



STUDY OF PATTERNS OF HORMONAL RECEPTORS (ER, PR AND HER-2) IN CARCINOMA BREAST

Obstetrics and Gynaecology

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ABSTRACT

Introduction- Expression of oestrogen receptors (ER) and progesterone receptors (PR) is a very powerful and useful predictor in breast cancer.

Material and methods- Retrospective observational study was carried out to find out the pattern of Oestrogen, Progesterone and HER-2 receptors in women with carcinoma breast and to co-relate ER, PR and HER-2 receptor pattern in breast cancer with histological type and tumour size.

Results- Out of total 115 cases of breast carcinoma, 35 % were negative for all three receptors (ER, PR, HER 2), 24% were positive for ER and PR receptors, 17% were positive only for HER 2 receptor, 13 % were positive only for ER and 9.56% cases were positive for all three receptors.

Conclusion- Triple negative tumours were common in the present study indicating unsatisfactory response to either chemotherapy or radiotherapy. Co relationship between hormonal receptors status and grade and size of tumour could be established.

KEYWORDS

Cancer Breast, Estrogen Receptors, Progesteron Receptors, Her 2 Receptor

INTRODUCTION

Breast cancer is the commonest cancer among urban Indian women and the second commonest in the rural women, accounting for 25% of all cancer cases.^{1,2} Expression of oestrogen receptors (ER) and progesterone receptors (PR) is a very powerful and useful predictor in the management of breast cancer. Assessment of receptor expression profile allows clinicians to predict breast cancer response to hormonal treatment^{3,4}. The higher the content of ER and PR in breast cancer, the greater the likelihood of response to hormonal therapy^{5,6}. In patients with advanced breast cancer, in those classified as ER(-)/PR(-) the response rate to hormonal treatment is 10%, in the group of ER(-)/PR(+) patients it is 32%, in patients with ER(+)/PR(-) it is 40%, and in patients with ER(+)/PR(+) it is 73%³.

Lobular and tubular cancers are characterized by presence of a high incidence of oestrogen and progesterone receptors. In these types of cancers, receptors are present in a greater percentage of cases than in other carcinomas^{7,8}. Many researchers have documented that the ER and PR expression is in inverse relation to the size of the primary tumor^{7,9}. Expression of oestrogen receptors is also associated with age and menopausal status. It is frequently detected in breast cancers in postmenopausal women than in premenopausal women and more frequently in older women than younger ones. HER2 (human epidermal growth factor) is a protein that can affect the growth of some cancer cells. It is found on the surface of normal breast cells. Some breast cancer cells have a very high number of HER2 receptors. Among every 100 women with breast cancer 15–25% are HER 2 positive cancers which tend to grow more quickly than HER 2 negative breast cancers.⁹

MATERIAL AND METHODS-

Present study was a retrospective record based observational study, carried out at department of Radiation oncology attached to tertiary care hospital in rural area. Study objectives were to find out the pattern of Oestrogen, Progesterone and HER-2 receptors in women with carcinoma breast and to co-relate ER, PR and HER-2 receptor pattern in breast cancer with histological type, tumor size. In the present study, 115 diagnosed cases of carcinoma breast, who were investigated and treated during one year period (January 2016 - December 2016), at hospital were included for analysis. Diagnosis confirmation by histopathology of breast tissue and IHC receptor analysis for oestrogen, Progesterone and HER-2 were considered as inclusion criteria. Cases with non availability of Histopathology report and IHC for ER, PR, HER-2 receptor report were excluded from the study. Institutional ethics committee approval was taken before start of the study. Record based data in relation to the age, marital status, parity, histo-pathological type, histological grading, staging and presence or absence of oestrogen, progesterone and HER-2 receptors in the tumor tissue was collected, compiled and tabulated. Statistical analysis was done using Z test and Chi-Square test.

RESULTS-

It was observed that maximum number of cases (42.62 %) of breast cancer belonged to age group of 40-49 years. Maximum number of cases (96.50 %) of breast cancer were multi-para. Majority of the women (96%) of cancer breast were married. 58% cases of cancer breast were in advanced stage (Stage III and IV) at the time of diagnosis. Maximum number of cases (53.04%) of cancer breast had tumor size of T2. Only 20% cases displayed with T1 tumor size. Maximum cases of breast cancer were tumor was in grade II & III category. Highest number of cases (95%) were of infiltrating ductal carcinoma of breast.

Highest number of cases had grade II tumor (44.32%), followed by grade III tumor (28.86%). Highest number of cases had stage II tumor (30.92%), followed by stage III tumor (28.86%). Overall, 16.49% cases had stage II and grade II tumor.

In the present study, Out of total 115 cases of breast carcinoma, 35 % were negative for all three receptors (ER, PR, HER 2), 24% were positive for ER and PR receptors, 17% were positive only for HER 2 receptor, 13 % were positive only for ER and 9.56% cases were triple positive. (Table 1) Out of 109 cases of infiltrating duct carcinoma, 38 (35%) were triple receptor negative, 25 (23%) were positive for ER and PR and 19 (17%) were negative for ER and PR, 11 (10%) were triple receptor positive. Out of 2 cases of medullary carcinoma, 1 was triple receptor negative and another was ER and PR negative but HER positive. (Table 2). Out of 115 cases of cancer breast, 61 (53%) cases had tumour size of 2-5 cms (T2). Among cases of T2, 38% were triple receptor negative and only 7 percent were triple receptor positive. (Table 3)

DISCUSSION-

Breast cancer is the commonest cancer in women. Owing to the lack of awareness of this disease and in absence of a breast cancer screening program, the majority of breast cancers are diagnosed at a relatively advanced stage. In a study from New Delhi¹⁰, the histo-morphological types seen in breast cancer patients indicates that invasive ductal carcinoma not otherwise specified was found to be the most common type (88%) followed by infiltrating lobular carcinoma (3.7%), colloid carcinoma (1.1%), ductal carcinoma in situ (1.1%), and metaplastic types (0.9%). At SGPGIMS Lucknow too, IDC is the commonest variety, with very few non-invasive cancers. In the present study, the commonest morphological type was infiltrating ductal carcinoma (94.78%). Medullary carcinoma of breast was seen in 1.76% cases. The percentage of cases with mucinous, papillary, invasive adenocarcinoma, infiltrating lobular carcinoma was 0.86% each. The morphological type of cancer breast observed in the present study co relate with the observations of other studies.

The average breast tumor size in most centers is well over 5 cm, with

almost 2/3 of these being grade III or II. At a major cancer centre in the city of Mumbai, 70% patients were reported as having grade III disease¹¹. A high proportion of patients were reported to have a high S-phase fraction, aneuploidy and other bad prognostic features on histology. At SGPGI Lucknow, the average tumor size has been 5.4 cm. The Indian cancer registries too provide similar figures. In the present study 20% cases had tumor size of less than 2 cms. Tumor size of 2-5cms was observed in 53% cases. Two third of the cases had tumor size above 2cms. The presentation seems similar in many other developing countries¹².

In the present study, 44% cases had grade II tumor and 68% cases had grade II plus III tumor. Similar observations were reported from other Indian studies.¹⁰⁻¹² Late detection of cancer breast was seen in the present study. Only 9% cases were detected in stage I whereas 32%, 31% and 28% cases were detected in stage II, III and IV respectively. Similar observations were reported in other studies.¹⁰⁻¹² Illiteracy, fear of cancer detection, poor awareness, socio cultural norms, lack of screening facilities, high cost of treatment are some of the contributory factors in late detection of cancer breast cases.

Oestrogen (ER) and progesterone receptors (PR) are found positive in only 20–45% of Indian patients. ER-positive rates were reported to be lower in Indian patients than those in western countries. Not all patients in India undergo hormonal receptor testing as evident from the study in Delhi which showed only 35.5% of patients had receptor testing¹³. At SGPGIMS, over the last decade, only about 45% patients have been found ER- and/or PR-positive (ER+/PR+). At TMH Mumbai, the ER+ status was found in 33%, and PR+ in 46% of patients¹⁴. According to some, the low ER+ and PR+ status in Indian patients may actually be due to improper immune-staining techniques used. A study from a major hospital in Mumbai reported that the ER-/PR+ reported on IHC were actually due to suboptimal manual assays, and when the same tumors were evaluated using well standardized international kits, they were found ER+/PR+¹⁵. HER2/neu or c-erb-B2 status – another clinically useful variable – is found positive in about 20% of Indian patients (SGPGIMS Lucknow).

In the present study, all cases of cancer breast with receptor status assessment, were enrolled in the study. As majority of cases reported in late stages, they were dependant on either chemotherapy or hormonal therapy. In the present study, 34.78% cases were triple negative and 9.56% cases were triple positive. The high rate of negative receptor status is likely to be responsible for poor prognosis following treatment in Indian population. Thirty eight cases out of forty cases of infiltrating cancer breast were triple negative. Similar receptor status was reported in other studies¹³⁻¹⁴. It was observed that 53.04% cases of cancer breast had tumor size of 2-5cms and 20% of these tumors were triple receptor negative. Highest number of cases of breast cancer with tumor size of T2, were triple negative for receptors.

In the present study, the highest number of cases had grade II tumor (44.32%), followed by grade III tumor (28.86%). Highest number of cases had stage II tumor (30.92%), followed by stage III tumor (28.86%) 16.49% cases had stage II and grade II tumor. It was observed that tumor grading was increasing with advanced tumor stage. Similar findings were reported by other research workers.¹³⁻¹⁵

Conclusion-

Expression of oestrogen receptors (ER) and progesterone receptors (PR) is a very powerful and useful predictor in breast cancer. Assessment of receptor expression profile allows clinicians to predict breast cancer response to hormonal treatment. The higher the content of ER and PR in breast cancer, the greater the likelihood of response to hormonal therapy. Infiltrating duct carcinoma continues to be the commonest morphological cancer. The advanced disease state needs either chemotherapy or hormonal therapy for prolonging life and improving the five year survival. Thorough evaluation of each case before planning the treatment is essential. Assessment of oestrogen, progesterone and HER 2 status help in treatment planning and prognostication of response to hormonal therapy. Triple negative tumors were common in the present study indicating unsatisfactory response to either chemotherapy or radiotherapy. Co relationship between hormonal receptors status and grade of tumor, size of tumor and morphological tumor could be established in the study.

Table-1 Distribution Of Cases As Per Of Receptor Status

SR.NO	RECEPTOR STATUS	NO (%)
1	ER -, PR -, HER 2 -	40(34.78)
2	ER +, PR +, HER 2 -	28(24.34)
3	ER -, PR -, HER 2 +	20(17.39)
4	ER +, PR -, HER 2 -	15(13.04)
5	ER +, PR +, HER 2 +	11(09.56)
6	ER -, PR +, HER 2 +	01(0.86)
7	ER +, PR -, HER 2 +	0(0.00)
8	ER -, PR +, HER 2 -	0(0.00)

Table-2 Co-relationship Of Receptor Status With Histological Type Of Cancer Breast

SR NO	RECEPTOR PATTERN	HISTOLOGICAL TYPE OF BREAST CANCER						TOTAL (%)N=115
		IDC	MC	IAC	PC	MC	ILC	
1	ER -, PR -, HER 2 -	38	01	01	-	-	-	40(34.78)
2	ER +, PR +, HER 2 -	25	-	-	01	01	01	28(24.34)
3	ER -, PR -, HER 2 +	19	01	-	-	-	-	20(17.39)
4	ER +, PR -, HER 2 -	15	-	-	-	-	-	15(13.04)
5	ER +, PR +, HER 2 +	11	-	-	-	-	-	11(09.56)
6	ER -, PR +, HER 2 +	01	-	-	-	-	-	01(0.86)
7	ER +, PR -, HER 2 +	0	-	-	-	-	-	0(0.00)
8	ER -, PR +, HER 2 -	0	-	-	-	-	-	0(0.00)

Table-3 Co-relationship Of Receptor Status With Size Of The Tumour

SR. NO	RECEPTOR PATTERN	TUMOUR SIZE				TOTAL (%)
		T1	T2	T3	T4	
1	ER -, PR -, HER 2 -	10	23	06	01	40(34.78)
2	ER +, PR +, HER 2 -	05	16	07	00	28(24.34)
3	ER -, PR -, HER 2 +	01	10	08	01	20(17.39)
4	ER +, PR -, HER 2 -	05	08	0	02	15(13.04)
5	ER +, PR +, HER 2 +	02	04	03	02	11(09.56)
6	ER -, PR +, HER 2 +	0	0	1	0	01(0.86)
7	ER +, PR -, HER 2 +	0	0	0	0	00(0.00)
8	ER -, PR +, HER 2 -	0	0	0	0	00(0.00)

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