

Comparison of Histological Grade of Breast Tumours with Hormone Receptors ER/PR/HER-2-NEU Status

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Abstract:

Background: Carcinoma breast, accounts for about 23% of all cancers in women worldwide. Correlation of various prognostic variables of breast carcinoma helps us in assessment of prognosis and to assess the response to treatment. This study aimed to correlate the histological grade of the tumour with hormone receptor expression.

Materials and Methods: This was a prospective study, conducted by the Department of Pathology, in a government medical college for a period of 6 months. Histopathological examination and ER, PR, Her-2- neu status was assessed for 50 patients who had underwent mastectomy. Hormone receptor status was then correlated with histological grade of the tumour.

Results: Majority of the samples were found to be diagnosed as Infiltrating Ductal Carcinoma No Special Type with Ductal Carcinoma In Situ (IDC-NOS-DCIS) (50%). Most of the cases belonged to grade II carcinoma. Correlation of histological grading with the hormone status indicates that the hormone receptor expression decreases with increasing grade of the tumour and was found to be statistically significant.

Conclusion: Hormone receptor expression carries an inverse relationship with the histological grade of the tumor. Evaluating the prognostic factors helps us to provide better treatment and to understand the prognosis of the patient.

Keywords: Breast carcinoma; Her-2-neu; Hormone receptors; Prognostic factors.

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Introduction

Carcinoma breast became the second most common malignant tumour next to cervical cancer, accounting for about 23% of all cancers in women worldwide. Incidence of breast tumours increases rapidly with age [1]. Most common neoplasm of breast is the tumour arising from the epithelium, most common being adenocarcinoma (95%) [2]. Infiltrating ductal carcinoma of breast is the common type accounting for about 70% [3]

Various prognostic factors in invasive breast carcinoma includes patient's age, tumour size, lymph node status, metastasis, nuclear grade, histological grade, type of tumour, hormone receptor – ER,PR and Her2 neu status [3].

A single strongest parameter with prognostic significance is the hormone receptor status (ER,PR). It helps us to determine the suitability of patients for hormonal therapy [3]. Her-2- neu is an oncogene, member of human epidermal growth factor receptor. Overexpression and amplification of her-2-neu indicates high rate of recurrence and

mortality. Quantitative measurement of these receptors are made by immunohistochemistry. Studies have found that ER,PR expression is in correlation with the degree of differentiation of tumour, Grade 1 tumours were well differentiated tumours with increased ER,PR expression and Grade 3 poorly differentiated tumours with lowest ER,PR expression [4]. Correlation of the prognostic variables helps us in assessment of prognosis, estimating survival rate, predicting metastatic rate, determining treatment and to assess the response to treatment. This study aimed to correlate the grade of the tumour with hormone receptors

Materials and Methods

This study was conducted by the Department of Pathology in a government medical college for a period of 6 months. 50 patients of breast cancer posted for surgery were included in this study. Excision and incision biopsies, benign lesions, inflammatory lesions of breast were excluded from this study.

Procedure: After getting Ethical clearance from the institutional ethical clearance committee and informed consent from the patients, 50 Mastectomy specimens were collected, cut and fixed in 10% formalin for 6-24 hrs. Gross examination of specimen – overall size, nipple, areola, tumour size, margins and nodal status was studied. They are processed in automatic tissue processor, embedded in paraffin wax and routine H&E staining was done to assess the histological grading. These tumours were histologically graded according to Modified Bloom Richardson Elston grading system. [2] Tissue sections were then subjected to immunohistochemistry. The tissue sections were taken in chrome alum coated slides, deparaffinised and antigen retrieval was done by pressure cooker heating method using EDTA buffer solution and the slides were stained with monoclonal antibodies ER,PR & Her-2-neu. Allred scoring was used to

determine the hormone receptor status. Positivity of ER,PR was noted by intensity of nuclear staining and proportion of positive cells.

Her-2-neu scoring was done by analysing membranous staining by the tumour cells. In this study, ER, PR, Her-2- neu status was then correlated with histological grade of the tumour. Data then entered in excel sheet and analysis was done using Chi Square test in SPSS software version.

Results

The mean age of the respondents was found to be 55.3 + 9.9 years. Among the study participants, 34% participants were aged > 60 years. The participants aged between 41 to 50 were 32% and the patients aged between 51 to 60 were 26%.

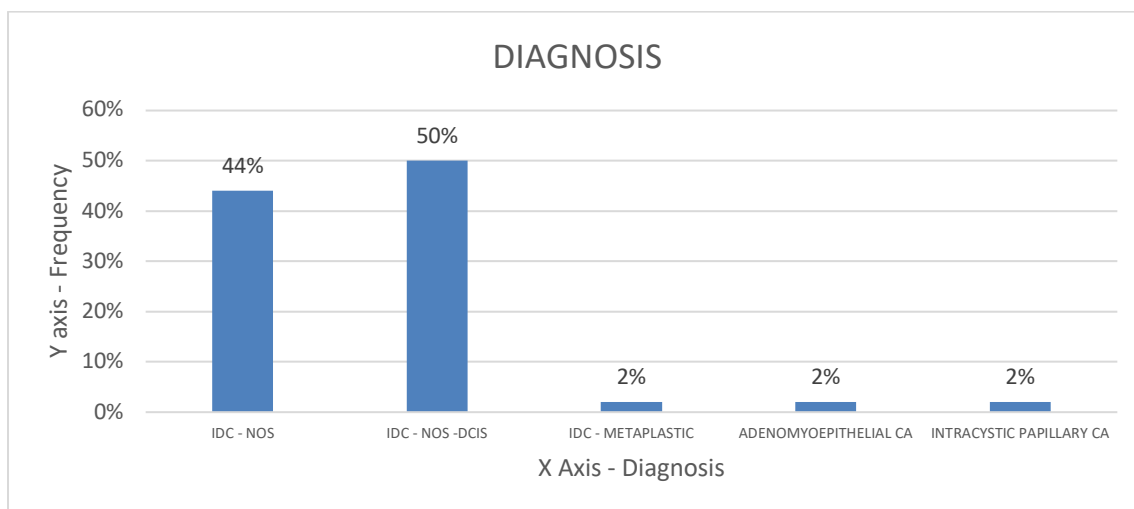


Figure 1: Distribution of type of cancer in the observed samples

FIG 1 shows the distribution of type of cancer in the observed samples, Majority of the samples were diagnosed as Infiltrating Ductal Carcinoma Non-Specific Type with Ductal Carcinoma in Situ (IDC-NOS-DCIS) (50%), followed by Infiltrating Ductal

Carcinoma Non-Specific Type (IDC-NOS) (44%). Diagnosis of Infiltrating Ductal Carcinoma (IDC) Metaplastic type, Adeno myoepithelial carcinoma, Intra cystic Papillary Carcinoma, each accounts for 2% of the total study population.

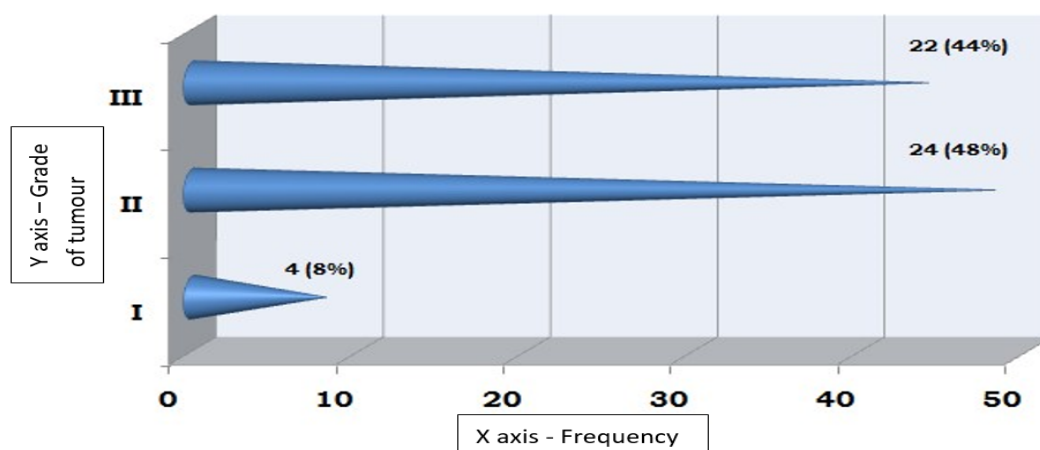


Figure 2: Distribution of study participants based on the grade of Infiltrating Ductal Carcinoma.

As per FIG 2, we found that majority of the participants had grade II tumour (48%). The study participants with grade III were 44%, while the cases in grade I were 8% of the study population. On analysis of immunohistochemical expression of ER,PR and Her-2-neu receptors, 52% of cases were found to be ER Positive, 50% of cases were found to be PR positive, 52% of cases were found to be Her-2-neu positive. Most of the breast tumours

were found to be ER/PR positive which accounts for about 48% and Her-2-neu negative which was found to be about 78%. Triple negative tumours carrying worst prognosis accounts for about 32%. Table 1 - Out of 50 cases studied, 8% of cases were found to be grade 1. Among grade 1 tumours, 3 cases were found to ER/PR positive (75%) and Her-2-neu negative (100%), 1 case was reported as triple negative tumour (25%).

Table 1: Comparison of grade of the tumours with hormone receptor status.

Hormone Receptor Status	GRADE 1(%) n- 4	GRADE 2 (%) n - 24	GRADE 3 (%) n - 22
ER +/ PR+	3 (75%)	18(75%)	3 (13%)
ER+/PR -	0	1 (4.1%)	0
ER-/PR+	0	0	0
HER 2 NEU +	0	3(12.5%)	8 (36%)
HER 2 NEU -	4 (100%)	21 (87.5%)	14 (63%)
Triple positive	0	1 (4.1%)	1 (4.5%)
Triple negative	1(25%)	3 (12.5%)	12 (54.5%)

Table 2: Correlation between Estrogen Receptors and Grade of Infiltrating Ductal Carcinoma (n = 50)

Estrogen Receptor	Grade of IDC			Test of significance Chi Square test
	I	II	III	
Negative	1 (25%)	5 (20.8%)	19 (86.3%)	0.001*
Positive	3 (75%)	19 (79.1%)	3 (13.6%)	
Total	4	24	22	

Table 3: Correlation between Progesterone Receptor (PR) and Grade of Infiltrating Ductal Carcinoma (n = 50)

Progesterone Receptor	Grade of IDC			Test of significance
	I	II	III	
Negative	1(25%)	6 (25%)	19 (86.3%)	0.001*
Positive	3 (75%)	18 (75%)	3 (13.6%)	
Total	4	24	22	

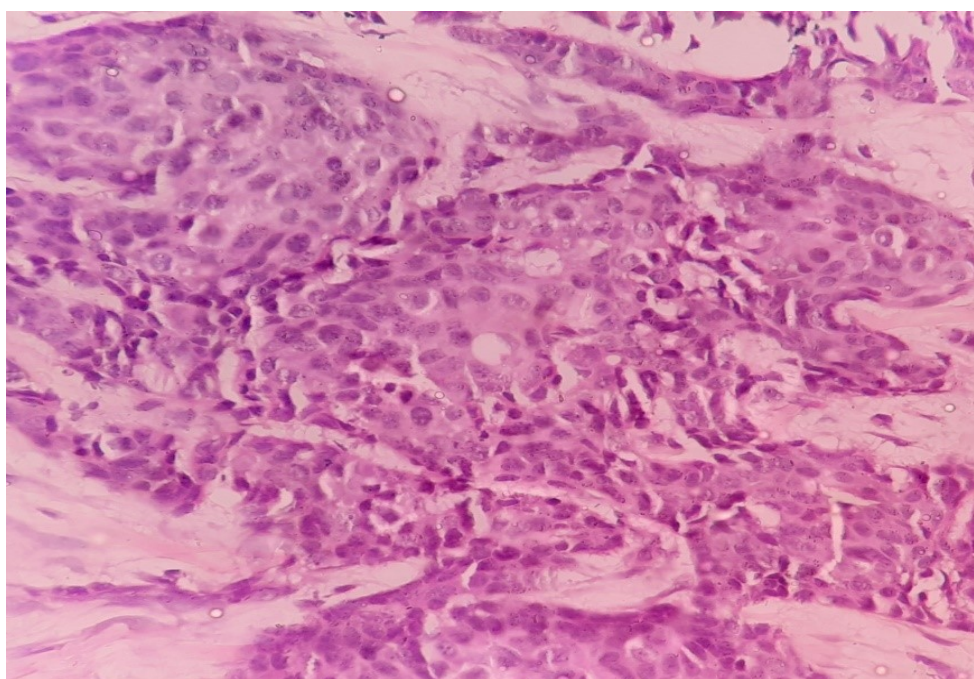


Figure 3: Histopathological picture showing Grade II infiltrating ductal carcinoma (40X, H&E)

48% cases was found to be of grade II tumour (table 3) (Fig 3), out of which 18 cases were found to be ER/PR positive (75%) and Her-2-neu negative(87.5%), 3 cases were found to be triple negative tumours (12.5%). 1 case was found to be a triple positive tumour(4.1%). One case was reported as ER+/PR (4.1%).

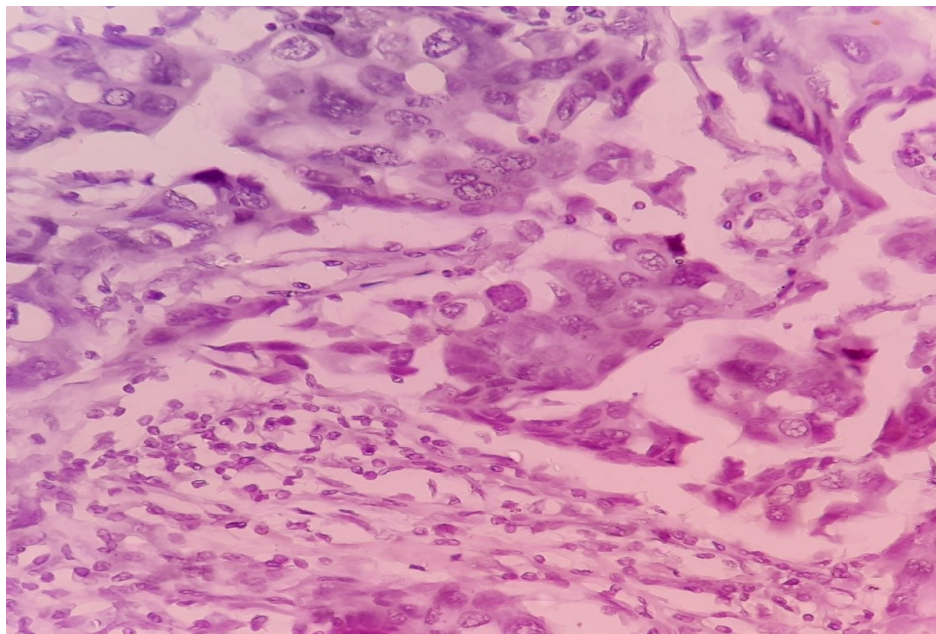


Figure 4: Histopathological picture showing Grade III infiltrating ductal carcinoma (40X, H&E)

Our results showed a significant increase in the expression of Estrogen receptors among the Grade I, Grade II tumours, and significant decrease in grade III tumours (Fig 4). Grade III tumours shows more of ER negativity. As per Table -2, ER expression decreases with increasing grade of the

tumor and was found to be statistically significant. (p value – 0.001).

As per Table 3, PR expression also has an inverse relationship with the grade of the tumour and was found to be statistically significant. (p value – 0.001)

Table 4: Correlation between HER 2 NEU receptor and Grade of Infiltrating Ductal Carcinoma (n = 50)

HER 2 NEU receptor	Grade of IDC			Test of significance
	I	II	III	Chi Square test
Negative	4 (100%)	21 (87.5%)	14 (63.6%)	0.001*
Positive	0	3 (12.5%)	8 (36.3%)	
Total	4	24	22	

Table 4 showing the correlation between Her-2-neu with the grade of infiltrating ductal carcinoma proves that Her-2-neu positivity was more in grade III tumours. Her-2-neu positivity was high in grade II and grade III tumours than grade I and was found to be statistically significant. Her-2-neu status increases with increasing tumour grade.

Discussion

This study was conducted to correlate the prognostic variables such as the grade with the hormonal receptor expression. On analysing the observed samples, incidence of Grade II tumours was common and this is concordant with the study proposed by Vedashree et al [3], Muhammad et al [24], Geethamala et al [4], Sepideh et al [29]. As per the current study, among analysis of 50 cases, 52% of case shows ER positivity while 50% cases show PR positivity and 78% of cases show Her-2-

neu positivity. Incidence of ER, PR and Her-2-neu positive tumours were more common than negative tumours. On Correlation of grade with hormone receptor expression, it has been found that ER/PR positivity was more in grade I and II tumours. Grade III tumours were more of ER/PR negative. While Her-2-neu expression is more in grade III tumours when compared to grade I and grade II. This correlation is found to be statistically significant with p value <0.05. This result was accordant with the study made by Vedashree et al [3], Amit mittal et al [27], Sepideh et al [29], Muhammad et al [24], Geethamala et al [4]. Grade of Infiltrating Ductal Carcinoma (Grade I, Grade II and Grade III) were co-related with the presence of Progesterone Receptor. Progesterone receptor were interpreted into two categories namely, negative and positive. Ours results showed a significant increase of the Progesterone Receptor among the

tumors belonging to grade I and grade II tumors, while participants with grade III tumours showed a significant decrease in the progesterone receptor and it is concordant with the results of Aryandaro et al [5], Vedashree et al [3], Sepideh et al [29], Muhammad et al (24). Aryandaro et al described that low grade tumours express ER receptors than high grade tumours.[5] Kenneth et al observed raising levels of ER, PR expression in well differentiated (grade I) and moderately differentiated (grade II) breast carcinomas. [24] Lakshmi K. Mudduwa found that expression of hormone receptors had an inverse relationship with the tumour grade. [6] Kenneth Mc Carty et al and Rosemary R. Milis have obtained a significant association between ER, PR status and histological grade of the tumour.[7,8]

In the present study we co-related, Grade of Infiltrating Ductal Carcinoma (Grade I, Grade II and Grade III) with the presence of HER 2 NEU receptor. HER 2 NEU receptor were interpreted into two categories namely, negative and positive. Our results showed that the positivity of HER 2 NEU was more in the grade III tumors, The presence of the receptors was significantly lower among the participants with grade I and grade II tumours.

Her-2-neu expression was more in grade III tumours and was concordant with results observed by Vedashree et al [3] but Geethamala et al [4] study shows that no significant relationship between Her-2-neu and grade of the tumour.

Conclusion

50 samples of breast carcinoma were analysed and found that Grade II tumours were more common than grade I and grade III. ER/PR and Her-2-Neu positive tumours were more common and it has significant correlation with the grade of the tumour. ER/PR expression was more in Grade I and II tumours while grade III tumours were ER/PR negative. Her-2-neu expression was more in Grade III tumours and was negative in grade I and II tumours. Thus, hormone receptor expression carries an inverse relationship with the grade of the tumour.

Ethical approval: Institutional Ethical committee, KAP Viswanadham government medical college. IEC.NO.55/2018

Highlights: Grade and Hormone receptor status of the patient was analysed before. But the correlation of the grade and the hormone receptor status helps to analyse the prognosis of the patient in a better way which also paves the way to the newer molecular classification of breast carcinoma.

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