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Research Article

A Correlative Study Of Estrogen Receptor, Progesterone Receptor, HER2-neu CD 10 Expression In Carcinoma Breast.

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ABSTRACT

Breast carcinoma has emerged as one of the most dreadful diseases among women major cause of cancer death among women in less developed countries.ER, PR and HER2-neu assessments can be done in routine are useful prognostic and therapeutic markers of breast cancer. However, stromal markers are now emerging as novel markers in assessing the prognosis of invasive breast cancer and have not been studied extensively till date as stroma plays a key role in modulating tumour invasion and metastasis. Aim of this study is to assess the expression of CD10 in breast cancers and its correlation with ER/PR/HER2-neu markers , histological grade and stage of the tumour Amongst ER/PR positive cases proportion of Grade I (60.0%) cases was found to be significantly higher than that of Grade II (15.0%) and Grade III (0.0%) and HER2-neu positive cases difference in the proportion of Grade I (20.0%), Grade II (20.0%) and Grade III (30.0%) was not found to be statistically significant. Proportion of Grade II (60.0%) and Grade III (80.0%) CD10 positive cases was significantly higher as compared to Grade I (p=0.012). Stage I & II cases was higher as compared to Stage III among ER/PR positive cases (21.4% vs. 14.3%) and in CD10 positive cases (64.29% vs. 52.38%) but these differences were not found to be statistically significant. Though Stage III cases was higher as compared to Stage I & II among HER2-neu positive cases (23.8% vs. 21.4%) but this difference was also not found to be statistically significant. In the study, proportion of ER/PR negative cases was significantly higher among CD10 positive cases (p=0.028) but in case of HER2-neu negative cases was not significantly higher among CD10 negative cases (80.00%). These findings are in general support that CD10 expression on the evaluation of independent association of ER, PR and HER2-neu shows a strong negative correlation with ER/PR only, however, with respect to independent association of HER2-neu, the evidence lacks strength and hence the findings in present study could be justified.

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INTRODUCTION

Breast carcinoma has emerged as one of the most dreadful diseases among women that has both physical as well as emotional impacts. Despite an improvement in clinical management during the last few decades, it continues to be a major cause of cancer death among women in less developed countries. Research in recent years has shown that breast cancer is immunogenic, and multiple putative tumour-associated antigens (TAAs), such as HER2-neu are observed in cancer[1]. There are some other hormonal markers like ER & PR that also provide a useful information regarding the breast cancer as well as its prognosis.

Estrogen receptor (ER) and progesterone receptor (PR) expression jointly define distinct phenotypic and molecular characteristics and sensitivity to adjuvant hormonal therapies [2,3]. There are studies that have evaluated breast cancer survival rates according to ER/PR status along with some other molecular markers like HER2-neu[3]. It has been shown that these parameters together might have the ability to further help in identifying treatment gaps where progress could be made in order to increase the treatment outcome. It has been shown that screening helps to identify early stage breast cancer[4], however hormonal therapy is useful only to those with hormone receptor-positive disease[5,6]. HER2-neu is also called as an Epidermal growth factor receptor 2 (ERBB2). It has gained much attention as a possible prognostic marker. In 15-30% of breast cancers, HER2-neu over-expression is due to gene amplification [7,8]. Its amplification and over-expression is associated with the poor prognosis in patients with axillary lymph node metastases[9]. HER2-neu can be a predictive marker in response to adjuvant therapy and endocrine therapy[10].

ER, PR and HER2-neu assessments can be done in routine, are relatively cheap, reliable and helpful in therapeutic decision making. They are also useful for the prognosis of breast cancer. However, stromal markers are now emerging as novel markers in assessing the prognosis of invasive breast cancer and have not been studied extensively till date as stroma plays a key role in modulating tumour invasion and metastasis. This justifies the study of new stromal marker CD10 in the prognosis of invasive breast carcinoma. CD10 is also known as a common acute lymphoblastic antigen (CALLA) which is a zinc dependent metalloproteinase. It is also found and give its expression in bone marrow lymphoid stem cells, endometrial stromal cells, pro-B lymphoblasts cell and mature neutrophils. Some studies conclude that stromal expression of CD10 is associated with biological aggressiveness in many epithelial malignancies[11,12,13,14,15]. Stromal expression of CD10 has been reported positively in myoepithelial cells of normal breast tissues.

Hence, our study was proposed to assess the expression of CD10 in breast cancers and its correlation with ER/PR/HER2-neu markers, histological grade and stage of the tumour.

MATERIAL AND METHODS –

This case-control study was conducted in the Department of Pathology in Era's Lucknow Medical College & Hospital, Lucknow, a charitable tertiary care facility that caters to patients with almost all the demographic profiles. With all the newly diagnosed patients of breast lump in the study period of eighteen months from November 2015 to April 2017. The study was approved by Ethical Committee of the Institute and an informed consent was obtained from all the subjects. A total of 70 cases were enrolled in the study, out of which 35 cases were malignant breast lesions and 35 cases were non-malignant breast lesions. Based on histopathological diagnosis, 35 cases (50.0%) of malignant breast lesions were diagnosed as Invasive ductal carcinoma and rest 35 cases (50.0%) of non-malignant breast lesions were benign tumour diagnosed as Fibroadenoma. These benign cases of Fibroadenoma were taken as control.

Demographic information of all the subjects was obtained and laboratory investigations were done which were recorded

on a separate Patient Record Form for each subject. All the new cases of breast lump presenting within the study period were included. The exclusion criteria were any previously diagnosed as well as treated cases of breast cancer and any patients with double malignancy, immunodeficiency diseases or any other associated chronic debilitating disorder which is likely to interfere with detection of marker. Tissue sections were taken from surgically resected breast specimen and excisional breast biopsies and were subjected for routine histopathological processing and H&E staining. Histopathological diagnosis and grading of malignant cases was done on H&E stained section into Grade I, Grade II and Grade III based on Nottingham grading system[16,17].TNM Classification of Breast carcinoma[18].

Immunohistochemistry –

ER, PR, HER2-neu and CD10 were assessed by IHC staining on formalin-fixed paraffin-embedded tissue sections cut into approximately 3-4µm. For ER- FLEX Monoclonal Rabbit Anti-Human Estrogen Receptor α, clone EP1, Ready-to-use (Dako) was used to detect estrogen receptor in human breast cancer, semi-quantitatively in high pH. This antibody labels estrogen receptor-positive cells and assesses ER status in breast carcinoma. For PR- FLEX Monoclonal Mouse Anti-Human Progesterone Receptor, clone PgR 636, Ready-to-use (Dako) was used to detect progesterone receptor in human breast cancer, semi-quantitatively in high pH. This antibody labels progesterone receptor-positive cells and assesses PR status in breast carcinoma. For HER2-neu- Anti-ErbB-2/HER2 (AN471-5ME,10ME) Rabbit Monoclonal antibody (BioGenex Automated Staining system) was used to detect over expression of ErbB2 in breast carcinoma. For CD10- Membrane Metallo-endopeptidase Rabbit Polyclonal antibody (Proteintech) was used to detect CD10 stromal expression in breast carcinoma.

Evaluation of IHC staining pattern –

The results were evaluated according to the intensity of staining pattern of the scoring system used for ER/PR, HER2-neu and CD10 in malignant cases.

Interpretation of ER and PR Results by Allred Method[19]

Proportion score	**Observation**	**Intensity score**	**Observation (PS)**	**(IS)**
0	None	0	None	
1	1%	1	Weak	
2	1-10%	2	Intermediate	
3	10-33%	3	Strong	
4	33-66%			
5	66-100%			
Total score	Sum of Proportion score and int		**Interpretation**	
0-2			Negative	
3-8			Positive	

Interpretation of HER2-neu scoring[20]

Staining pattern	Score	HER2-neu overexpression
No staining or membrane staining <10% tumor cells	0	Negative
Faint/perceptible membrane staining in >10% tumor cells	1	Negative
Weak to moderate complete membrane staining in >10% tumor cells	2	Weak
Strong complete membrane staining in >10% tumor cells	3	strong

Interpretation of CD10 Scoring[20]

Score	CD10 Staining
Negative	<10% stromal positive cells/core
Weak	10-30% stromal positive cells/core
Strong	>30% stromal positive cells/core

STATISTICAL ANALYSIS –

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. The values were represented in Number (%) and Mean±SD. All the p values <0.05 were taken as significant.

RESULTS –

A total of 70 cases fulfilling the inclusion criteria were enrolled in the study. Out of 70 cases, 35 cases (50.0%) were malignant diagnosed as Invasive ductal carcinoma and rest 35 cases (50.0%) were benign diagnosed as Fibroadenoma which were taken as controls in the study. Out of 35 malignant cases, 5 cases (14.29%) were found to be Grade I, 10 cases (28.57%) were of Grade III and remaining 20 cases (57.14%) were of Grade II. Only 1 case (2.86%) of Stage I tumour was found. Stage II comprised of 13 cases (37.14%) and remaining 21 cases (60.00%) were of Stage III. None of the Stage IV case was found in the study.

Table no. 1 shows the distribution of cases according to histopathological diagnosis of the study population. (figure 1,2,5)

Table 1: Histopathological Distribution of Malignant and Benign Cases.

Histopathological Diagnosis		No. of cases	Percentage
Malignant- **Invasive Ductal Carcinoma**		35	50.0
Nottingham Grading			
Grade I	5 (14.29%)		

Grade II	20 (57.14%)		
Grade III	10 (28.57%)		
pTNM Staging			
Stage I	1 (2.86%)		
Stage II	13 (37.14%)		
Stage III	21 (60.00%)		
Stage IV	0 (0.0%)		
Benign – **Fibroadenoma**		35	50.0

Out of a total of 70 cases, the range of age for malignant cases varied from 25-80 years and for benign cases was 14-55 years. Mean age of malignant cases (45.66±12.18 years) was found to be higher as compared to benign cases (24.83±8.77 years). Proportion of those of younger age cases was higher in benign as compared to the malignant cases while proportion of older age cases was higher in malignant cases. Difference in age of malignant cases and benign cases was found to be statistically significant ($p<0.001$). (Table no. 2)

Table 2: Comparison of Age group among Malignant and Benign Cases .

Age Group (years)	**Malignant (n=35)**		**Benign (n=35)**		**Total**	
	No.	**%**	**No.**	**%**	**No.**	**%**
≤20 yrs	0	0.00	14	40.00	14	20.00
21-30 yrs	4	11.43	13	37.14	17	24.29
31-40 yrs	9	25.71	7	20.00	16	22.86
41-50 yrs	13	37.14	0	0.00	13	18.57
51-60 yrs	6	17.14	1	2.86	7	10.00
>60 yrs	3	8.57	0	0.00	3	4.29
	χ^2=38.586 (df=5); p<0.001					
Min-Max (Median)	25-80 (45.00)		14-55 (22.00)		14-80 (35.00)	
Mean±SD	45.66±12.18		24.83±8.77		35.24±14.87	

Out of 70 cases enrolled in the study, 26 cases (37.14%) were ER/PR positive. In 35 malignant cases, 6 cases (17.14%) were ER/PR positive and in 35 benign cases, 20 cases (57.14%) were ER/PR positive. Out of 70 cases, 9 cases (12.86%) were HER2-neu positive. Among 35 malignant cases, 8 cases (22.86%) were HER2-neu positive and among 35 benign cases, only 1 case (2.86%) was positive. Staining of HER2-neu was weak positive in the benign case. Out of 70 cases, 21 cases (30.0%) were CD10 positive. Among 35 malignant cases, 20 cases (57.14%) were CD10 positive and among 35 benign cases, only 1 case (2.86%) was positive. Staining of CD10 was weak positive in the benign case. (Table no. 3)

Table 3: Expression of ER, PR, HER2-neu and CD10 in Malignant and Benign cases.

	Total	Malignant (n=35)		Benign (n=35)	
		No.	%	No.	%
ER positive	26	6	17.14	20	57.14
PR positive	26	6	17.14	20	57.14
HER2-neu positive	9	8	22.86	1	2.86
CD10 positive	21	20	57.14	1	2.86

Out of 35 malignant cases, 5 (14.29%) were found to be Grade I, in which 3 cases (60.0%) were ER/PR positive, only 1 case (20%) was HER2-neu positive and no case of CD10 was found positive. 20 cases (57.14%) were found to be Grade II, in which 3 cases (15.0%) were ER/PR positive, 4 cases (20%) were HER2-neu positive and 12 cases (60.0%) were CD10 positive. Grade III had 10 cases (28.57%) in which no case was ER/PR positive, 3 cases (30.0%) were HER2-neu positive and 8 cases (80.0%) were CD10 positive. Only 1 case (2.86%) of Stage I tumour was found which was only CD10 positive. Stage II comprised of 13 cases (37.14%) in which 3 cases (23.1%) were ER/PR positive, 3 cases (23.1%) were HER2-neu positive and 8 cases (61.5%) were CD10 positive. Remaining 21 cases (60.00%) were of Stage III, in which 3 cases (14.3%) were ER/PR positive, 5 cases (23.8%) were HER2neu positive and 11 cases (52.4%) were CD10 positive. None of the Stage IV case was found in the study. (Table no. 4)

Table 4: Association of ER, PR, HER2-neu and CD10 with Grade & Stage of Malignant Cases

	Total	ER positive		PR positive		HER2-neu positive		CD10 positive	
		No.	%	No.	%	No.	%	No.	%
Malignant: IDC	35	6	17.1	6	17.1	8	22.9	20	57.1
Nottingham Grade (n=35)									
Grade I	5	3	60.0	3	60.0	1	20.0	0	0.0
Grade II	20	3	15.0	3	15.0	4	20.0	12	60.0
Grade III	10	0	0.0	0	0.0	3	30.0	8	80.0
Stage (n=35)									
Stage I	1	0	0.0	0	0.0	0	0.0	1	100.0
Stage II	13	3	23.1	3	23.1	3	23.1	8	61.5
Stage III	21	3	14.3	3	14.3	5	23.8	11	52.4
Stage IV	0	0	0.0	0	0.0	0	0.0	0	0.0

Amongst ER/PR positive cases proportion of Grade I (60.0%) cases was found to be significantly higher than that of Grade II (15.0%) and Grade III (0.0%) and HER2-neu positive cases difference in the proportion of Grade I (20.0%), Grade II (20.0%) and Grade III (30.0%) was not found to be statistically significant. Though proportion of Grade II (60.0%) and Grade III (80.0%) CD10 positive cases was higher as compared to Grade I CD10 positive cases (0.0%) and this difference was found to be statistically significant (p=0.012). (table no. 5) (Figure2,4,6,7,8,9)

Table 5: Comparison of ER, PR, HER2-neu and CD10 among different Grades of Malignant Cases.

	Total (n=35)	Grade I (n=5)		Grade II (n=20)		Grade III (n=10)		Statistical significance	
		No.	%	No.	%	No.	%	χ^2	P
ER positive	6	3	60.0	3	15.0	0	0.0	8.599	0.014
PR positive	6	3	60.0	3	15.0	0	0.0	8.599	0.014
HER2-neu positive	8	1	20.0	4	20.0	3	30.0	0.405	0.817
CD10 positive	20	0	0.0	12	60.0	8	80.0	8.867	0.012

Out of the 70 cases studied, Stage I & II cases was higher as compared to Stage III among ER/PR positive cases (21.4% vs. 14.3%) and in CD10 positive cases (64.29% vs. 52.38%) but these differences were not found to be statistically significant. Though Stage III cases was higher as compared to Stage I & II among HER2-neu positive cases (23.8% vs. 21.4%) but this difference was also not found to be statistically significant. (table no.6)

Table 6: Comparison of ER, PR, HER2-neu and CD10 among different Stages of Malignant Cases

	Total (n=35)	Stage I+II (n=14)		Stage III (n=21)		Statistical significance	
		No.	%	No.	%	χ^2	P
ER positive	6	3	21.4	3	14.3	0.302	0.583
PR positive	6	3	21.4	3	14.3	0.302	0.583
HER2-neu positive	8	3	21.4	5	23.8	0.027	0.869
CD10 positive	20	9	64.29	11	52.38	0.486	0.486

Out of the 70 cases in the study, proportion of ER/PR negative cases was higher among CD10 positive cases (95.00%) as compared to CD10 negative cases (66.67%). This association was found to be statistically significant (p=0.028) but in case of HER2-neu, negative cases was higher among CD10 negative cases (80.00%) as compared to CD10 positive cases (75.00%). This association was not found to be statistically significant (p=0.727; NS). (Table no. 7)

Table 7: Correlation of CD10 with ER/PR and HER2-neu in Malignant Cases

		CD10 Negative (n=15)		CD10 Positive (n=20)		Statistical significance	
		No.	%	No.	%	χ^2	P
ER	Negative	10	66.67	19	95.00	4.844 (df=1)	0.028
	Positive	5	33.33	1	5.00		
PR	Negative	10	66.67	19	95.00	4.844 (df=1)	0.028
	Positive	5	33.33	1	5.00		
HER2-neu	Negative	12	80.00	15	75.00	0.122 (df=1)	0.727
	Positive	3	20.00	5	25.00		

Figure :1 Photomicrograph of Invasive Ductal Carcinoma -Grade 1 (H&E,100X)

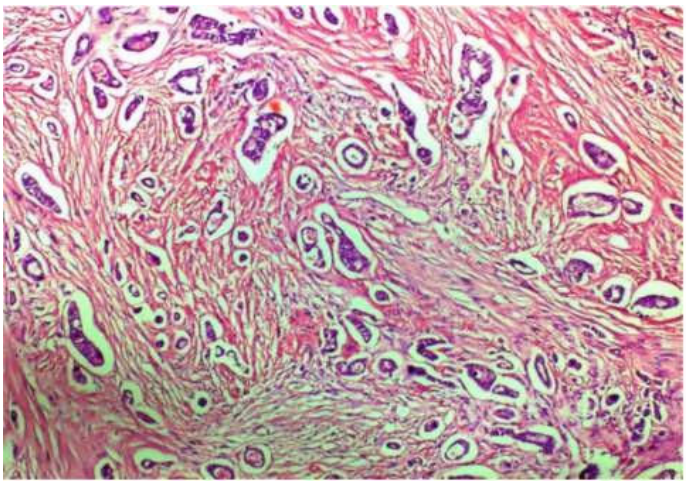


Figure :2 Photomicrograph of Invasive Ductal Carcinoma -Grade 1 (IHC for CD10,100X)

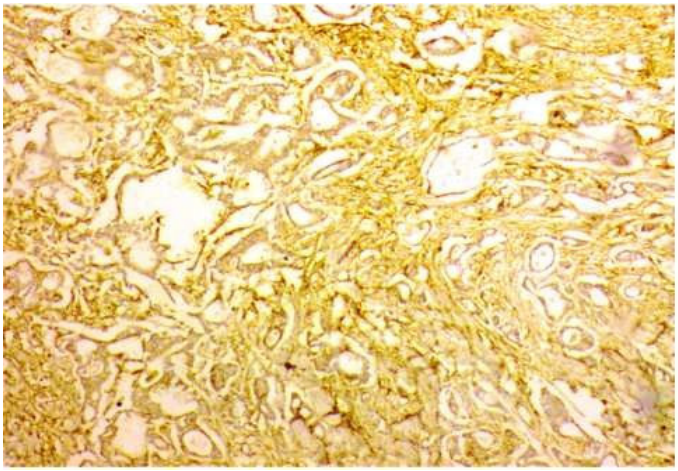


Figure :3 Photomicrograph of Invasive Ductal Carcinoma -Grade 2 (H&E ,100X)

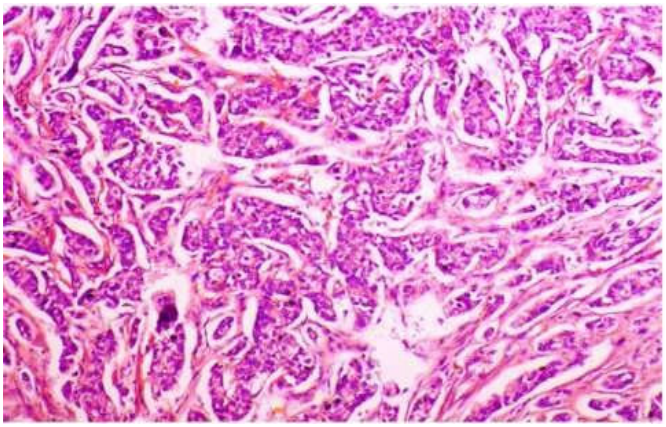


Figure :4 Photomicrograph of Invasive Ductal Carcinoma -Grade 2 (IHC for CD10,100X)

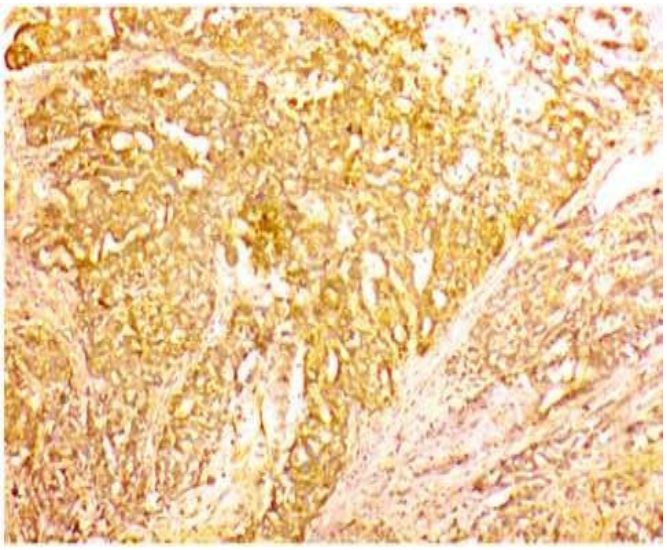


Figure :5 Photomicrograph of Invasive Ductal Carcinoma -Grade 3 (H&E,100X)

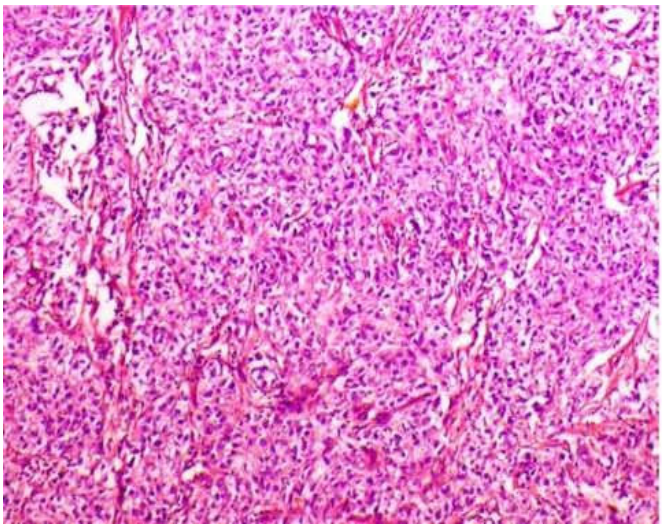


Figure :6 Photomicrograph of Invasive Ductal Carcinoma -Grade 3 (IHC for CD10,100X)

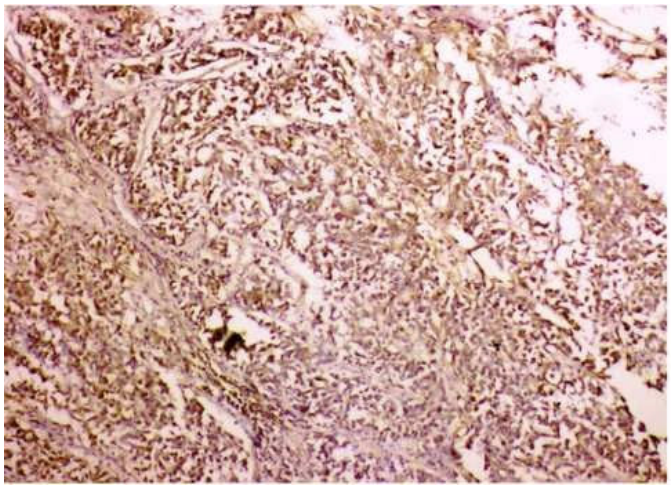


Fig.7: Photomicrograph of Invasive Ductal Carcinoma showing positivity for ER (IHC, 400X)

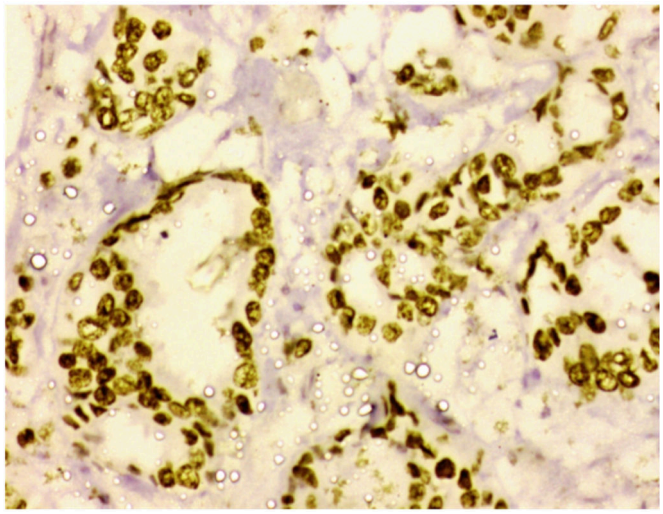


Fig.8: Photomicrograph of Invasive Ductal Carcinoma showing positivity for PR (IHC, 400X)

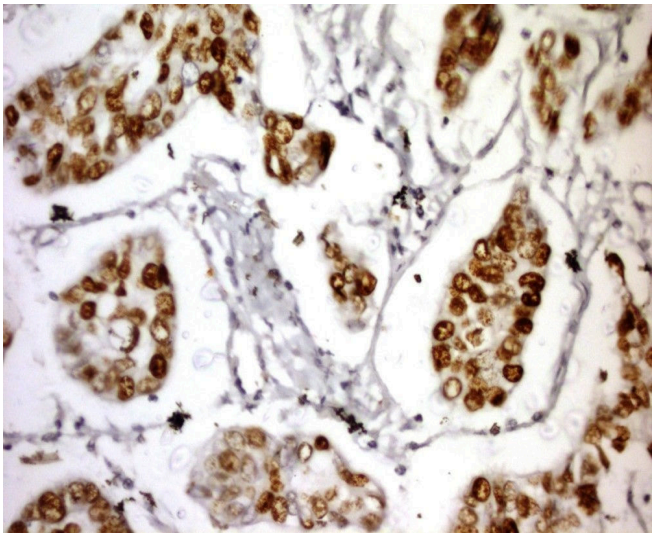
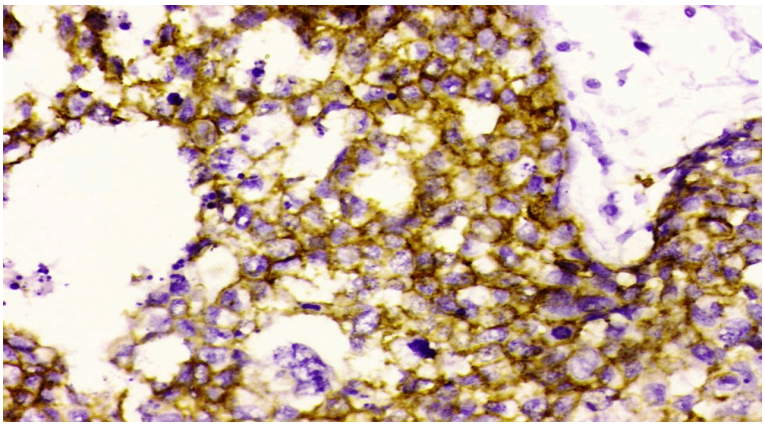


Fig.9: Photomicrograph of Invasive Ductal Carcinoma showing positivity for HER2-neu (IHC, 400X)



DISCUSSION

Diagnosis of breast cancer is often followed by the question regarding its metastatic potential, predicted response to treatment and survival of the patient. In addition to traditional prognostic factors including tumour grade and stage, hormonal markers such as Estrogen and Progesterone receptors and HER2-neu expression have emerged for survival prediction. The detection of these IHC markers has played a major role in planning treatment strategy. However, attempts are often made to find out other markers that have an independent correlation and such recognition of new markers would be able to predict invasive and metastatic tumour potency which could help in making the proper treatment decisions.

As breast cancer is an epithelial malignancy, the prognosis of breast cancer is related to the number and types of oncogenes activated in the epithelial cells. However, stroma plays a key role in modulating tumour invasion and metastasis. Stromal markers are now emerging as novel markers in assessing the prognosis of invasive breast carcinoma and have not been studied extensively till date. CD10 which is also called Neprilysin and Common Acute Lymphoblastic Leukemia/Lymphoma Antigen (CALLA) is a zinc-dependant metalloproteinase which are produced by myofibroblasts. CD10 is highly expressed in kidney, lung tissues and in many other tissue.

Multiple studies have shown that the expression of CD10 in stromal cells is associated with more biologically aggressive tumours[21]. Considering the usefulness of stromal CD10 expression as a marker of aggressive tumours, the present study was proposed to assess stromal CD10 expression and its correlation with ER, PR, HER2-neu, tumour grade and stage in breast carcinoma cases. For this purpose, this study was designed comprising of 70 cases out of which 35 cases of malignant breast tumour (invasive ductal carcinoma) and 35 benign breast tumour (fibroadenoma) were enrolled, the purpose was to find out whether CD10 can measure the aggressiveness of tumours and has any correlation with IHC status of ER, PR, HER2-neu and with tumour grade and stage.

We found in our study, that the age range of patients enrolled ranged from 14 to 80 years. Mean age of malignant cases was 45.66 years as compared to 24.83 years for benign cases. Majority of cases were in age group 41-60 years (54.3%). Kumar *et al.*[22] in their study reported the mean age of malignant cases as 50.5 years. The age profile of malignant cases in the present study was similar to that of a recent study from Karnataka (India)[23] that has also reported the age of majority of their cases in the age group 41-60 years.

In the present study, expression of both hormonal markers ER and PR were more common in benign (57.14%) as compared to malignant (17.14%) cases whereas expression

of HER2-neu was more common in malignant (22.86%) as compared to benign (2.86%). CD10 expression was also more common in malignant (57.14%) as compared to benign (2.86%) cases. Similar to findings of our study, Gupta *et al.*[24] in their study reported expression of ER/PR in the majority of benign cases (96% and 100%) as compared to malignant (32% and 42%) respectively. Hormonal profile of benign cases generally shows a high prevalence of ER/PR positivity. In a descriptive study, Nizze*et al.*[25]reportedER positivity in 72.7% and PR positivity in 90.9% of their fibroadenoma cases. However, in IDC cases, ER positivity was seen in 70% and PR positivity was seen in 61% cases.

In the present study, CD10 stromal positivity was seen in 20 out of 35 (57.14%) cases in malignant cases. However, in 1 (2.9%) benign case it showed weak positivity in stroma. With respect to expression of CD10 in benign breast tumours, most of the literature coincides with the present study reporting low stromal expression in normal or benign breast tissue. Similar to findings of the present study, Ibrahim *et al.*[26] also showed low CD10 expression rate in benign (16.7%) cases. In their study, they also included borderline and malignant cases and found the expression rates to be 60% and 80% in borderline and malignant cases respectively. Gupta *et al.*[24]too in their study reported CD10 expression in 11.1% benign, 77.8% of borderline and 87.5% of malignant cases. However, the expression rate in malignant cases in the present study was not that high as reported in these studies[24,26] one of the reasons for this could be a low prevalence of cases in Grade III (28.67%) and stage IV (0%).

We found that on evaluating the positivity rate of ER/PR, HER2-neu and CD10 expression with grades of malignancy, a significant decline in ER/PR positivity with increasing grade of breast carcinoma. It was seen that both ER/PR were positive in 60% of Grade I and none of the Grade III cases and found this difference to be significant statistically. However, no significant trend with HER2-neu scores was seen. Thus indicating that a negative ER/PR status was related with higher grade of breast cancer. A number of previous studies have shown ER/PR positivity to be associated with good prognosis[27,28]. Biswal*et al.*[29] in their study showed ER positivity in 57.1% of Grade II and 16.7% of Grade III and PR positivity in 40.0% of Grade II and 23.3% of Grade III cancer. In their study, they observed HER2-neu positivity in 8.6% of Grade II and 80% of Grade III cancer patients. These results are similar to the findings in the present study. In another study, Yadav*et al.*[30]showed ER positivity in 51.2% of Grade I, 47.8% of Grade II and only 5% of Grade III tumours thus showing a significant association as observed in the present study. They observed PR positivity in 46.5% of Grade I, 42.0% of Grade II and 11.1% of Grade III cases and HER2neu positivity in 58.7% of Grade I, 58.1% of Grade II and 54.5% of Grade III lesions and did not show a significant association between Grade and HER2-neu positivity.

In association with grade and CD10 expression is concerned, in the our study we found that the expression of CD10 to be increasing with increasing grade of cancer. Mohammadizadeh*et al.*[31] in their study also found no or weak CD10 expression 33.3% of Grade I, 80% of Grade II and 91.47% of Grade III patients thus showing that expression levels tended to increase with increasing grade of cancer. Taghizadeh-Kermani A *et al.*[32] too in their study showed weak to strong CD10 expression in 31.8% of Grade I, 62% of Grade II and 92.9% of Grade III breast cancer cases. Jana *et al.*[33] in their study showed CD10 positivity in 26% of Grade I, 57% of Grade II and 68% of Grade III tumors and found this association to be significant.

In the present study, a total of 14 (40%) of the breast cancer cases were in Stage I & II while remaining 21 (60%) were in Stage III. On evaluating the association of ER/PR, HER2-neu as well as CD10 expression for positivity, there was no significant association of any of these markers with the stage. One of the reasons

for this probably was dominance of Stage II and III cases only. In the present study, we had only 1 (2.86%) case of Stage I. In different studies, the relationship with stage and ER, PR, HER2-neu status and CD10 expression has been reported to be of varying nature. Most of the studies did not assess the stage and correlated with it. Shaikh*et al.*[34] also did not find a significant association between of ER, PR, HER2-neu expression with tumour stage. Thus the supportive evidence is much divided regarding association of ER, PR and HER2-neu positivity with tumour stage.

In our study, association of CD10 expression with ER/PR, it was found that CD10 expression was significantly associated with ER/PR negative status. However, we failed to find out a significant association of HER2-neu with CD10 expression. These findings are partially in agreement with the observations of Puri*et al.*[20], who observed that CD10 expression correlated strongly with ER/PR negativity and HER2-neu positivity. In the present study, we also failed to replicate their results for HER2-neu expression. Arora*et al.*[35] in their study found ER negative status to be strongly correlated with CD10 expression. However, in their study they did not assess PR and HER2-neu status. Taghizadeh-KermaniA*et al.*[32] in their study also found ER/PR status to be inversely correlated with CD10 expression as observed in the present study. However, in their study, they did not make an assessment of HER2-neu status. The findings of Nema and Narang[36] also showed a significant association between with CD10 expression and ER status but failed to replicate it for PR or HER2-neu. One of the reasons for this was low positivity rate for HER2-neu in our study (22.9%). Nema and Narang[36]on the other hand showed a high HER2-neu positivity (70%) and failed to deduce a relationship between HER2-neu status and CD10 expression. Mohammadizadeh*et al.*[31] in their study also failed to find out a significant association between CD10 expression and HER2-neu status.

These findings are in general support that CD10 expression on the evaluation of independent association of ER, PR and HER2-neu shows a strong negative correlation with ER/PR only, however, with respect to independent association of HER2-neu, the evidence lacks strength and hence the findings in present study could be justified.

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