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To study the estrogen (ER) and progesterone (PR) receptor in case of primary and metastatic breast cancer

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***Abstract*---**Background: Worldwide, breast cancer is the most common invasive cancer in women. It comprises 22.9% of invasive cancers in women[1] and 16% of all female cancers[2]. It accounts for 15% of cancer deaths worldwide. Objective: to study the expression of ER/PR on breast cancer by immunocytochemistry on fine needle aspiration smears. Material and Methods: A prospective study was carried out on 120 cases of breast lump, referred from various clinical Departments to cytopathology lab of a tertiary care center in North India, during September 2018 to March 2020. Two sets of Fine Needle Aspirate smears were obtained from breast lump and palpable lymph node, if present. Both sets of smear were air dried and fixed in propyl alcohol for 1-2 hours. First set of smear was used for cytology, in which cytology was positive, the second set of smear were packed in aluminum foil and preserved at -20 degree Celsius. Slides were then stained for ER and PR receptor. Later on when patient undergone surgery findings were correlated with histopathology. Results : The most common symptom was breast lump (87.5%) with tumour size of 2.0-5.0 cm. ER were positive in 65.0% cases, PR were positive in 57.5% and ER+/PR+ in 55.0% of cases.. Most of the cases showed moderate staining. Conclusion: ER and PR status correlates well with histopathological grading and other clinico-cytopathological

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parameters. Tumor diagnosis, grading and prognosis by evaluation of ER and PR status on FNAC material in breast carcinoma are simple, quick and reliable method. Hence, immunocytochemical assessment of ER and PR status should be incorporated as a routine investigation

***Keywords*---**estrogen receptor, progesterone receptor, immunocytochemistry, breast carcinoma.

Introduction

In 2020, breast cancer caused 685,000 deaths worldwide [1] The number of cases worldwide has significantly increased since the 1970s, a phenomenon partly attributed to the modern lifestyles.[3,4] The incidence of breast cancer varies greatly around the world, lower in developing countries and greater in the developed countries. Breast cancer cells have receptors on their surface and in their cytoplasm. Breast cancer cells may or may not have three important receptors, ER, PR and HER2/neu. ER positive cancer cells depend on estrogen for their growth, so they can be treated with drugs to block estrogen effects (e.g. tamoxifen), and generally have a better prognosis. HER2/neu positive breast cancer had a worse prognosis. Cells with none of these receptors are called basal-like or triple negative cancer.

The presence of estrogen and progesterone receptors in the cancer cell is important in guiding treatment. Those who are negative for these specific receptors will not be able to respond to hormone therapy, and this can affect their chance of survival depending upon what treatment options remain, the exact type of the cancer, and how advanced the disease is. Therefore, it is proposed to see the expression of ER/PR on breast cancer by immunocytochemistry on fine needle aspiration smears.

Material and Methods

A cross-sectional study was carried out in the department of pathology at a tertiary care centre in north India, between September 2018 to March 2020. Specimen in the form of Fine Needle Aspirate smears were obtained from patients of breast carcinoma referred to cytopathology lab from Department of Surgery. Study population: female patients, diagnosed with breast carcinoma based on fine needle aspiration cytology, irrespective of their age, caste, religion, educational and socioeconomic status were included in the study. Female patients, those were diagnosed with benign breast diseases or denied to participate in this study were excluded from the study. Sample size: sample size was calculated considering the study 120

Patients those referred from various departments for breast lump, nipple discharge and skin dimpling and those were referred to the tertiary care from primary health center, community health center, private labs and private clinics for second opinion were subjected for FNAC. Four slides were prepared, out of which two slides were used for cytology to confirm and rule out the malignancy, and two slides were air dried, fixed in propyle alcohol for 1-2 hours, packed in

aluminium foil and preserved at – 20 degree Celsius. These preserved slides were used for study of ER/PR status.

Statistical analysis

The data was collected using a pre-formed paper sheet, entered in the MS Excel sheet and cleared. Categorical data was presented in the form of percentages and continuous data was presented in the form of means and standard deviation. Analysis of the data, binominal proportional and Chi square analysis were employed to determine the significant correlation of positive rate in hormone receptors of primary and metastatic sites. P-value less than 0.05 was regarded as a significant difference. SPSS-25 software was used for statistical analysis.

Results

Among the 120 participants, mean age was 50.58 ± 9.02. Most of the patients (45%) were in age group between 41 to 50 years while only 3 patients in the age group between 71 to 80 years. Table 1

Table 1: Age distribution of patients studied

Age (in years)	Number of patients	%
31-40	12	10.0
41-50	54	45.0
51-60	36	30.0
61-70	30	12.5
71-80	3	2.5
Total	120	100.0

Breast lump was the commonest symptom in 105 cases (87.5%), followed by breast lump with pain in 9 cases (7.5%) and skin involvement in 6 cases (5%). In most of the patients, size of the lump was between 2.0 to 5.0 cm. Table: 2

Table: 2 – distribution of patients according to the size of breast lump

Size (cm)	Number of patients	%
<2.0 square cm	6	5.0
2.0-5.0 square cm	105	87.5
>5.0 square cm	9	7.5
Total	120	100

Immunocytochemistry was reactive in 65% cases for estrogen receptor and in 57.5 % for progesterone receptor. (Table: 3) In our study 8 cases (20%) had nodal metastasis, 10 cases (25%) had reactive lymphadenitis

Table 3: Distribution according to reactivity and Intensity of ER and PR staining

Intensity	Estrogen receptor		Progesterone receptor	
Staining	No. of patients	%	No. of patients	%

	(n=120)		(n=120)	
Negative	42	35.0	51	42.5
Positive	78	65.0	69	57.5
• Mild	12	10.0	6	5.0
• Moderate	63	52.5	60	50.0
• Severe	03	2.5	3	2.5

Of 120 cases, 66 (55%) were ER+/PR+, 4(10%) were ER+/PR- (Table: 4)

Table 4: ER/PR

ER/PR	No. of patients (n=40)	%
ER+/PR+	66	55.0
ER+/PR-	12	10.0
ER-/PR+	03	2.5
ER-/PR-	39	32.5

Table – 5 : Correlation of cytological grade according to ER/PR status[13]

Tumor grade	ER+/PR+	ER+/PR-	ER-/PR+	ER-/PR-
1	81.1	13	1.8	4.1
2	74.2	13	2.4	10.4
3	44.4	12.1	4.4	39.1

Discussion

Breast cancer is the most common cancer among women in India and in many regions of the world. Constant research on prognostic and predictive markers of breast carcinoma is going on. ER and PR are the important markers among them. So, we took to study these important prognostic markers and correlate with the grading of breast cancers. In the present study, age at presentation ranged from 33-76 years with a mean age of 50.58 years, in another study on Indian population by Raina V et al,[07] the median age at presentation was 47 years and according to the study by Joshi K et al,[06] the mean age ± SD was 49.7± 10.29. So these results are similar to the result of this study and significantly lower than most Western figures.

In this study, in most of the cases (87.5%), size of tumors was between 2 to 5cms, according to a study by Raina V et al,[07] the majority (86.4%) had a lump size > two cm. Lymph node metastases was seen in 25% in our study which was in comparison with study by Onitilo AA et.al[09], Zafrani B et al[10] and Huang JH et al [11] reported 31.0%, 37.0% and 35.4% positivity respectively. In various studies, R. Kim et al[12], Dunnwald KL et al[13] and Nadji M et al[14] ER and PR expression was 62.1%, 63.0% and 55% respectively, which is almost similar to our study which shows 55% of ER and PR expression.

In study by Dunnwald KL et al[13] among grade 1 tumors 81.1% were ER+/PR+ and only 4.1% were ER-/PR-, where as among grade III tumors 39.1% were ER-/PR- and only 44.4% were ER+/PR+. Results of our study were comparable to

other studies. There are some limitation of this study, when performing immunocytochemical analysis it is important to remember that no marker is 100% specific or sensitive. Thus, one should use panels of antibodies and not rely too much on any individual result. There is a danger of false_negative results in cytosmear, particularly if the antigen is only focally present.

Conclusion

In the recent years with outstanding advances in diagnosis of breast cancer, immunocytochemistry can be taken as reliable method of diagnosis. immunohistochemistry takes much more times. This will result early diagnosis, improved quality of life with significant decline morbidity and mortality in women living with the disease. Prognosis and management of breast cancer are influenced by classic variables such as histologic type and grade, tumor size, lymph node status, status of hormone receptors- ER and PR, same can be achieved by immunocytochemistry. ER and PR status correlates well with histopathological grading and other clinicocytopathological parameters. Cytologically higher grade (confirmed on histology) is associated with ER/PR negativity. Hence, immunocytochemical assessment of ER and PR status should be incorporated as a routine investigation. Tumor typing, grading and evaluation of ER and PR status on FNAC material in breast carcinoma are simple, quick and reliable method.

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