Comparison of ER, PR Reactivity Pattern with Histologic Grade, Tumor Size and Lymph Node Status in Breast Cancer

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Abstract

Background & Aims: There is positive correlation of ER and PR with degree of tumor differentiation and survival and response to hormone therapy are most favourable among women who are receptor positive. **Materials and Method:** The present study was carried out at our institute P.D.U. Medical college, Rajkot. A Total of 130 cases of breast carcinoma were taken into consideration which included of modified radical mastectomies and tru cut biopsies.Data including age, tumor size, and histological grade and lymph node status retrieved from pathology department. **Results:**Maximum number 42 of cases were seen in 41-50 years age group.128 cases of breast carcinomas were found affecting females and 02 were found affecting males. Out of 130 cases 66 cases have ER, PR receptor positive. Out of 130 cases 90 cases were stage 2 and out of them 50 were ER , PR positive,83 cases were grade 2 and of them 46 were ER,PR positive,75 cases were lymph node stage N0 and out of them 37 were ER ,PR positive. **Conclusion:** There is significant decrease in mortality and tumor recurrences with hormone therapy. There is positive correlation of ER,PR status with histological grade of tumor and lymph node metastasis. As the positivity was seen to decrease with advancing histological grade. It was also observed that the positivity decrease with increasing metastasis and the lymph node involvement. But there is no statistically significant correlation found between ER PR positivity and Histological Grade, Tumor Size & Lymph Node Status in this study.
Keywords: ER, PR, Breast Cancer.

Introduction

Breast carcinoma has a major impact on health of women. Cancer of the breast is the most common cancer among women in many regions in India and has overtaken cancer cervix[1]Presently 75000 new cases occur in India every year. Breast cancer survival is linked to early detection and timely appropriate treatment. Prognosis and management of breast carcinoma are influenced by the classic variables such as histological type and grade, tumor size, lymph node status, estrogen,progesterone receptor status[2]

The approach to management of breast carcinoma has undergone enormous changes over the last 20 years. Today, the choice of conservative and reconstructive surgery is more popular than mastectomy. Such changes are accompanied by increasing range of systemic, hormonal and cyto toxic drugs used in both adjuvant and neoadjuvant settings.

Identification of biomarkers plays a paramount role in treatment, management and prognosis of breast carcinoma. Determination of hormonal status is an important primary assessment at the time of diagnosis of breast carcinoma. With an established positive correlation of ER and PR with the degree of tumor differentiation, determination of ER and PR status on breast biopsy specimens, prior to therapeutic intervention is advocated as a standard practice. Survival and response to hormone therapy are most

favourable among women who are receptor positive.[3] With these prognostic, the need for accurate and precise assessment of ER,PR, expression in breast carcinoma is critical in the determination of patients appropriate for treatment with these drugs. Immunohistochemistry is an important tool in precise histopathological diagnosis.[4]

Survival and response to hormone therapy are most favourable among women who are receptor positive, intermediate for tumors discordant on receptor status and least favourable for receptor negative patients.[4]

Materials and Method

The study was carried out at our institute P.D.U. Medical college& Civil Hospital, Rajkot. The duration of the study was from August 2017 to July 2021. A total of 130 cases of breast carcinoma were taken into consideration which included of Modified radical mastectomies and the tru-cut biopsies. The immunohistochemistry of these specimens received were done.

All the mastectomy specimens received were properly bisected and fixed in 10% formalin for 18-24 hours. The sections of mass were preserved in Buffered neutral formalin and sections passed were used in IHC study. Detailed gross examination pertaining to overall size of the specimen, nipple and areola, margin status and nodal status were carefully studied.

Histological grading was done by modified Bloom and Richardson scoring system. Representative samples are taken from tumor, margins all four quadrants, nipple and areola and lymph nodes.

The tissues were processed in various grades of alcohol and xylol or egg albumin using automated histokinette. Paraffin blocks were prepared and sections of 5 micron thickness were cut in microtome using disposable blades and stained with hematoxylin and eosin.

Representative blocks were chosen for IHC. Sections for immunohistochemistry were also cut in microtome using disposable blades. Slides coated with chrome alum or egg albumin were used. Sections were subjected to antigen retrieval using pressure cooker technique using citrate retrieval solution (pH 6) and then treated by Horse Radish Peroxidase(HRP) polymer techniques.

Coated slides after antigen retrieval were taken through following stages. Treatment with peroxidase block for inhibiting endogenous peroxidase in the tissue for 5 minutes.

- Washed twice in TRIS buffer for 5 minutes.
- Application of power block for blocking non-specific antibody reaction.
- Application of primary and secondary antibody then wash with TRIS buffer.
- Application of super enhancer and washed in TRIS buffer.
- Application of DAB (diaminobenzidine) chromogen for 5 minutes –this is cleaved by enzyme to give coloured product at antigen slides.
- Washed in distilled water and are counter stained with hematoxyline then mounted with DPX.

Results

Table 1 shows the incidence of breast carcinoma in different age groups in our study. The youngest patient was 29 years old and oldest patient was 85 years old .Maximum number of cases were seen in 41-50 years age group. Mean age group was 50.51years. 74% of the cases were more than 40 years.

Out of 130 cases taken into study 128 cases of breast carcinoma were those affecting and only 2 cases were found affecting males (Table 2).

According to table 3, after applying Yates Chi square test for correlation of ER PR positivity with histological grade, tumor size, lymph node metastasis, tumor stage p value is 0.95, 0.98, 0.97, 0.96 respectively.

Table 1: Age Wise Distribution of Breast Carcinoma

Age (Years)	Cases Number	%
21-30	4	3.07
31-40	30	23.07
41-50	42	32.31
51-60	30	23.1
61-70	20	15.38
71-80	4	3.07
Total	130	100
Mean	50.51	
95 % CI	49 – 55	
Range	21 – 80	

Table 2: Sex Wise Distribution of Breast Carcinoma

Sex	No of Cases	%
Male	2	1.5
Female	128	98.5
Total	130	100

Table 3: Clinical Grade, Tumor Size, Lymph Node, Tumor Size Wise Distribution In Breast Carcinoma And Correlation With ER, PR Status

	ER Positive	PR Positive
Grade 1	18	18
Grade 2	46	38
Grade 3	2	1
Yates p value: 0.95		
<2.0 cm	8	6
2-5 cm	56	50
>5 cm	2	1
Yates p value: 0.98		
N0	38	36
N1	18	15
N2	8	5
N3	2	1
Yates p value: 0.97		
Tumor Stage		
T1	4	4
T2	50	46
T3	10	6
T4	2	1
Yates p value: 0.96		

Figure 1: ER/PR Positive in Breast Cancer
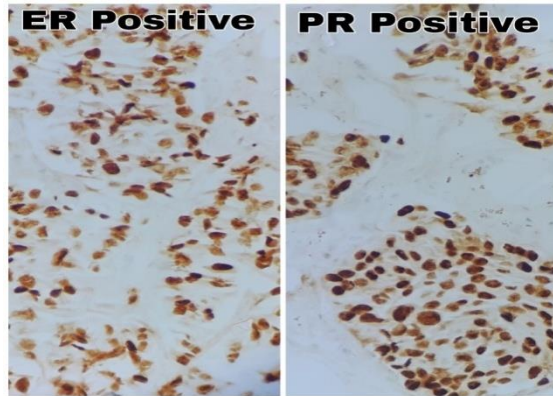
Discussion

Incidence of breast carcinoma is increasing in India. Prognosis is related to a variety of clinical, pathological and molecular features which include stage of the carcinoma, histologic type, grade and lymph node metastasis. Estogen and progesterone receptor have with increasing importance, influenced the management of this malignancy.

The study included 130 cases of breast carcinoma whose ER/PR studies were done. Maximum number of cases were diagnosed as ductal carcinoma-NST type.

Most of the breast carcinomas were diagnosed on right side with involvement of the upper outer quadrant. It included of the modified radical mastectomies and the trucut biopsies of the breast tissue.

As seen in table 1, mean age of patients included in our study was 50.51 years. 80.9% of cases were more than 40 years of age. Maximum number of cases were in the age a group of 41-50 years. 74% of the cases were more than 40 years.

Our results are in concordance with the study conducted by Dr. R. Narmadha, Kilpauk Medical College, where mean age of patients was 50.18 years. 80.9% of the cases were more than 40 years of age.Maximum number of cases were In the age group of 41-50 years. Even in the study carried out by Azizun-Nisa at Karachi the mean age was 45.5 years and 66% of the patients were,<50years of age at diagnosis.

Of the total 130 cases necrosis was seen in only in 32 cases this is contradictory to the study carried out by Azizun where 105 cases out of 150 cases had necrosis. Where as in current study the fibrosis was present In about 127 cases out of 130 cases and the findings are consistent with study of Azizun at Agakhan university where fibrosis was involved in 94% of the cases.

The hormone receptor status of breast carcinoma can predict the response to adjuvant endocrine therapy. In a study conducted by Pritilal et al[5] at New York with 3655 breast carcinomas, ER was positive in 71.6% and PR in 47.4%.

This study conducted in western population. According to Lakhmini K.B.Mudduwa[6] the prevalence of hormone receptor positive breast cancer in Asian countries has found to be lower than western world where more than 50% tumors express hormone receptors.However, the number of studies performed on this topic is much less in the Asian communities compared with the western world.LjiljanaHuipic et al[7] conducted a study in Croatia with 242 cases and found ER positivity in 37.5%,PR positivity in 40.6% of the cases.Azizun Nisa et al[8] studied 150 cases in Karachi and found that ER and PR was positive in 32.7%and 25.3%of cases respectively. But the results of our study shows that overall ER positivity is 53% and PR positivity is 50%.It is not as low as the positivity seen in Asian countries ,nor as high as those seen in western countries.Overall positivity rate for ER and PR differs possibly because of difference in techniques of evaluation.[9]

Nulliparity, late age at first birth, early age at menarche, higher body mass index and the use of hormone replacement therapy have all been associated with increased risk of developing an ER+ tumour but with a decreased risk of developing an ER- tumour. Young patients have high levels of circulating oestrogens and a correspondingly low expression of steroid receptors, which is reflected in their tumours. There appears to be a variation in steroid receptor positive in the Asian population.[10]

Hormone receptor expression decreases with increasing tumour size but no statistically significant association between the two variables. With increasing histological grade there is decrease in number of positive cases of ER and PR .No significant correlation has been noted between the tumour size and the ER/PR positivity. LakminiK.B.Mudduwa has found a significance inverse relation with the grade and ER,PR expression in his study. His study also shows no significant association of hormone receptor status with tumour size and lymph node metastasis[6].Kenneth McCarty and Rosemary. R. Millis et al have also obtained similar results of association between ER,PR, status and histological grade but no association with other prognostic variable.[11,12]

Table 4: Comparative Study of Association of Histological Grade With ER/PR Status

Histological grade	Number of ER/PR+cases		
	Present Study	Puvitha et al	Azizun et al
1	52%	85%	7%
2	55%	40%	40%
3	15%	25%	2%

As seen in the above table no 4 the ER/PR + positivity decrease with increase in grades in the current study and current study and the study at Coimbatore medical college.[14] The results vary in different studies but the positivity is seen more in grade 1 and 2 as compared to grade 3.The ER/PR positivity is seen to be more in grade 2 rather than in grade 1 in the current study.

Table 5: Correlation of Tumour Size With ER/PR + Status In Different Studies.

Tumour size	Number of ER/PR + cases		
	Current study	Puvitha et al	Azizun et al
1-2CM	28.57%	50%	9%
2-5CM	60.21%	41%	26%
>5CM	25%	33.33%	14%

As per data in table 5 the study at Coimbatore college shows a significant decrease in the positivity of ER/PR with increase in tumour size. Where as in the present study and that by Azizun shows no such significant decrease in positivity as the positivity is seen in size 2-5 cm of tumour.

Table 6: Comparative Study of Lymph Node Status & ER/PR Positivity In Breast Carcinoma

Lymph node status	Number of ER/PR +cases		
	Current study	Puvitha et al	Azizun et al
1	51.51%	29%	11%
2	50%	50%	13%
3	33.33%	46.66%	25%

As per the table 6 there is a statistical correlation seen of decreasing ER/PR positivity with higher grade of lymph node involvement. The findings are contradictory to the other two studies where there is no such correlation seen.

This study shows results of association between ER,PR status and other prognostic variables comparable to most of the studies conducted especially in Asian population.Presence of hormone receptors correlates well with response to hormone therapy. There is a significant decrease in mortality and tumour recurrence with hormone therapy. So, determination of ER,PR status is essential in all cases irrespective of clinical staging and lymph node metastasis.

Conclusion

Positivity was seen to decrease with advancing histological grade. It was also observed that the positivity decreases with increasing metastasis and lymph node involvement.On applying Yates chi square test p value is not <0.05, so there is no statistically significant correlation of ER PR positivity with histological grade, tumor staging, size and lymph node status.

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