

Correlation of Histological Grade with Hormone Receptors and Her 2 Neu In Carcinoma Breast - A Tertiary Centre Study

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ABSTRACT

Introduction: Hormone receptors and Her 2 Neu status are now widely accepted as prognostic markers and to decide therapeutic modality in breast carcinoma. The aim of this study was to analyze the receptor status in breast carcinoma with histopathological characteristics of the tumor.

Material and Methods: In the present study, immunohistochemical assay of 60 tumor block of patients of breast carcinoma was performed to know the hormone receptor status as well as histological examination.

Results: 60 breast cancer specimen were available for immunohistochemical testing for ER/PR. The result of the study showed that only 3.33% cases were ER+/PR+, 7.66% cases ER+/PR-, 9.33% ER-/PR+ and 80% cases were ER-/PR-. Expression of ER and PR was found to be significantly associated with tumor grade.

Conclusion: The Estrogen receptor and Progesterone Receptor negative cases were found in high grade disease on histological evaluation. Their status should be ascertained in all cases of breast carcinomas. Triple negative breast carcinomas have poorer prognosis as they tend to be of high grade.

Keywords: Breast Carcinoma; Estrogen Receptor; Progesterone Receptor; Her 2 Neu

INTRODUCTION

Carcinoma breast is the most frequent cancer among females worldwide. In India, it is the second most common cancer among females after carcinoma cervix. It is leading cause of cancer death in women aged 40 to 44 years, and second leading cause of cancer death for women overall¹. Breast cancer represents about 12% of all new cancer cases and 25% of all cancers in women². Although, incidence of breast cancer is low in India as compared to western countries, it is associated with poor prognosis and high mortality, may be due to late presentation when it in advanced stages³. Numerous variables such as histological type and grade, tumor size, lymph node status, status of hormonal receptors- estrogen receptor (ER) and Progesterone receptor (PR) of tumor influence the prognosis and management of breast carcinoma⁴. With advent of adjuvant hormonal or chemotherapeutic regimens determination the ER, PR and human epidermal growth factor receptor-2 (Her2/neu) receptor status in breast cancer has become practice as receptor positive status confer survival advantage in these patients^{2,5}. It is well known that strong ER-positive cases benefit from endocrine therapy alone^{4,5}.

PR status is also independently associated with overall and disease free survival. Patients with ER, PR positive

tumors have a better prognosis than patients with negative expression⁶. Hormone receptors study is not routinely measured as it is expensive and is still considered a research tool in many parts of our country. This could adversely impact decision making regarding treatment protocol and sometimes patients are treated empirically with tamoxifen which is not always required. The present study was planned keeping in mind predictive importance of receptor status for the prognosis of illness and application of appropriate therapy. The objective was to determine receptor status and its correlation with histopathological Grade of the tumor in an Indian population.

MATERIAL AND METHODS

This was a retrospective study carried out in a tertiary care centre in Central India. Samples of Sixty patients with histological proven diagnosis of breast carcinoma from January 2016 to October 2017 were selected for this study. Modified radical mastectomy specimens were subjected to histopathological examination and Immunohistochemical (IHC) analysis. Clinical details were archived from the files. Specimens were routinely fixed 24-48 hours in 10% neutral buffer formalin and were grossly examined and representative tissue bits were taken according to standard guidelines and then processed. 4 micron sections were stained with routine hematoxylin and eosin (H&E) stain. Samples were histologically graded according to Modified Bloom-Richardson-Elston (MRB) grading system. MRB grade was obtained by adding up the scores for tubule formation, nuclear pleomorphism and mitotic count⁷. Each of which was given 1, 2 or 3 points. This resulted in a total score of between 3 and 9. The final grading was given as below

1. 3 to 5 points – grade I
2. 6 to 7 points – grade II
3. 8 to 9 points – grade III.

ER / PR and Her-2Neu status was evaluated by IHC technique with monoclonal antibodies (DAKO) using

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antigen-antibody Streptavidin immunoperoxidase method⁸. Positive and negative controls were simultaneously run with each batch of IHC staining. Tumors that showed strong complete membranous staining in > 10% cells were taken as positive for Her-2neu. Nuclear staining was taken as positive for estrogen and progesterone receptors⁹. ER/PR expressions were assessed by Quick scoring which is based on assessment of proportion score and intensity score¹⁰. The 2 scores are added together for a final score with 8 possible values. A simplified Allred score groups 0 and 2; 3 and 4; 5 and 6; and 7 and 8 for 4 possible values (Tables 1 and 2).

RESULTS

Sixty cases of breast carcinomas cases were ascertained for ER/ PR status in relation to histological grading of tumor. In the present study female patients with breast carcinoma were aged between 24-79 years with youngest being 24 years and oldest 79 years. The mean age was 54.1 years. Majority (63%) were in age group of 40 to 59 yrs. The morphological categories were infiltrating ductal carcinoma, not otherwise specified (51cases- 85%) followed by medullary carcinoma (6 cases, 10%); infiltrating lobular carcinoma, mucinous carcinoma and infiltrating papillary carcinoma 1 (1.66%) case each.

Score	% of Positive Cells
0	0
1	< 1
2	1-10
3	11-33
4	34-66
5	66-100
Intensity Score	Intensity of positivity
0	None
1	Weak
2	Intermediate
3	Strong

Table-1: Proportion Score

Total Score	Interpretation
0,2	Negative
3-8	Positive

Table-2: The Proportion and Intensity score added together for total score

Histological Grade	No of cases	Percentage
Grade I	6	10%
Grade II	32	53.33%
Grade III	22	36.66%

Table-3: Histological grade of Tumours

Histological grade of Tumour	No of Cases	ER Positive	ER Negative
Grade I	6	2	4
Grade II	32	8	24
Grade III	22	2	20

Table-4: Histological grade Vs ER status

Histological grade of Tumour	No of Cases	PR Positive	PR Negative
Grade I	6	2	4
Grade II	32	12	20
Grade III	22	0	22

Table-5: Histological grade Vs PR status

Histological grade of Tumour	No of Cases	ER/PR copositive	ER/PR conegative
Grade I	6	2	2
Grade II	32	8	24
Grade III	22	0	22

Table-6: Histological Grade Vs ER/PR copositivity

Histological grade of Tumour	No of Cases	Her 2 Neu Positive	Her 2 Neu Negative	Her 2 Neu Equivocal
Grade I	6	4	2	0
Grade II	32	14	14	4
Grade III	22	10	08	4

Table-7: Histological grade Vs Her 2Neu status

The most frequent tumor grade was grade II (53.33%) followed by grade III (36.66%) and grade I (10%) (Table 3). The result of the study showed that only 3.33% cases were ER+/PR+, 7.66% cases ER+/PR-, 9.33% ER-/PR+ and 80% cases were ER-/PR-. Expression of ER and PR found to be significantly associated with tumor grade (p=0.02) (Tables 3-6). Her 2Neu status was as per table 7.

DISCUSSION

ER, PR and her2/neu are well-established procedures in routine breast cancer management mainly as prognostic factors for adjuvant hormone therapy^{11,12}. In our study, we found expression of ER to be only 20% and PR only 23.33%. Hormonal receptor status has shown that overall positivity rate for ER and PR is lower in India as compared to Western literature^{2,13}. In European and American population, 60-80% patients were found with positive receptor expression¹⁴. This may be due to lower average age at diagnosis or racial difference.

The tumor grade II were more common in our study followed by grade III and I contrast to other studies^{1,2,5,15}. Increased histological grade and late presentation possibly reflects lack of health awareness and miscellaneous social taboos in this part of the country. In our study, ER and PR correlated well with grade I (p=0.001 and p=0.02 respectively). Tumor grade is one of the important predictors of tumor behavior in breast cancer. Our results confirmed that non-reactivity of hormonal receptors increases with increase in tumor grade. Infiltrating ductal carcinoma was the most common histological type similar to other studies followed by medullary carcinoma in our study where as in other studies Infiltrating lobular carcinoma being the second most common type^{2,16}.

Triple-negative breast cancer (TNBC) is defined as a that group of breast carcinomas that are negative for ER, PR and

HER2/neu. In our study, of 60 cases, we found 8 such tumors. All 8 cases were infiltrating ductal type of carcinomas. All of them were of grade II or III. 75% had lymph node metastasis and lymphatic vessel invasion and 62.5% had tumor necrosis. Our results showed that TNBC had poor prognostic characteristics as compared with other subtypes of breast cancers. Other authors have also found similar results^{6,17}. Although patients with TNBC tend to have a poor prognosis, only chemotherapy is expected to be effective because no therapeutic targets have yet been established.

Our study also reveals for a non-significant association between expression of ER/ PR and lymph node metastasis. Similar results have been documented in other studies¹⁸.

CONCLUSION

Immunohistochemical analysis of ER, PR and Her2 Neu is widely accepted to have prognostic implications and are vital in deciding treatment modality. This study confirms that receptor expression of ER and PR is significantly associated with tumor grade. However, No association with node metastasis and ER, PR expressions was observed. High percentage of grade II and III tumours in our centre highlights the need to increase health awareness in this area in order to decrease the morbidity and mortality. Further functional analysis of ER, PR and Her 2Neu receptors are needed to investigate the effects of compounds in inhibiting cancer in humans. These findings can have profound impact in breast cancer treatment.

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