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Original Article

ESTROGEN AND PROGESTERONE RECEPTOR STATUS IN BREAST CANCER- ITS RELATION TO AGE, AXILLARY LYMPH NODE STATUS, TUMOUR'S MAXIMUM DIMENSION AND GRADE OF TUMOUR

Md. Hasanuzzaman [1], Md. Mizanur Rahman[2], Md. Johirul Islam[3], Md. Ashraf-Ul Haque[4], Md. Setabur Rahman[5], Md. Mafizur Rahman[6]

Abstract

Background: Carcinoma of the breast is one of the most common malignancies of women in our country. The current study was conducted with the objective of assessing Oestrogen receptor (ER) and progesterone receptor (PR) status of carcinoma breast for correlation with age of the patient, tumor dimension, axillary lymph node metastasis and histologic grade.

Methodology: One hundred and nineteen female breast cancer patients operated at the surgical oncology department of National Institute of Cancer Research & Hospital were selected by non-probability sampling method and operated specimens were sent for immunohistochemical study of the Oestrogen receptor and progesterone receptors. Statistical analysis was conducted using SPSS version 12 for Windows software. P-value 0.05 or less was considered as significant.

Result: Mean age of the patients was 41.64 years (95 % CI 39.8, 43.5). About 87% of the ER+ and PR+ patients had tumour dimension < 5 cm. The predominant morphology was infiltrating duct cell carcinoma. Out of 66 ER+ cases 63 were the patients of Infiltrating duct cell carcinoma and in 63 PR+ cases 60 were the patients of same histological type. The majority of the cases presented as grade II (59.1%) followed by grade III (33.9%). Sixty percent patients had axillary lymph node metastasis. Majority of the patients (51.3%) expressed both the receptors in their breast tissue while around 43% of the patients did not show any receptor.

Conclusion: ER and PR expression in breast cancers in the current study was found to be comparable to published national and international data. Assessment of prognostic markers for the clinical management of breast cancer patients is strongly advocated to provide best therapeutic options.

Key words: Breast cancer, Oestrogen and progesterone receptor status, Axillary lymph node status, Type & grade of breast cancer.

1. Surgical Oncology Department, National Institute of Cancer Research & Hospital (NICRH)
2. Surgical Oncology Department, National Institute of Cancer Research & Hospital (NICRH)
3. Cancer Epidemiology Department, National Institute of Cancer Research & Hospital (NICRH)
4. Department of Surgery, Kushtia Medical College, Kushtia
5. Surgical Oncology Department, National Institute of Cancer Research & Hospital (NICRH)
6. Radiation Oncology Department, National Institute of Cancer Research & Hospital (NICRH)

Correspondence to: Dr. Md. Hasanuzzaman, Surgical Oncology Department, National Institute of Cancer Research & Hospital (NICRH)

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Introduction

Breast cancer is a type of cancer originating from breast tissue, most commonly from the inner lining of milk ducts or the lobules that supply the ducts with milk. Breast cancer is a disease of humans and other mammals; while the overwhelming majority of cases in humans are women, men can sometimes also develop breast cancer[1]. Breast cancer is by far the most frequent cancer among women with an estimated 1.38 million new cancer cases diagnosed in 2008 (23% of all cancers), and ranks second overall (10.9% of all cancers). It is now the most common cancer

both in developed and developing regions with around 690 000 new cases estimated in each region[2].

The primary risk factors for breast cancer are female sex, age, lack of childbearing or breastfeeding, higher hormone levels, race and economic status[3,4]. The genes associated with hereditary breast-ovarian cancer syndromes usually increase the risk slightly or moderately; the exception is women and men who are carriers of BRCA mutations. These people have a very high lifetime risk for breast and ovarian cancer, depending on the portion of the proteins where the mutation occurs. Instead of a 12 percent lifetime risk of breast cancer, women with one of these genes have 60 percent risk on an average [5].

In more recent years, research has indicated the impact of diet and other behaviors on breast cancer. These additional risk factors include a high-fat diet, alcohol intake, obesity, and environmental factors such as tobacco use, radiation, endocrine disruptors and shiftwork[6]. Estrogen and progesterone receptors (ER, PR) with increasing importance influenced the management of the malignancy[7]. With an established positive correlation of ER and PR with the degree of tumor differentiation, determination of ER and PR status on biopsy specimens prior to therapeutic intervention is advocated as standard practice [8].

The presence of hormone receptors (ER and PR) in the tumor tissue correlates well with the response to hormone therapy[9]. Tumors that are better differentiated are more likely to be ER and PR positive and have a relatively better prognosis[10-11]. PR is a surrogate marker of a functional ER and as valuable in predicting the behavior of breast carcinoma. It is expressed in 60-70% invasive breast carcinomas with a higher positivity in older age and postmenopausal women. Loss of PR by tumor cells is associated with a worse prognosis [12]. Patients with larger tumors, poorly differentiated morphology, increased number of axillary lymph node metastases and higher stage tumors have more chance of an ER and PR negative status [13]. With the dramatic improvement in our understanding of steroid hormone receptor and prognosis of the patient, determination of estrogen and progesterone receptor status has become a standard practice in the treatment of breast cancer.

Materials and Methods

This cross-sectional observation study was carried out in the department of Surgical Oncology of NICRH from January 2009 to October 2010. The study was approved by the Ethical Review Committee of NICRH and informed consent was taken from each patient before their enrollment in the study. One hundred and nineteen newly diagnosed female breast cancer patients were enrolled in the study. Sampling was convenient and purposive. The specimen or block of tissue was sent for immunohistochemical examination to specialized diagnostic centers.

Results

Statistical analysis was conducted using SPSS version 12 for Windows software. Continuous data were expressed in mean±SD. Parametric data were evaluated by independent sample "t" test & categorical data were evaluated by Chi-squre ($\div^2$) test as needed. Level of significance for all analytical tests was set as 0.05 & p=d"0.05 was considered significant. Majority of the patients (61, 51.3%) expressed both the receptors in their breast tissue while 51 (42.9%) patients were both receptors negative. Only a handful number of patients had ER +ve but PR –ve (4.2%) or vice versa (1.7%) receptor expression. Most patients (85.7%) were pre-menopausal (< 50 year), the median age was 60 years. Patients of 50 years or less expressed ER and PR almost identically (52 and 51% respectively). Older patients expressed more ER marker than PR (76.5 and 64.7% respectively). These differences, however, were not statistically significant (Table 1). Table 1 also showed distribution of patients by tumour dimension and receptors status. It was found that 52 (78.8%) of the ER + patients had tumour dimension equal or less than 5 cm while 14 (21.2%) of the ER + patients had tumour dimension more than 5 cm. Fifty (79.4%) PR + patients had tumour dimension equal or less than 5 cm and 13 (20.6%) ER + patients had tumour dimension more than 5 cm. From table 1 it is evident that patients (35, 29.4%) without lymph node metastasis express more Estrogen Receptor than patients with axillary lymph node metastasis (31, 26.1%). This difference is statistically significant ($\div^2$= 9.922 (df=1); p <0.01). Most of the patients had grade II (68, 59.1%) tumours followed by grade III (39, 33.9%). Only 8 (7%) patients had grade I tumours. Initially, ER and PR reactivity increased with increasing tumour grade, i.e. from grade I to grade II but decreased thereafter, from grade II to grade III (Table 1). Table 2 showed distribution of the patients by PR, ER scores and age group. It was found that PR expression increased with increasing age. Patients of 36-50 years age group expressed more of the receptors. Like PR expression, ER expression also increased with increasing age. Patients of 36-50 years age group expressed more of the receptors as well.

Table -I

Correlation of receptor status with age, lymph node metastasis and grade of the tumour

Status	Variables		p-value
	Age		
Marker	≤ 50 yrs old	> 50 yrs	
	n (%)	n (%)	
ER+	53 (52.0)	13 (76.5)	0.60
PR+	52 (51.0)	11 (64.7)	0.294
	Tumour dimension		
	≤ 5 cm	> 5 cm	
ER +	39 (86.7)	6 (13.3)	.077
PR +	38 (86.4)	6 (13.6)	.101
	Estrogen Receptor		
Lymph Node	Positive	Negative	
Metastasis	31 (26.1)	40 (33.6)	0.002*
No metastasis	35 (29.4)	13 (10.9)	
Grade	**n (%)**	**ER+, PR+**	
I	8 (7.0)	5, 5	
II	68 (59.1)	36, 36	
III	39 (33.9)	22, 19	

*significant

Table-II

Distribution of the patients by PR score, ER score and age group

Age group	Score 0		Score 2-3		Score 4-6		Score =7	
	PR Score	ER Score	PR Score	ER Score	PR Score	ER Score	PR Score	ER Score
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
=35	18 (32.1)	18 (34.0)	2 (13.3)	6 (22.2)	17 (44.7)	9 (34.6)	1 (10.0)	5 (38.5)
36-50	32 (57.2)	31 (58.5)	9 (60.0)	15 (55.6)	18 (47.4)	13 (50.0)	5 (50.0)	5 (38.5)
>50	6 (10.7)	4 (7.5)	4 (26.7)	6 (22.2)	3 (7.9)	4 (15.4)	4 (40.0)	3 (23.0)
Total	56 (100.0)	53 (100.0)	15 (100.0)	27 (100.0)	38 (100.0)	26 (100.0)	10 (100.0)	13 (100.0)

Discussion

This is an immunohistochemical analysis of Estrogen and Progesteron receptor status in 119 breast cancer patients which showed that majority of the patients (61, 51.3%) expressed both the receptors in their breast tissue while 51(43%) patients were both receptors negative. Mostafa MG et al. reported 69% ER positive, 72.3% PR positive in a study of 1042 study subjects in Bangladesh[14]. In the present study the expression of ER & PR was almost identical in the patients aged 50 years or less. However, older patients expressed more ER marker than PR. This finding matched with the finding of Mostafa GM et al[14]. Azizun Nissa et al. also reported that ER positivity increased with rising age[15]. In his study Desai SB et al.[16] and Nerukar A Y [17] also came to this inference that ER & PR status showed a higher incidence of reactivity with advancing age. We found that about

87% both ER & PR positive patients had tumor dimension 5 cm or less. Azizun Nissa et al. stratified tumor dimension into 3 groups[15]. She found that small tumor expressed more ER & PR receptor than larger one. However, Desai SB et al. did not find such correlation in their study[16]. Dunnwald LK et al. found tumor dimension to modify the relationship between ER & PR status and relative risk of mortalities[18]. He reported that this risk of mortalities is particularly high among women whose tumor were more than 5 cm in dimension. From our study it is evident that initially ER & PR reactivity increased with increasing tumor grade but decrease thereafter. Only 7% patients had grade I tumor but 59% patients present with grade II tumor and about 34% patients had grade III tumor. Out of 66 ER+ cases 63 were the patients of Infiltrating duct cell carcinoma and in 63 PR+ cases 60 were the patients of the same histological type. This result is supported well by the study of Mostafa MG et al.[14]. He reported that higher histological tumor grade was associated with lower hormonal receptor status and he concluded that higher histological grade is a poor predictor of hormone receptor status. Azizun Nissa et al. also showed in her study that both ER & PR positivity decreased with increasing grade [15]. She reported 70% ER positivity in grade I, 48% in grade II and only 3.5% in grade III. This finding was statistically significant ($p<0.001$). Desia SB et al. in their study found that ER & PR reactivity decreased with increasing tumor grade [16]. We examined the ER & PR status and axillary Lymph Node (LN) metastasis. We found patients without LN metastasis expressed more ER & PR than with LN metastasis. This difference is statistically significant. These findings contradict the finding of Mostafa GM et al[14]. He rather observed that cases with nodal metastasis were more frequently hormonal receptor positive. Our sample size was very small as compared with his study. This could be the cause of such different finding. On the other hand the findings of Desia SB et al. failed to find any correlation with ER & PR status and LN metastasis [16]. Balleine et al. also confirmed similar findings of no association[19]. In published literature, approximately 50% of tumours are ER+ PR+, 25% ER- PR-, 20% ER+ PR- and 5% ER- PR+ [20]. Present study has showed a high proportion of both receptor positive and negative cases (51% and 43% respectively). In 1992 Redkar et al. have reported a higher incidence of steroid receptor non–reactivity in breast cancer patients in India[21]. This can be partially explained by the younger age of patients and higher grade of tumours in their practice. This particular observation is also true for our country. Mostafa GM et al. in his study found that younger patients are more likely to have higher grade tumors and higher grade is a poor predictor of hormone receptor status [14]. Young patients have high levels of circulating estrogens and a correspondingly low expression of steroid receptors which is reûected in their tumours. There appears to be a variation in steroid receptor positivity in the Asian population. Chariyalertsak and colleagues reported lower rates of (36.1%) ER and (45.8%) PR reactivity in breast cancer cases in Thailand [22]. In contrast, a Chinese study recorded 73.5% and 65.5% of ER and PR reactivity in their analysis of 200 breast cancers [23]. Most of pre-menopausal patients expressed both the receptors identically but older patients expressed more ER. Patients without axillary lymph node metastasis expressed more ER and PR than patients with lymph node metastasis. Most of the patients had grade II tumours followed by grade III. Initially, ER and PR reactivity increased with increasing tumour grade, i.e. from grade I to grade II but decreased thereafter, from grade II to grade III. The present study showed reactivity of steroid receptors more on moderately differentiated tumours.

In conclusion, it can be said that ER and PR expression increases with increasing age and decreases with increased tumour dimension, increased grade and axillary lymph node metastasis. The use of these receptors markers should be made popular amongst the experts who specially deal with carcinoma breast as these facilities are provided in some specialized centres of Bangladesh at reasonable cost.

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