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Original Article

Correlation of Various Clinico-Pathological Parameters with Estrogen Receptor and Progesterone Receptor Status in Malignant Breast Lesions

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Abstract

Breast carcinoma is emerging as the common most malignancy globally. In India, the rate of cervix cancer is decreasing while breast cancer is on the increase, especially in urban areas. Breast carcinoma continues to be a major health problem despite a decrease in mortality rate over the past 2 decades. The aim of this study is to determine if any correlation exists between estrogen receptor (ER) and progesterone receptor (PR) with respect to age, menopausal status, grade, tumor size and lymph node status in breast carcinoma. A total 50 cases of invasive duct cancers were included in this study. This study was on histopathology of excised specimens of 50 females with breast carcinoma operated by trained doctors. The hormone receptors were assessed immunohistochemically and compared with patient's age, menopausal status, grade, tumor size and lymph node status of tumor. Correlating the above factors with hormone receptor status, increase positivity of ER / PR in post menopausal age group (66.67%), small tumor size (83.33%), moderately differentiated tumors (76.67%) and negative lymph node status (56.67%) was found. Assessment of hormone receptors for clinical management of breast cancer patients is strongly advocated to provide prognostic information and better therapeutic options.

Keywords: Breast Carcinoma; Estrogen; Progesterone.

Introduction

Breast carcinoma continues to be a major health problem despite a decrease in mortality rate over the past two decades. There is difference in survival and mortality in breast carcinoma patients with similar clinicopathological features. This is because of difference in prognostic factors. Clinicopathologic variables like tumor size, histologic grade, nodal metastases, age may help in predicting the prognosis. Since mid 1990s the use of predictive molecular markers in breast cancer has revolutionized the approach for management and prognosis of breast carcinoma. Receptor status is now commonly established by an immunohistochemical (IHC) assay using monoclonal antibodies. These assays have the advantage of allowing only tumor cells to be assessed for receptor status. They can also be conducted relatively inexpensively on routinely processed tissue sections with no need for specialized equipment. Approximately 50 to70 per cent of breast cancer patients have been found to contain estrogen and progesterone receptor (ER and PR). Several studies have indicated that ER PR positive tumors have a better survival and favorable host-tumor relationship. The aim of this study is to determine if any correlation exists between estrogen receptor (ER) and progesterone receptor (PR) with patient's age, menopausal status, grade, tumor size and lymph node status in breast carcinoma.

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Methods

A total 50 cases have been included in this study. This study was conducted on histopathology of

excised specimens of 50 females with breast carcinoma in the department of pathology, who were operated by trained doctors in surgical department of Sriram Chandra Bhanja Medical College and Hospital (SCBMCH). Histopathological examination of 50 excised specimens was conducted by using conventional H&E stain. Immunohistochemical evaluation of ER & PR were undertaken on formalin fixed paraffin embedded tissue sections by using Novocastra's Ready to use mouse monoclonal antibody and Novolink polymer Detection system. The hormone receptors were assessed immunohistochemically and compared with prognostic parameters like patient's age, menopausal status, grade, tumor size and lymph node status of tumor. Cancers were graded according to Elston and Ellis' [8] modification of Bloom and Richardson's [5] original classification from 1957. Tumour typing was performed according to WHO [17]. Currently there is no single recommended system worldwide. A simple method known as 'Quick score' system (table 2) was described by Leake et al, [12] which takes into account the summation of the proportion of tumor cells showing the proportion of stained cells (0 = no nucleus stained, 1 = <1% nuclei stained, 2 = 1-10% nuclei stained, 3 = 11-33% nuclei stained, 4 = 34- 66% nuclei stained and 5 = 67-100% nuclei stained) and the intensity of staining (0 = no staining, 1 = weak staining, 2 = moderate staining and 3 = strong staining). Final score is obtained by adding scores from the 2 categories to give a maximum score of 8. Tumors with score < 2 are termed negative while those with score >2 are termed positive.

Differences in tissue processing and technical procedure may produce variable results. Hence, controls used are fresh autopsy / surgical specimens processed in same manner as patient's sample. The results of immunohistochemistry were noted down in tabular forms. The number of cases in each category was also expressed in the form of percentages. The Chi-square test was was used to find the correlation between these parameters and ER and PR expression.The result was considered statistically significant if p value was less than 0.05. The commercially available statistical software (PAST version 3.04 for Windows; Øyvind Hammer, Natural History Museum, University of Oslo) was used for data analysis. This study was conducted according to the Ethical Committee of SCBMCH and the institution took care of the entire financial burden for the completion of this prospective research study.

Results

Out of the 50 cases (Table 1) invasive ductal carcinoma (IDC NST) were 84% (42/50), ductal carcinoma in situ (DCIS) were 8% (4/50), invasive lobular carcinoma (ILC) were 2% (1/50), lobular carcinoma in situ (LCIS) were 2% (1/50) and mucinous carcinoma were 4% (2/50). Among the study group (Table 2 A), 50% belonged to 41-50 years age group, 16% belongs to <41 years age group, 17% belongs to >50 years of age group and mean age was found to be 48.52 years. 80% (40/50) of patients were of postmenopausal age group (Table 2 B) and rests 20% were premenopausal. 6 out of 50 (12%) patients were at T_1stage tumor size (Table 2 C), 36 out of 50 (72%) presented at T_2 stage, 8 out of 50(16%) patients were at T_3 stage and during study period there were no patients in T_4 stage. 8 out of 50 (16%) patients had grade I tumor (Table 2 D), 37 out of 50 (74%) patients had grade II and the rest 5 out of 50(10%) patients belonged to grade III. 20 out of 50 (40%) patients were without nodal involvement (Table 2 E), 26 out of 50 (52%) patients were presented at N_1 stage and the rest 4 out of 50 (8%) were at N_2 stage. There were no patients in N_3 stage during the study period.

Discussion

Breast carcinoma is a disease of tremendous heterogeneity in its clinical behavior. The present study was designed to evaluate the various prognostic factors of breast cancer. The prognostic factors which were taken into account were age, menopausal status, size of the tumor, histologic grading, lymphnode status, and expression of hormone receptors (ER and PR). Out of the 50 cases included in this study (Table 1), Invasive ductal carcinoma (IDC NST) was the largest group, accounting for 84% (42/50) of all the cases which is similar to the finding of Azizun et al. [2] who found the predominant morphology (85.3%) to be IDC. In the study group (Table 2 A) the common age group to be affected was 41-50 year and the mean age was found to be 48.52 years. Kamil et al, [11] found the commonest age group to be affected is 40-49 year whereas Azizun et al, [2] reported the mean age of the patient was 48.3yrs having breast carcinoma. Barnes et al, [3] in their study showed that age was not related to ER PR status. In our study (Table 2 A), among the total ER PR positive cases majority 50% (15/30) belonged to 41-50 years age group, similarly among ER PR negative patients majority 71.43% (5/7) were of 41-50 years of age

group. The data obtained in our study was statistically insignificant (p-value>0.05). So our study was consistent with Barnes et al, [3] and showed no significant relationship between ER PR status and age of the patients.

Regarding the menopausal status (Table 2 B), Hawkins et al, [10] were of view that ER+ve tumors were found in 61% of postmenopausal patients. Our study is consistent with the above study (Table 2 B) as 66.67% of ER+ve PR+ve patients were postmenopausal while only 33.33% of ER+ve PR+ve patients were premenopausal. This correlation between estrogen, progesterone receptors and menstrual status of the patients was found to be statistically significant (p-value<0.05). Regarding the size of the tumor at presentation (Table 2 C) in the study of Azizun et al, [2], most of the patients (53%) were at T_1 stage but Kamil et al, [11] found the average size of tumor to be 5.4cm (T_3 stage). Barnes et al, [3] revealed that ER+ ve tumors were smaller than ER-ve tumor, while Allegra et al, [1] found no correlation between steroid hormone receptor positivity and size of the tumor. In our study (Table 2 C) most of the tumor in ER+ ve PR+ ve group were at T_2 stage (83.33%) , 13.33% were at stage T_1 and only 3.33% ER PR+ve were at T_3 stage, whereas in ER–ve PR –ve group 85.71% were at stage T_2 and 14.29% were in stage T_3, while there was none in T_1 stage. The above results revealed that ER PR+ve tumor were of smaller size (p-value=0.01).

In the present study group (Table 2 D), 74% of the patients had grade II i.e. moderately differentiated tumor, 16% had grade I i.e. well differentiated tumor and the rest 10% of the patients belonged to grade III i.e., poorly differentiated tumor which is similar with finding of Azizun et al [2] who reported 55.3% tumors belonging to grade II (Table 2 D). Out of 30 ER PR +ve tumors 23 (76.67%) cases are moderately differentiated whereas 23.33% belong to grade I and there was none in grade III. In comparison to ER PR+ve tumors 42.86% ER PR-ve cases are poorely differentiated (grade III). Barnes et al. [3] in their study on relationship between hormone receptor status and ductal carcinoma in situ concluded that ER positivity decreases significantly for high grade tumor. Ratnatunga et al [14] noted that most of the low grade tumors are associated with hormone receptor positivity which is consistent with our finding (p-value=0.01).

In the nodal involvement (Table 2 E) Azizun et al, [2] found 71.3% patients with nodal metastasis. Allegra et al, [1] in their study showed that ER positive group patients had a high proportion of node negative patients. While Fatima et al, [9] found no significant correlation between ER PR status and lymph node metastasis. Our study is consistent with Allegra et al, [1] which showed that in contrast to ER PR-ve tumors higher percentage of ER PR+ ve tumors were without node involvement. Correlating the nodal status and hormone receptor (Table 2 E**),** it was found 56.67% patients of ER+ve PR+ve group were without any lymph node involvement whereas in ER-ve PR-ve group 71.43% and 28.57% of the patients had nodal involvement in the form of N_1 and N_2 respectively. There was no N_3 so not included in the table. The correlation of ER PR and lymph node status was statistically significant **(**p-vaue<0.05**)** which showed that in N_1 stage there was more ER PR –ve patients than that of stage N_2. Barnes et al, [3] in their study showed that 73% of ductal carcinoma were ER +ve ,61% were PR+ve, 60% ER PR+ve, 13% ER+ve PR-ve, 9% ER-ve PR+ve. The present study was consistent with Barnes et al, [3] Majority of the patients were ER PR+ve i.e. 60% (30/50), 18% (9/50) were ER-ve PR+ve, 14% (7/50) were ER-ve PR-ve and only 8% (4/50) were ER+ve PR-ve.

Table 1: Distribution of patients according to histologic types

Sl. No	Histological type		Number of cases (%)
1	Invasive ductal carcinoma (NST)	Without DCIS	42(84%)
2		With DCIS	4(8%)
3	Invasive lobular carcinoma	Without LCIS	1(2%)
4		With LCIS	1(2%)
5	Mucinous carcinoma		2(4%)
	TOTAL		50

Table 2: Correlation of various prognostic parameters with ER & PR expression in breast carcinoma (n=50)

Er/pr status / Prognostic parameters	Er+ve pr+ve no. (%)	Er+ve pr-ve no. (%)	Er-ve pr+ve no. (%)	Er-ve pr-ve no. (%)	Total no. (%)	*P* value
A. Age distribution (in years)						
<41	6 (20%)	0	2(22.22%)	0	8(16%)	p=0.64796 ≈0.65
41-50	15(50%)	2(50%)	3(33.33%)	5(71.43%)	25(50%)	
>50	9(30%)	2(50%)	4(44.44%)	2(28.57%)	17(34%)	
B. Menopausal status						
PRE MENOPAUSAL	10(33.33%)	0	0	0	10(20%)	p=0.039602 ≈0.04
POST MENOPAUSAL	20(66.67%)	4(100%)	9(100%)	7(100%)	40(80%)	
C. TUMOR SIZE						
T_1	4(13.33%)	1(25%)	1(11.11%)	0	6(12%)	p=0.012068 ≈0.01
T_2	25(83.33%)	2(50%)	3(33.33%)	6(85.71%)	36(72%)	
T_3	1(3.33%)	1(25%)	5(55.56%)	1(14.29%)	8(16%)	
D. Histopathological grade						
G_1	7(23.33%)	1(25%)	0	0	8(16)	p=0.013136 ≈0.01
G_2	23(76.67%)	2(50%)	8(88.89%)	4(57.14%)	37(74%)	
G_3	0	1(25%)	1(11.11%)	3(42.86%)	5(10%)	
E. Nodal involvement						
N_0	17(56.67%)	1(25%)	2(22.22%)	0	20(40	p=0.021929 ≈0.02
N_1	13(43.33%)	2(50%)	6(66.67%)	5(71.43%)	26(52%)	
N_2	0	1(25%)	1(11.11%)	2(28.57%)	4(8%)	
Total No. (%)	30(60%)	4(8%)	9(18%)	7(14%)	50	

Conclusion

The present study constitutes 50 patients, found infiltrating duct carcinoma (NOS) to be the predominant (84%) morphology. The mean age was calculated to be 48.52 years. Infiltrating ductal carcinoma, no special type (IDC – NST) was the commonest type of breast cancer seen in this study which matched with other similar studies. The most common age group affected was postmenopausal, i.e., above 45 years. The molecular markers ER, PR are the major driver for tumor cell proliferation and survival. Targeting these pathways therapeutically has remarkably improved the outlook of the patients. Steroid receptor assays in breast tumors represent the very first step of a general strategy to decipher the biological behavior of human breast cancer for clinical purposes. To this date, none of the other biological prognostic factors have gained general acceptance for clinical practice. Steroid receptor status still remains the only single biological parameter in use to suggest therapeutic directives for subgroups of breast cancer patients.

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References

1. Allegra JC, Lippman ME, Thompson EB and Simon R. An association between steroid hormone receptor and response to Cytotoxic chemotherapy in patients with metastatic breast cancer. Cancer Research 1978; 38: 4299-4.
2. Azizun N, Bhurgri Y, Raza F and Kayani N. Comparison of ER, PR and HER-2/neu (C-erb B 2) reactivity pattern with histologic grade, tumor size and lymph node status in breast cancer. Asian Pac J Cancer Prev2008; 9 (4): 553-6.
3. Barnes NLP, Boland GP, Davenport A, Knox WF and Bundred NJ. Relationship between hormone receptor status and tumor size, grade and comedo necrosis in ductal carcinoma in situ. Br J Surg 2005; 92: 429-34.
4. Bhagat VM, Jha BM and Patel PR. Correlation of Hormonal Receptor and Her-2/Neu Expression In Breast Cancer: A Study At Tertiary Care Hospital In South Gujarat. Natl J Med Res 2012; 2 (3): 295-8.
5. Bloom HJG and Richardson WW. Histological grading and prognosis in breast cancer. A study of 1409 cases of which 359 have been followed for 15 years. Br. J. Cancer1957; 11(3): 359-77.
6. Desai SB, Moonim MT, Gill AK, Punia RS, Naresh KN and Chinoy RF. Hormone receptor status of breast cancer in India: a study of 798 tumors. The Breast2000; 9 (5): 267-70.
7. Elston CW and Ellis IO. Pathological prognostic factors in breast cancer. The value of histological grade in breast cancer: experience from a large study with long-term follow-up. Histopathology 1991; 19:403-10.
8. Elston CW. The assessment of histological differentiation in breast cancer. Aust N Z J Surg 1984; 54(1): 11-5.
9. Fatima S, Faridi N and Gill S. Breast cancer: steroid receptors and other prognostic indicators. J Coll Physicians Surg Pak 2005; 15(4): 230-3.
10. Hawkins RA, Roberts MM and Forrest APM. Estrogen receptors and breast cancer. Current status. Br J Surg 1980; 67: 162-5.
11. Kamil M, Yusuf N, Khalid I, Islam R, Biswas M and Hashim H. Association between HER-2/neu over-expression and clinico-pathologic parameters of breast cancer in northern Malaysia. Ceylon Med J 2010; 55 (1): 9-13.
12. Leake R, Barnes D, Pinder S, Ellis I, Anderson L, Anderson T, Adamson R, Rhodes T, Miller K and Walker R. Immunohistochemical detection of steroid receptors in breast cancer: a working protocol. J Clin Pathol 2000; 53: 634-5.
13. Pourzand A, Fakhree MBA, Hashemzadeh S, Halimi and Daryani A: Hormone Receptor Status in Breast Cancer and its Relation to Age and Other Prognostic Factors. Breast Cancer: Basic and Clin Res. 2011; 5 87–92.
14. Ratnatunga N and Liyanapathirana LVC. Hormone receptor expression and Her/2neu amplification in breast carcinoma in a cohort of Sri Lankans. Ceylon Med J 2007; 52 (4), 133-6.
15. Schmitt FC, Andrade LM and De Lucca LA. Detection of estrogen receptor in formalin fixed and paraffin embedded breast carcinoma: correlation with histologic patterns. Rev Paul Med 1992; 110: 158-62.
16. Sofi GN, Sofi JN, Nadeem R, Shiekh RY, Khan FA, Sofi AA, Bhat HA and Bhat RA. Estrogen Receptor and Progesterone Receptor Status in Breast Cancer in Relation to Age, Histological Grade, Size of Lesion and Lymph Node Involvement. Asian Pacific J Cancer Prev 2012; 13(10): 5047-52.
17. World Health Organization, Histologic Typing of Breast Tumors, 2nd edn. vol. 2, Geneva, Switzerland: WHO; 1981.