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EXPRESSION OF ESTROGEN AND PROGESTERONE RECEPTORS IN BREAST CARCINOMA

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ABSTRACT **Background:** Breast carcinoma is the most common malignant tumor and the leading cause of death in women worldwide. Of the various parameters, expression of hormone receptors in particular estrogen receptor(ER) and progesterone receptor (PR) is significant**. Study design:** 50 cases of proven breast carcinoma diagnosed in the Department of Pathology, Katuri Medical College and Hospital, Guntur from October 2013 to October 2015 which includes 50 prospective cases. **Results:** In the present study 70% expressed estrogen receptors and 64 expressed progesterone receptors. Of 50 cases, 64% were ER+/PR+, 6% were ER+/PR- and remaining 30% were ER-/PR-. Histological grading in correlation with ER/PR positivity was found to be statistically significant (p <0.001). **Conclusion:** Prognosis and management of breast cancer are influenced by classic variables such as histological type and grade, tumor size, lymph node status, status of hormone receptors- ER and PR.

KEYWORDS :

INTRODUCTION: Breast carcinoma is the most common malignant tumor and the leading cause of death in women worldwide.It is of serious concern owing to the rising incidence of the disease in the last 5-10 years[1]. Women diagnosed with breast cancer have relative survival rates of 96 %, 79%, and 67% and 60 % for 1, 5, 10 and 15 years respectively [2]. Various protocols are in use for the assessment of prognosis and also to assist further management of these cases. Of the various parameters, expression of hormone receptors in particular estrogen receptor(ER) and progesterone receptor (PR) are significant [3].Most of the studies positive association between the presence of estrogen and progesterone receptors in tumor cells and a favorable prognosis for both diseases free and overall survival [5]. The literature also includes several studies showing association between the presence of estrogen receptor and progesterone receptor and other indicators of good prognosis like post menopausal patients, small tumor size, low histological grade, low nuclear grade and low mitotic activity[3].

The estrogen receptor and progesterone receptor status in predicting response to hormonal treatment for breast carcinoma is well documented .The response rate is variable among various study groups [3].The hormone receptor expression in breast cancers in India is low4.

MATERIALS & METHODS: 50 cases of proven breast carcinoma diagnosed in the Department of Pathology Katuri Medical College and Hospital, Guntur from October 2013 to October 2015which includes 50 prospective cases. The haematoxylin and eosin (H&E) sections of the cases were retrieved from the records and screened for confirmation of diagnosis and selection of representative tumor paraffin blocks. The representative neoplastic tissue blocks (paraffin embedded) were cut at [3].0µ on Poly-L -Lysine coated slides. One of these sections was routinely stained with H&E. The histological grading of tumor was done on H&E stained sections according to Modified Bloom and Richardson grading.

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance.

RESULTS: In our study, age ranged from 32-73 years and the mean age ± SD was 51.10 ± 9.38years. Majority, 37 cases (74%) belonged to 41-60 years followed by 6 (12%) 61-70yrs.

Table 1: Age distribution of patients

Age in years	Number of patients	%
31-40	5	10.0
41-50	21	42.0
51-60	16	32.0
61-70	6	12.0
71-80	2	4.0
Total	50	100.0

Table 2: Morphological and Histological features

Size (cm)	Number of patients	%
<2.0 square cm	2	4.0
2.0-5.0 square cm	45	90.0
>5.0 square cm	3	6.0
Tubule formation	**Number of patients**	**%**
>75% of tumor	17	34.0
10-75% tumor	22	44.0
<10 % tumor	11	22.0
Nuclear pleomorphism	**Number of patients**	**%**
Minimal variation in size and Shape of nuclei	18	36.0
Moderate variation in size and shape of nuclei	21	42.0
Marked variation is size and shape of nuclei	11	22.0
Mitotoc score/10 hpf	**Number of patients**	**%**
0-5	19	38.0
6-10	23	46.0
>11	8	16.0
Total	50	100.0

On gross examination, 45 cases (90%) measured 2-5cms, followed by 3 cases (6%) between >5.0 cms and 2 cases (4%) ≤2cms. Majority, 22 cases (44%) had score-2, 17(34%) had score-1 and 11(22%) had score-3 for tubule formation Majority, 21 (42%) had score 2 followed by 18 (36%) with score 1 then 11 (22%) with score 3 for nuclear pleomorphism. In our study majority, 23 (46%) had score 2 followed by 19 (38%) with score 1 then 18(16%) with score 3 for mitotic rate.

Table 3: Histological (MBR) grade

Histological grade	Number of patients (n=50)	%
Grade I	21	42.0
Grade II	25	50.0
Grade III	4	8.0

Histological grading showed 25(50%) of cases to be grade-II followed by 21(42%) grade-I and grade III 4(8%). In our study the predominant histological subtype was Infiltrating ductal carcinoma (NOS) seen in 46(92%) cases, 2 cases were medullary carcinomas and 1 case each of papillary and mucinous carcinomas.

Table 4: Intensity of ER staining

Intensity of ER staining	Number of patients (n=50)	%
Negative	15	30.0
Positive	35	70.0
• Mild	3	6.0
• Moderate	30	60.0
• Severe	2	4.0
Intensity of PR Staining	**Number of patients (n=50)**	**%**
Negative	18	36.0
Positive	32	64.0
• Mild	2	4.0
• Moderate	28	56.0
• Severe	2	4.0

In our study 35(70%) cases showed positive for staining and 15(30%) cases were negative, Majority of them showed moderate intensity of staining 30(60%), 3(6%) cases were mildly stained and 2 (4%) cases were severe stained

Table 5: PR Staining

Intensity of PR Staining	Number of patients (n=50)	%
Negative	18	36.0
Positive	32	64.0
• Mild	2	4.0
• Moderate	28	56.0
• Severe	2	4.0

In our study 32(64%) cases showed positive for staining and 18(36%) cases were negative, Majority of them showed moderate intensity of staining 28(56%), 2(4%) cases were mildly stained and 2 (4%)cases were severe stained.

Table 6: ER/PR

ER/PR	Number of patients (n=50)	%
ER+/PR+	32	64.0
ER+/PR-	3	6.0
ER-/PR+	0	0.0
ER-/PR-	15	30.0

Of 50 cases, 32 (64%) were ER+/PR+, 3(6%) were ER+/PR- and remaining 15(30%) were ER-/PR-.

Table 7: Correlation of variables according to ER/PR status

Variables	ER/PR status			P Value
	ER+/PR+ (n=32)	ER+/PR- (n=3)	ER-/PR- (n=15)	
Tubule formation				
• >75% of tumor	14(43.8%)	1(33.3%)	2(13.3%)	0.357
• 10-75% tumor	13(40.6%)	1(33.3%)	8(53.3%)	
• <10 % tumor	5(15.6%)	1(33.3%)	5(33.3%)	
Nuclear pleomorphism				
• Minimal variation in size and Shape of nuclei	15(46.9%)	0(0%)	3(20%)	<0.001**
• Moderate variation in size and shape of nuclei	16(50%)	2(66.7%)	3(20%)	
• Marked variation is size and shape of nuclei	1(3.1%)	1(33.3%)	9(60%)	
Histological (MBR) grade				
• Grade I	2165.6%)	0	0	<0.001**
• Grade II	11(34.4%)	3(100.0%)	11(73.3%)	
• Grade III	0	0	4(26.7%)	

In all the three groups breast lump was the most common presentation. Tubule formation was better with ER +/PR+ group compared to ER-/PR- group. Higher nuclear pleomorphism was seen in ER-/PR- group compared to ER+/PR+ group, which was statistically significant($p<0.001$). In our study mean age among ER+/PR+ group was 49.09±7.79yrs compared to 54.00±5.57yrs in ER+/PR- and 54.80±11.97 in ER-/PR- group. In the entire three groups breast lump was the most common presentation. Tubule formation was better with ER +/PR+ group compared to ER-/PR- group. Higher nuclear pleomorphism was seen in ER-/PR- group compared to ER+/PR+ group, which was statistically significant ($p < 0.001$).

Table 8: Correlation of Histological features according to ER/PR status

Variables	ER/PR status			
	ER+/PR+ (n=32)	ER+/PR- (n=3)	ER-/PR- (n=15)	
Size (cm)				
• <2.0 square cm	1(3.1%)	0(0%)	1(6.7%)	0.208
• 2.0-5.0 square cm	30(93.8%)	2(66.7%)	13(86.7%)	
• >5.0 square cm	1(3.1%)	1(33.3%)	1(6.7%)	
Mitotic score /10 hpf				
• 0-5	13(40.6%)	1(33.3%)	5(33.3%)	0.558
• 6-10	14(43.8%)	2(66.7%)	2(13.3%)	
• >11	5(15.6%)	0(0%)	3(20%)	
Histological variability				
• Deep surgical margin	0(0%)	0(0%)	1(6.7%)	0.360
• Paget`s disease	0(0%)	0(0%)	1(6.7%)	0.360
• Necrosis	14(43.8%)	1(33.3%)	6(40%)	1.000
• Fibrocystic change	7(21.9%)	1(33.3%)	9(60%)	0.021*
• Desmoplasia	14(43.8%)	0(0%)	5(33.3%)	0.358
• Calcification	7(21.9%)	2(66.7%)	7(46.7%)	0.086+
• Lymphatic Invasion	6(18.8%)	1(33.3%)	5(33.3%)	0.389
• Perineural invasion	0(0%)	0(0%)	2(13.3%)	0.203
• Vascular invasion	6(18.8%)	0(0%)	7(46.7%)	0.097+

There was no difference in tumor size between the three groups. There was no significant difference between three groups with respect to mitotic rate. Fibrocystic changes was more common among ER-/PR- group which was statistically significant ($p<0.021$). Vascular invasion, calcification, lymphatic invasion and perineural invasion were more common among ER-/PR- group but it was not statistically significant. Desmoplasia and necrosis were more common among ER+/PR+ group but it was not statistically significant.

DISCUSSION:

Breast cancer being 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 becoming mandatory markers among them. So, we took to study these important prognostic markers and correlate with the histological grading of breast cancers. In the present study, age at presentation ranged from 32-73 years with a mean age of 51.10 years, similar observation was made by Joshi K et al [5]. In the present study 45(90%) tumors were 2-5cms, which was in comparison to other studies. In the present study 46(92.0%) were Invasive ductal carcinoma (NOS). Similar observation was made by Peiro G et al [6], Zafrani B et al[7] and Onitilo AA[8] et al. Other types of carcinomas had varied incidence in different studies.

Table 9: Histological grading in comparison with other studies

Authors	Grade I %	Grade II %	Grade III %
Zafrani B.et al	27.0	40.0	33.0
Le Doussal et al	11.0	55.0	34.0
Onitilo AA.et al	21.2	38.4	35.9
Peiro G et al	28.5	37.1	34.4
Present study	42.0	50.0	8.0

In the present study, histological grading was done using modified Bloom Richardson grading, majority 50% were grade II. Similar observation was made by Zafrani B et al[7], Le Doussal et al, Onitilo AA et al[8] and Peiro G et al[6]. In our study lymph node metastases was seen in 24% which was in comparison with study by Onitilo AA et al[8]

Table 10:ER and PR positive status in comparison with other studies

Immunohistochemical subtypes	R.Kim et al %	Dunnwald KL et al %	Nadji M et al %	Present study
ER+/PR+	62.1	63	55	64
ER+/PR-	12.3	13	20	6
ER-/PR+	5.0	3	0	0
ER-/PR-	20.5	21	25	30

Present study data are consistent with those of other published studies like those of R. Kim et al [9] and Lisa K D et al [10], in that ER and or PR expression was seen in around 64% of patients. Lal P et al, Ayadi L et a [11] and other studies in literature demonstrated high ER, PR positivity with IDC (NOS), papillary carcinomas and mucinous carcinomas. Results of our study were comparable with other studies. In our study histologic grading in correlation with ER/PR positivity was found to be statistically significant ($p < 0.001$). Among ER+/PR+ group 65.6% were grade 1, 34.4% were grade 2 and none of them were grade 3. Among ER+/PR- all were grade 2. Among ER-/PR- group 73.3% were grade 2 and 26.7% were grade 3 and none of them were belong to grade 1. In our study histologic grading in correlation with ER positivity was found to be statistically significant ($p < 0.001$). Among ER+ group 60% were grade 1, 40% were grade 2 and none of them were grade 3. Among ER- group 73.3% were grade 2 and 26.7% were grade 3 and none of them were belong to grade 1. In our study histologic grading in correlation with ER positivity was found to be statistically significant ($p < 0.001$). Among PR+ group 65.6% were grade 1, 34.4% were grade 2 and none of them were grade 3. Among PR- group 77.8% were grade 2 and 22.2% were grade 3 and none of them were belong to grade 1. In study by Nadji M et al[12] among infiltrating ductal carcinomas of no special type, all nuclear grade 1 tumors contained ER, where only 2.0% of nuclear grade 3 carcinomas showed ER positivity.

Table 11:Correlation of histological grade according to ER/PR status

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

In study by Dunnwald KL et al[10] among grade 1 tumors 81.1% were ER+/PR+ and only 4.1% were ER-/PR-, where as among grade tumors 39.1% were ER-/PR- and only 44.4% were ER+/PR+. Results of our study were comparable to other studies.

CONCLUSION:

In the recent years there have been outstanding advances in breast cancer diagnosis and management leading to earlier detection of disease and the development of more effective treatment. This has resulted in improved quality of life with significant decline in breast cancer deaths for those women living with the disease. Prognosis and management of breast cancer are influenced by classic variables such as histological type and grade, tumor size, lymph node status, status of hormone receptors- ER and PR. In this study an attempt was made to understand the correlation of ER and PR status with histopathological grading and clinicopathological parameters. In conclusion, ER and PR status correlates well with histopathological grading and other clinico-pathological parameters. Higher grade is associated with ER/PR negativity. Hence, immunohistochemical assessment of ER and PR status should be incorporated as a routine investigation. This along with histopathological grading will guide the clinicians to make correct choice of treatment protocols and helps in improved quality of life.

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