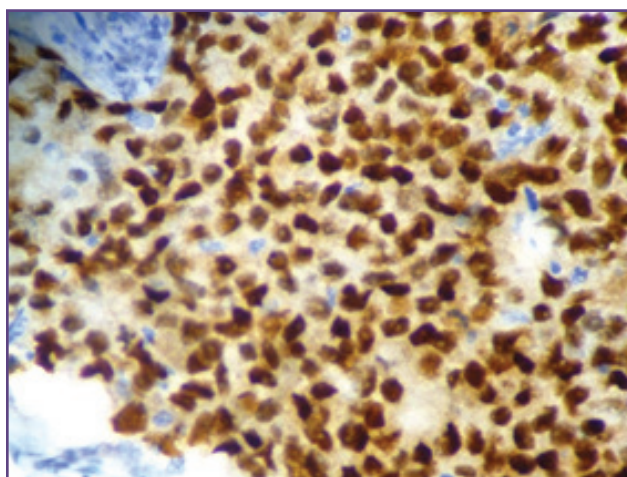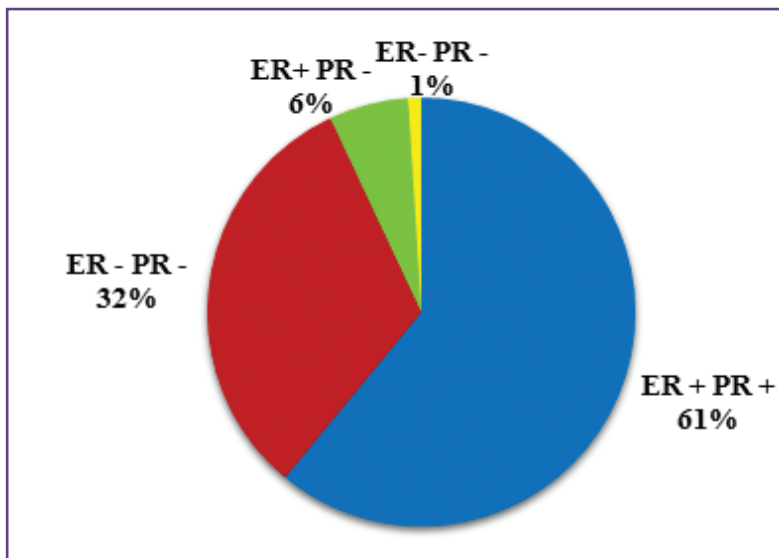
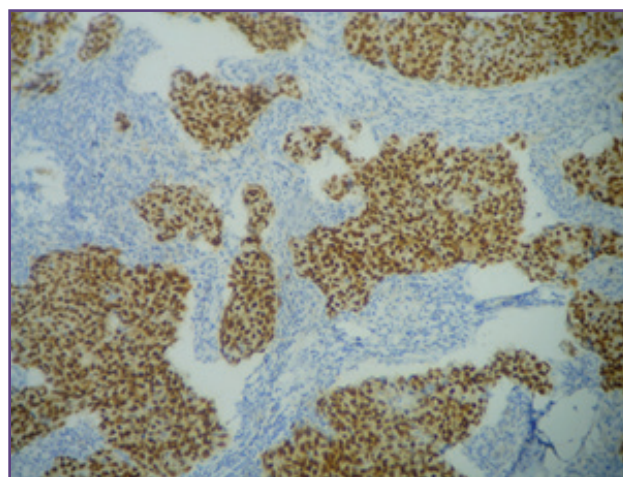**Fig. 1: Estrogen Receptor Positivity — Strong Intensity 40X.**

Fig. 2: Progesterone Receptor Positivity - Strong Intensity 10X.
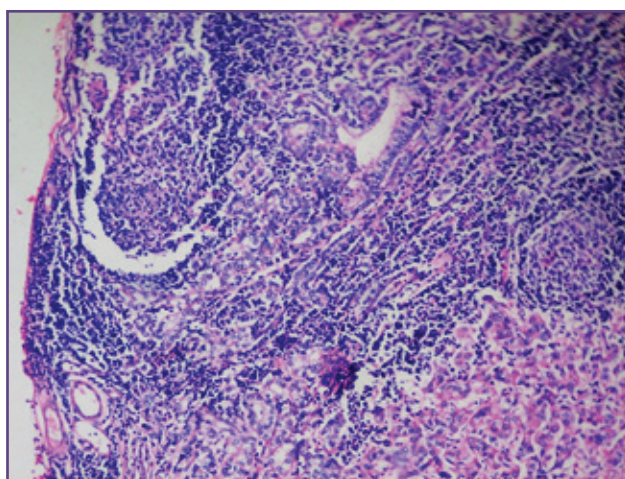

Fig. 3: Axillary Lymphnode Showing Metastasis From Infiltrating Duct Carcinoma Breast.

Christopher et al[6] have documented a prevalence of 76-78% of hormone receptor- positive breast cancers with a rise in the prevalence over the years.

Hormone receptor status in breast carcinomas : Hormone receptor status is an important prognostic factor in breast cancer. Estrogen receptor positivity in this study is 67% (Table 2) and progesterone receptor positivity is 62%. (Table 2) This is similar to the study by Pleason et al which showed that the estrogen receptors (ER) was positive in 63% of the cases, and the progesterone receptors (PR) in 64% of the cases.[7] A prevalence of 32.6% for ER- positive and 46.1% for PR- positive breast cancers has been documented in a study carried out in India by Desai et al.[8] A Jordanian study by Sughayer et al revealed 50.8% ER-positive tumors and 57.5% of PR- positive tumors in their study sample.[9]

In our study both ER & PR were positive (ER+PR+) were 61%, both receptors were negative (ER-PR-) were 32%, Only ER was positive in (ER+PR-) were 6%, only PR was positive (ER-PR+) in only 1% (Table 3). This was similar to the study by Sofi et al who studied 101 cases of which 67 (66.3%) cases were ER positive, 64 (63.4%) cases were PR positive. 61 (60.4%) cases were both ER and PR positive, 31 (30.7%) cases were both ER and PR negative, 6 (5.9%) cases were ER positive and PR negative and 3 (2.9%) cases were ER negative and PR positive. [10]

Our patients show much better receptor positivity as compared with studies done in rest of Asia (Fatima et al, 2005[11]; Kuraparthy et al 2007[12]; Mudduwa et al 2009[13]; Shet et al, 2009[14] where positivity for ER and PR ranges from as little as 28% to maximum of <60%. This difference may be due to genetic differences, however other factors like threshold for positivity, are responsible for atleast some of the difference. However studies in west (Dunnwald et al, 2007[15]; Kakarala et al, 2010[16] show ER positivity of more than 75% and PR positivity of more than 65% in caucasions and ER, PR positivity of 70% and 60% respectively. The prevalence of hormone receptor-positive breast cancer in Asian countries has been found to be lower than the western world where more than 50% tumors express hormone receptors. Christopher et al[17] have documented a prevalence of 76-78% of hormone receptor- positive breast cancers in the United States from 1992 to 1998 with a rise in the prevalence over the years.

Age distribution : In our study maximum number of cases were seen in the age group of 51-60 years with mean age 52.72 and standard deviation 10.056. 33% of the patients were in the age group 41-50, 36% of the patients were in the age group 51-60. (Table 2). This is in accordance with study by Christopher et al which showed an increase in incidence among 50 through 59 years old and no increase in the rates among women 60 years of age and above.[17] In this study, younger age group showed lower ER positivity while old and middle aged patients showed higher ER positivity. (Table 2) Similar was the finding with PR also with younger age group showing lower PR positivity. (Table 2) This is similar to the study by Paivi Jalava et al in which there was a slight positive correlation between the age of the patients and ER status whereas PR showed no correlation.[18]

Correlation of hormone receptor status positivity with other prognostic variables Tumor grade was considered as an important parameter in this study and calculated by Modified Bloom Richardson grading which takes into account nuclear pleomorphism, architectural differentiation and mitotic index. Each of the three variables was given a score ranging from 1 to 3 and the final grade was calculated by adding the scores of three variables. And it is graded as Grade1 (well differentiated)- scores 3 to 5, Grade 2 (intermediate)- scores 6 to 7, Grade 3 (poorly differentiated- scores 8 to 9).

Correlating the IHC results with the grade of the tumor we found that higher grade tumors showed more ER/PR negative status. Higher grade tumors showed more ER negative status 62.5% and PR negative status 56.2% respectively. In our study, majority were of grade 2 comprising 75%. Grade 3 and grade 1 constituted 16% and 9% respectively. This was similar to the study by Sofi et al[10] in which the majority of the cases presented as grade II (52.1%) and lymph node involvement was present in 65.2%. ER and PR were positive in 66.3% and 63.4% cases, respectively similar to our study increasing with rising age.

Nottingham Prognostic Index was calculated for all 100 patients. NPI was <5 in 68% of patients and more than 5 in 20%. NPI cases ranged between 2.4 and 9 with a mean of 4.464 and standard deviation 1.019. (Table 1) This is similar to study by Emad et al[19] in which The Nottingham Prognostic Index in these cases ranged from 2.3–7.6 (mean, 4.8). In our study, NPI did not show significant correlation with hormone receptor status.

In our study size of the tumor varies between 0.5 to 20 cm with a mean 3.653 and standard deviation of 2.516. Eight patients (Table 1) had a tumor size of < 2 cm, of which 50% were ER positive and 82 patients had size between 2 and 5 cm of which 70.7% were ER positive. Only 10 patients had size above 5 cm, among which 50% were ER positive. Eight cases had a tumor size of < 2 cm, of which 50% were PR positive and majority 82 cases had size between 2 and 5 cm of which 67.1% were PR positive. Only 7 cases were

above 5 cm, among which 30% were PR positive. This was statistically significant with a p value 0.035. This is similar to the study by Mudduwa which also showed majority of cases in the range between 2 and 5 cm.[13]

In our study 55% showed no axillary lymphnode involvement and 45% showed lymphnode involvement. Among the latter 30% of cases have less than 5 lymphnodes and 15% of cases had more than 5 lymphnodes. (Table 1) This is similar to study by Ann et al in which fifty- nine percent of patients were node- negative and 41% were node-positive.[20] In this study ER positivity showed significant correlation with lymph node metastasis. (p value: 0.013) Among the node positive cases, 82.2% were ER positive. Among less than 5 lymphnode involvement 83.3% showed positivity and above 5 lymphnode involvement 80% showed positivity (Table 3). Similarly among node positive cases, 73.3% were PR positive. Among less than 5 lymphnode involvement 76.7% showed positivity and 66.7% showed positivity among above 5 lymphnode involvement. (Table 3) PR positivity showed a borderline significance with lymph node metastasis (p value:0.087) This is similar to the study by Hussain et al in which hormone receptor status showed a significant positive correlation with lymphnode status with a p value of 0.004 and 0.022 respectively.[21]

In this study, distribution of the frequency of axillary nodal involvement in relation to tumor size was assessed– T1(< 2cm-50%); T2-(2-5cm-70.7%); T3(>5cm-50%) with a p value of 0.238 which was not significant. This was similar to Leonel et al[22] and Foulkes et al[23] which also showed no relation between size of the tumor and lymphnode involvement.

Conclusion

The findings in this study indicates that Estrogen and Progesterone receptor status is an important parameter in breast cancer. Estrogen receptor positivity in this study is 67% and progesterone receptor positivity is 62%. Maximum number of cases were obtained in the age group of 51-60 years. Hormone receptor positivity was found to be associated with increased lymphnode metastasis and lower grade tumors. Since there is a positive correlation with lymph node status and grade, Quick score can be considered as a reliable method for immunohistochemical evaluation.

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