

Research Article

A study of correlation of expression of ER, PR and HER2/neu receptor status with clinico-pathological parameters in breast carcinoma at a tertiary care centre

P. Urmila Devi¹, Uma Prasad¹, A. Bhagya Lakshmi^{1*}, G. Santa Rao²

¹Department of Pathology, Andhra Medical College/King George Hospital, Visakhapatnam, A.P., India

²Department of Surgery, Andhra Medical College/King George Hospital, Visakhapatnam, A.P., India

Received: 17 November 2014

Accepted: 8 December 2014

*Correspondence:

Dr. A. Bhagya Lakshmi,

E-mail: dr.a.bhagalaxmi@gmail.com

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ABSTRACT

Background: In English literature it is documented that the expression of ER and PR is low in Asian countries when compared to that of Western countries. HER2/neu over expression is uniform throughout the world. Studies have shown that triple-negative breast carcinomas are aggressive, likely to spread beyond the breast and recur after treatment. Aims and objectives: To correlate the expression of ER, PR and HER 2/neu with clinico-pathological parameters in infiltrating ductal carcinoma and other variants of breast carcinoma. To determine the clinicopathological parameters in triple negative cases.

Methods: This is a prospective study for a period of two years in the Department of Pathology, Andhra Medical College, a tertiary care centre. We received 111 mastectomy specimens during this period out of which 52 patients were funded under Arogyasri and were subjected for ER, PR, HER2/neu receptor study.

Results: In the present study total cases analyzed were 52. Infiltrating ductal carcinoma was 41/52 (78.84%) and other variants were 11/52 (21.15%). In our institute infiltrating duct cell carcinoma (NOS) type was the commonest type of carcinoma breast with significant group occurring in less than 45 years of age, 95 % of women were multipara with two or more children and triple negative tumors being 54.83%. In infiltrating ductal carcinoma ER, PR positive expression has no association with age and size of tumor. Their expression was higher in grade 1 tumors 83.3%. The ER, PR negative expression was more in size of tumor being greater than 2 cm; (92.5%), positive lymph nodes (51.8%) and stage II and stage III tumors (96.2%). HER2/neu negative expression was seen in 51.61% of cases. Triple negative receptor expression was seen in 54.83% of infiltrating ductal carcinoma. In the English literature medullary carcinoma is negative for HER2/neu expression but in the present study in 2 cases the expression for HER2/neu was positive.

Conclusion: In the present study significant group occurred in less than 45 years of age presenting in advanced stage of the disease. Triple negative cases were seen in 54.8% cases of infiltrating duct cell carcinoma indicating bad prognosis.

Keywords: Breast carcinoma, Clinicopathological parameters, Hormonal status, Triple negative cases

INTRODUCTION

Breast carcinoma is a heterogenous disease, with wide variation in clinical behavior. Breast carcinoma is no longer seen as a single disease but rather as a multifaceted disease comprised of distinct biological

subtypes with diverse natural history. Carcinoma breast has a varied spectrum of clinical, pathological and molecular features with different prognostic and therapeutic implications. The biological nature of the disease and clinical outcome are closely inter-linked. Over the last few decades there have been outstanding

advances in breast carcinoma management leading to earlier detection of disease and the development of more effective treatments resulting in significant decline in breast carcinoma deaths.

Because the hormonal receptors are well-known predictive factors of the response to the hormonal therapy in mammary carcinoma, their evaluation through immunohistochemical methods is absolutely necessary. The assessment of prognostic factors, in order to provide a prediction of outcome, has become an essential part of the histopathologist's role in the handling and histological reporting of invasive breast carcinomas.

Although many markers have been evaluated, it is well known that ER, PR and HER-2 expression is most useful in predicting response to therapy. In English literature it is documented that the expression of ER and PR is low in Asian countries when compared to that of Western countries. HER2/neu over expression is uniform throughout the world. Studies have shown that triple-negative breast carcinomas are aggressive, likely to spread beyond the breast and recur after treatment.

In the present study an attempt was made to evaluate the expression of HER-2/neu, Estrogen Receptor (ER) and Progesterone Receptors (PR) in breast carcinoma and to compare it with other prognostic parameters such as histological type and grade, tumor size, patients' age, and lymph node metastases.

METHODS

This is a prospective study for a period of two years at the department of Pathology, in a tertiary care centre. We received 111 mastectomy specimens during this period out of which 52 patients were funded under Arogyasri and were subjected for ER, PR, HER2/neu receptor study.

Specimens were thoroughly grossed according to standard protocol. The following data was recorded-tumor size, infiltration of the tumor to nipple and areola, posterior margin, adjacent breast changes, number of lymph nodes involved and size of lymph nodes. Relevant clinical data and demographic particulars were recorded.

Tissue was subjected to routine processing and sections were stained with H&E. The histopathological sections were diagnosed basing on WHO classification, and graded adopting Modified Blooms Richardson grading system.

The paraffin blocks were subjected to ER, PR, HER 2/neu receptor study.

Specimens have been processed by the HRP polymer method. Protein retrieval has been done by microwave technique. The following antibody clones have been used.1. Mouse anti-human estrogen receptor alpha clone

1D5, 2. Mouse anti-human progesterone receptor clone PgR636, 3. Rabbit anti-human c-erb-2 oncoprotein.

Staining pattern for ER and PR is confined to the nucleus. A positive staining is defined when more than 10% of cells take up the nuclear stain of any intensity. Breast ductal epithelial cells act as internal controls. Staining pattern for HER2/neu is confined to the cell membrane. The staining pattern was compared with the control slides provided by the company

ER, PR staining was quantified by using Allred score.¹² All the slides were quantified by giving proportional score based on the percentage of cells showing nuclear stain and intensity score based on intensity of staining.

The Proportional Score (PS) is as follows:

1. 1% of cells showing nuclear stain
2. 10% cells showing nuclear stain
3. 33% cells showing nuclear stain
4. 66% cells showing nuclear stain
5. 100% cells showing nuclear stain

Intensity score (IS) is as follows:

- 0 - Negative
- 1 - Weak staining
- 2 - Intermediate staining
- 3 - Strong staining

Total Score (TS): sum of proportional score + intensity score.

Total score greater than 2 is considered positive for significant expression of ER and PR.

Immunohistochemical assessment of HER2/neu overexpression was graded as

Table 1: Immunohistochemical assessment of HER2/neu overexpression grading.

Score report	HER2 protein assessment	Staining pattern
0	Negative	No staining is seen or membrane staining in <10% of invasive tumour cells
1+	Negative	Faint/barely perceptible membrane staining detected in >10% of invasive tumour cells
2+	Equivocal	Weak to moderate complete membrane staining in >10% of invasive tumour cells or <30% with strong complete membrane staining
3+	Positive	Strong complete membrane staining in >30% of invasive tumour cells

HER2/neu over expression more than 30% (score 3+) is considered as positive. In equivocal cases (score 2+) has to be confirmed by FISH. P value was calculated for individual prognostic markers using Chi-square test and results were tabulated.

RESULTS

In the present study total cases analyzed were 52. Infiltrating ductal carcinoma was 41/52 (78.84%) and other variants were 11/52 (21.15%).

In the present study the various clinico-pathological parameters in 41 cases of infiltrating ductal carcinoma were analyzed. The age range of occurrence of carcinoma breast was between 23 to 80 years. The mean age was 51.5 years. 22/41 (53.6%) cases were seen in perimenopausal and menopausal age group with 19/41 (46.3%) of cases occurred below 45 years of age and the youngest being 29 years.

Out of 41 cases with infiltrating ductal carcinoma 40/41 (97.5%) was seen in females and one case occurred in male. Nulliparity is considered as a risk factor for carcinoma breast but in the present study 33/39 (80.4%) cases of infiltrating ductal carcinoma had children less than 2 and 6/39(14.6%) had children more than 2 in number. One case had history of nulliparity.

The size of tumor was more than 2 cm in 37/41(90.2%) of cases. The grade of tumor was well differentiated (grade 1) (Figure 1, 2) in 28/41 (68.2%) and grade 2 in 9/41 (21.9%) and grade 3 in 4/41 (9.75%) of cases.

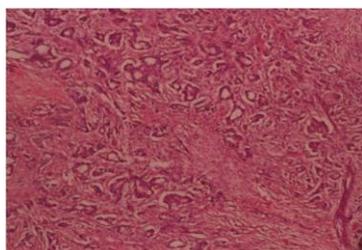


Figure 1: Duct cell carcinoma (NOS) type with tubules, (Grade 1) (H&E; 100x).

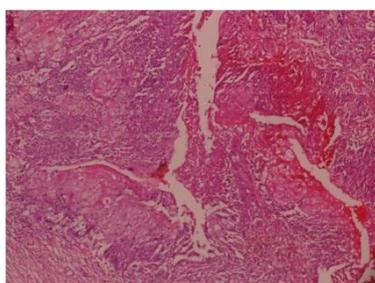


Figure 2: Mataplastic carcinoma - Ductal epithelial cells with squamoid change showing abundant eosinophilic cytoplasm, nucleus with prominent nucleoli and keratin material (H&E; 100x).

Metastatic lymph nodes was seen in 22/41 cases (53.6%) with less than 4 lymph nodes involved in 12/22 (54.5%) of cases. Out of 22 cases with positive lymph nodes 81.8% showed vascular invasion and necrosis was seen in 90.9% of cases. In the present study 26/41 (63.4%) and 12/41 (29.2%) presented with stage I and stage II disease respectively (Table 2).

Table 2: Clinico-pathological parameters in infiltrating ductal carcinoma - 41 cases.

Clinical pathological parameters	Number of cases	Percentage
Age		
≤45 years	19	46.3
>45 years	22	53.6
Parity		
≤2 children	33	80.4
>2 children	06	14.6
Tumor size		
≤2 cm	04	9.75
>2 cm	37	90.2
Histological grade		
Grade 1	28	68.2
Grade 2	09	21.9
Grade 3	04	9.75
Vascular invasion	11	26.8
Necrosis	16	39
Lymph node metastasis		
Negative	19	46.3
Positive	22	53.6
Number of lymph nodes involved		
≤4 lymph nodes	12	54.5
>4 lymph nodes	10	45.4
Size of lymph nodes		
≤2 cm	16	72.7
>2cm	06	27.2
AJCC staging		
Stage I	03	7.3
Stage II	26	63.4
Stage III	12	29.2
Stage IV	Nil	Nil

Out of 41 cases of infiltrating ductal carcinoma positive expression of both ER and PR was seen in 12/41 (29.2%) of cases (Figure 3, 4). In 27/41 (65.8%) showed negative expression of both ER and PR. One case each showed ER positive and PR negative expression and ER negative and PR positive expression. 10/41 (24.3%) showed HER2/neu membrane positivity with score of 2+ meaning equivocal reaction, which has to be confirmed by FISH. HER2/neu membrane positivity with score 3 is shown in 5/31 (16.1%) (Figure 5) and negative expression in 16/31 (51.61%) of cases (Table 3).

On correlating ER and PR expression of infiltrating ductal carcinoma with various clinico-pathological

parameters, the observations in the present study was that ER, PR positive expression has no association with age and size of tumor. Their expression was higher in grade 1 tumors 10/12 (83.3%). The ER,PR negative expression was more in size of tumor being greater than 2 cm; 25/27 (92.5%), positive lymph nodes 14/27 (51.8%) and stage II and stage III tumors being 26/27 (96.2%) (Table 4).

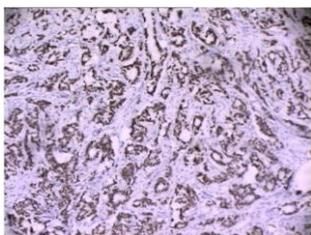


Figure 3: Duct cell carcinoma NOS showing ER positive nuclear staining (IHC-100x).

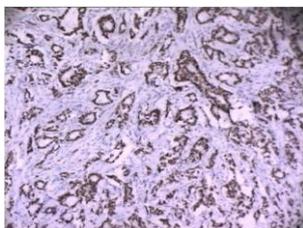


Figure 4: Duct cell carcinoma NOS showing PR positive nuclear staining (IHC-100x).

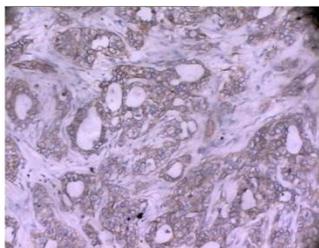


Figure 5: Duct cell carcinoma NOS showing HER2/neu membrane staining (IHC-100x).

Table 3: Expression of ER, PR and HER2/neu in cases of infiltrating ductal carcinoma - 41.

	Number of cases	Percentage
ER expression/PR expression		
ER+/PR+	12	29.2
ER+/PR-	01	2.4
ER-/PR+	01	2.4
ER-/PR-	27	65.8
	41	
HER2/neu		
Positive	05	12.19
Negative	26	63.41
Equivocal	10	24.39
	41	

Table 4: Correlation of ER, PR expression with clinico-pathological parameters in infiltrating ductal carcinoma.

Clinico-pathological parameters	ER+/PR+ (N=12)	ER-/PR- (N=27)	P value
Age			
≤45 years	06	13	0.91
>45 years	06	14	
Tumor size			
≤2 cm	02	02	0.37
>2 cm	10	25	
Histological grade			
Grade 1	10	17	0.71
Grade 2	01	07	
Grade 3	01	03	
Lymph node metastasis			
Negative	05	13	0.34
Positive	07	14	
Number of lymph nodes involved			
≤4 lymph nodes	05	07	0.78
>4 lymph nodes	02	07	
AJCC staging			
Stage I	02	01	0.60
Stage II	06	19	
Stage III	04	07	
Stage IV	00	00	

Out of 41 cases with diagnosis of infiltrating duct cell carcinoma in 10 cases the expression of HER2/neu was equivocal. Excluding them in 31 cases, HER2/neu over expression was seen in 5/31(16.1%) of cases and HER2/neu negative expression in 16/31(51.61%) of cases. Out of 41 cases with diagnosis of infiltrating duct cell carcinoma in 10 cases the expression of HER2/neu was equivocal. On correlating the HER2/neu negative expression with clinic pathological parameters, negative expression was seen in the age group more than 45 years; 15/26 (57.6%), tumor size more than 2 cm; 24/26 (92.3%) grade 1 tumors; 19/26 (73%), positive lymph nodes 14/26(53.8%) and stage II , stage III tumors being 24/26 (92.3%) (Table 5).

Out of 41 cases of infiltrating ductal carcinoma in 10 cases HER2/neu is equivocal. Excluding them in 31 cases the combined expression was ER+/PR+/HER2 -ve: 9/31 (29.0%), ER-/PR-/HER2/neu +ve: 5/31 (16.12%), ER-/PR-/HER2-ve (Triple negative): 17/31 (54.83%). Out of 17 cases of infiltrating duct cell carcinoma which were triple negative, the clinic pathological parameters in these cases were greater number of cases were in age more than 45 years; 12/17 (70.5%), tumor size greater than 2cm; 16/17 (94.1%), grade 1 tumors 12/17 (70.5%), positive lymph nodes 9/17 (52.9%), number of lymph nodes more than 4;5/17 (29.4%) and stage II, stage III tumors being 16/17 (94.1%) (Table 6).

Table 5: Correlation of HER2/neu expression with clinico-pathological parameters in infiltrating ductal carcinoma.

Clinico-pathological parameters	HER2/neu +ve(N=5)	HER2/neu -ve(N=26)	P value
Age			
≤45 years	02	11	0.10
>45 years	03	15	
Tumor size			
≤2 cm	00	02	0.4
>2 cm	05	24	
Histological grade			
Grade 1	02	19	0.04
Grade 2	01	06	
Grade 3	02	01	
Lymph node metastasis			
Negative	02	12	0.8
Positive	03	14	
Number of lymph nodes involved			
≤4 lymph nodes	01	07	0.2
>4 lymph nodes	02	07	
AJCC staging			
Stage I	00	02	0.7
Stage II	03	15	
Stage III	02	09	
Stage IV	00	00	

Table 6: Clinico-pathological parameters in triple negative cases.

Clinico-pathological parameters	Triple negative cases (N=17)
Age	
≤45 years	05
>45 years	12
Tumor size	
≤2 cm	01
>2 cm	16
Histological grade	
Grade 1	12
Grade 2	05
Grade 3	00
Lymph node metastasis	
Negative	08
Positive	09
Number of lymph nodes involved	
≤4 lymph nodes	04
>4 lymph nodes	05
AJCC staging	
Stage I	01
Stage II	11
Stage III	05

Luminal type A tumor is ER and PR positive with HER2/neu-negative expression associated with low or

moderate tumor grade; 11/41(26.8%). In the present study basal like (triple negative tumor) were 17/41 (41.4%) being the commonest molecular subtype (Table 7).

Table 7: Molecular subtypes.

Molecular subtypes	Number of cases	Percentage
Luminal type A	11	26.8
Luminal type B	00	00
Basal like	17	41.4
HER2/neu	05	12.1

Medullary carcinoma (Figure 6), mucinous carcinoma (Figure 9) tubular carcinoma are grade 1 tumors and more commonly seen beyond 45 years of age 8/11 (72.7%). One case of male breast carcinoma was seen with histopathological diagnosis of tubular carcinoma (Figure 11, 12, 13, 14, 15). The tumor size was more than 2 cm in all these cases. 9/11 (81.8%) were negative for lymph nodes with 2 cases showing metastatic lymph nodes. 10/11 (90.9%) presented with stage II disease (Table 8).

Triple negative receptor expression was seen in metaplastic carcinoma, invasive papillary carcinoma (Figure 10) and invasive lobular carcinoma (Figure 8). In the English literature medullary carcinoma is negative for HER2/neu expression but in the present study in 2 cases the expression for HER2/neu was positive (Table 9) (Figure 7).

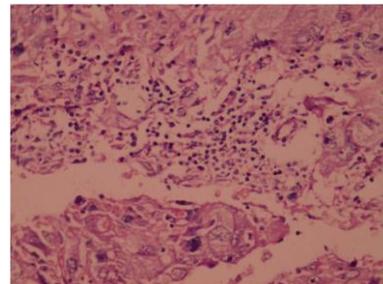


Figure 6: Medullary carcinoma with tumour cells arranged in syncytial sheets with lymphocytic aggregates. (H&E; 100x).

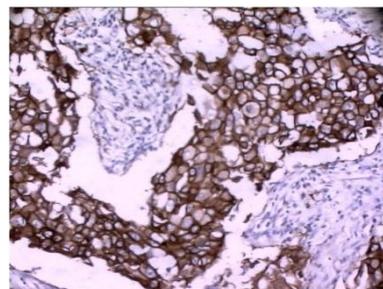


Figure 7: Medullary Carcinoma showing HER2/neu Membrane staining strong positive-3+ (IHC; 100x).

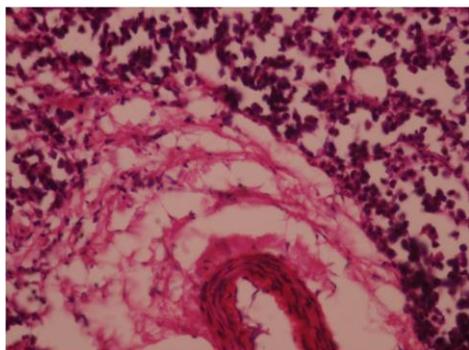


Figure 8: Lobular carcinoma showing small round uniform cells with targetoid pattern (H&E; 100x).

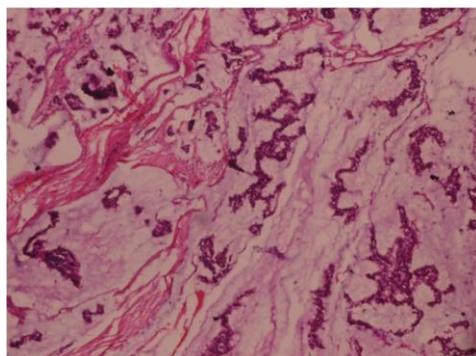


Figure 9: Mucinous carcinoma showing tumour cells with uniform round hyperchromatic nuclei floating in mucin pools (H&E; 100x).

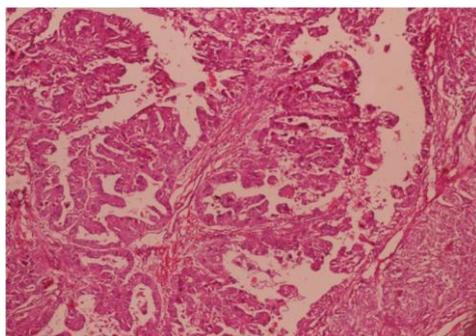


Figure 10: Papillary carcinoma show tumour cells arranged in papillary fronds with pleomorphic nuclei and abundant eosinophilic cytoplasm (H&E; 100x).

Table 8: Other variants of carcinoma breast-11 cases.

Other variants of carcinoma breast	Number of cases	Percentage
Medullary carcinoma	04	36.3
Tubular carcinoma	02	18.1
Invasive lobular carcinoma	01	9.09
Metaplastic carcinoma	02	18.1
Invasive papillary carcinoma	01	9.09
Mucinous carcinoma	01	9.09

Table 9: Clinico-pathological parameters and expression of ER,PR and HER2/neu in other variants of carcinoma breast - 11 cases.

Clinical pathological parameters	Number of cases	Percentage
Age		
≤45 years	03	27.2
>45 years	08	72.7
Parity		
≤2 children	07	63.6
>2 children	03	27.2
Tumor size		
≤2 cm	00	00
>2 cm	11	100
Vascular invasion	01	9.09
Necrosis	02	18.1
Lymph node metastasis		
Negative	09	81.8
Positive	02	18.1
Number of lymph nodes involved		
≤4 lymph nodes	01	9.09
>4 lymph nodes	01	9.09
Size of lymph nodes		
≤2 cm	01	9.09
>2cm	01	9.09
AJCC staging		
Stage I	00	00
Stage II	10	90.9
Stage III	01	9.09
Stage IV	00	00
ER/PR/HER2/neu status		
ER+/PR+	02	18.18
ER-/PR-	09	81.81
HER2/neu positive	02	18.18
HER2/neu negative	09	81.81



Figure 11: Clinical photograph of male carcinoma breast.



Figure 12: Gross of male carcinoma breast.

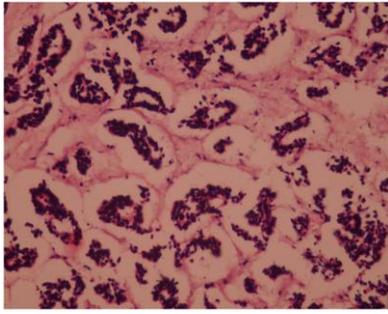


Figure 13: Tubular carcinoma male breast showing round tumor cells arranged in tubules with angulations (H&E; 100x).

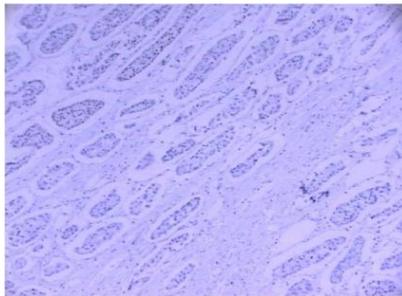


Figure 14: Tubular carcinoma with ER positive in 10% of cells (IHC - 100x).

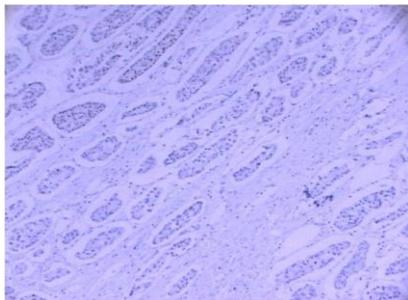


Figure 15: Tubular carcinoma with PR positive in 10% of cells (IHC - 100x).

DISCUSSION

Breast cancer accounts for 19-34% of all cancer cases among women nationally. As per the data from national and regional cancer registries, it is the commonest cancer and is listed as the second leading site among women. The age-standardized incidence rates vary from 9-28.6 per 100000 women, the lowest being from the rural area-based registry Barshi. The majority of the patients seek medical advice when the disease is fairly advanced. Early breast carcinoma constitutes only 30% of the breast cancer cases seen at regional cancer centers in India, whereas it constitutes 60-70% of cases in the developed world. There is no prospective or retrospective published case series on early carcinoma of breast from India. There is a paucity of data regarding breast carcinoma in the developing world; hence individual institutes should have

the knowledge of the various clinico-pathological parameters of carcinoma breast specific for their region.

In the present study 52 mastectomy cases were assessed for clinico-pathological parameters and for expression of estrogen, progesterone receptors and over expression of human epidermal growth factor receptor 2. Out of 52 cases of carcinoma breast 41 (78.8%) were infiltrating duct cell carcinoma and other variants were 11 (21.1%).

Clinico-pathological parameters in infiltrating ductal carcinoma

In the present study the mean age at presentation of carcinoma breast was 51.5 years. 54% of cases occurred in the post-menopausal age group with 46% occurring less than 45 years of age. In the study by Lobna Ayadi et al.¹ 51.6% of cases occurred in less than 50 years of age with median age of 51 years and 46% of cases occurred in less than 45 years. In the study by Vinod Raina et al.² 49.7% of cases occurred in less than 45 years and 48.5% cases in greater than 45 years. In the study by Sunita Saxena et al.³ of New Delhi reported that the median age of occurrence of carcinoma breast was 47.8 years.

In English literature one of the major risk factor for carcinoma breast is nulliparity. In the present study out of 52 cases only one case had history of nulliparity and two cases were men with carcinoma breast. Women with less than or equal to two children were 80.4% and more than two children were 14.6%. The size of the tumor greater than 2 cm in the present study was 90% and less than 2cm was 10%. In the study by Menaka DS. Lokuhetty et al.⁴ 58% cases had size of tumor more than 2 cm. Lobna Ayadi et al.¹ documented in their study that in 12.9% the size of tumor was less than 2cm and in 87% greater than 2 cm. Lakmini KB. Mudduwa et al.⁵ in their study reported that 14.5% of tumors was less than 2 cm and in 85.5% the tumor was more than 2 cm. In the study by Zubair Ahmed et al.⁶ the tumor size was less than 2 cm in 7.5% of cases and 92.4% of cases with tumor size more than 2 cm.

The commonest histological type was infiltrating duct cell carcinoma (NOS) type constituting 78.8% of cases in the present study. In the studies by Vinod Raina et al.,² Menaka DS. Lokuhetty,⁴ Lobna Ayadi et al.¹ were 92.8%, 86.3% and 83.8% respectively. Infiltrating duct cell carcinoma is graded using modified Bloom Richardson grading system into three grades. In the present study grade 1 tumors were 68.2%, grade 2 tumors were 21.9% and 9.75% tumors were grade 3. In the study by Zubair Ahmed et al.⁶ of Karachi Pakistan documented 4.17 % as grade 1 tumors, grade 2 were 75.83% and grade 3 tumors as 20%. Lakmini KB. Mudduwa et al.⁵ reported 14.6% as grade 1 tumors, 36.4% as grade 2 tumors and 49% as grade 3 tumors. The grade 1, grade 2 and grade 3 tumors in the study by Lobna Ayadi et al.¹ was 10.9%, 63.2% and 25.8%.

In the present study lymph node metastasis in infiltrating duct cell carcinoma was seen in 53.6% of cases and negative for metastasis in 46.3% of tumors. In 72.7% of cases the size of lymph nodes was less than 2 cm with 27.2% showing lymph node size of more than 2 cm. The number of lymph nodes positive for metastasis, less than 4 in number was 55% and those more than 4 were 45%. In the studies by various authors like Zubair Ahmed et al.,⁶ Lakmini KB. Mudduwa et al.,⁵ Seho Park et al.,⁷ Lobna Ayadi et al.¹ and Menaka DS. Lokuhetty⁴ documented lymph nodes positive for metastasis as 74.77%, 57.7%, and 27.8%, 65% and 41% respectively. Vascular invasion was seen in 26.8% of cases in the present study and out of these cases with vascular invasion, 81.8% of cases showed lymph node metastatic deposits. In the study by Zubair Ahmed et al.⁶ vascular invasion was seen in 35.8% of cases. Tumor necrosis was seen in 39% of cases in the present study and commonly associated with moderate and high grade tumors. In these cases with tumor necrosis lymph node metastasis was seen in 62.5% of cases with 60% of the involving more than 4 lymph nodes. In the study by Zubair Ahmed et al.⁶ tumor necrosis was seen in 63.33 % of cases.

In the present study 63.4% of the tumors presented in stage II disease, 29.2% in stage III disease and 7.3% in stage I disease. In the study by Vinod Raina et al.² stage III tumors were 35.2%.

Clinico-pathological parameters in other variants of carcinoma breast

In the present study medullary carcinoma constituted 7.69%, tubular carcinoma 3.8%, invasive lobular carcinoma 1.9%, metaplastic carcinoma 3.8%, invasive papillary carcinoma 1.9% and mucinous carcinoma in 1.9% of cases. Vinod Raina et al.² documented 2.9% of lobular carcinoma, medullary carcinoma 1.4% and Lobna Ayadi et al.¹ reported 3, 8% of invasive lobular carcinoma, 3.2% mucinous carcinoma and 0.6% as metaplastic carcinoma. In the present study a case of tubular carcinoma and a case of infiltrating duct cell carcinoma was seen in male breast. These non-ductal tumors were more common in the age group of more than 45 years (72.7%). All the cases showed tumor size of more than 2 cm. Eighty one percent of cases did not show lymph node metastasis and 90.9% of cases presented in stage II.

Hormonal receptor status and HER2/neu overexpression in infiltrating duct cell carcinoma and other variants of carcinoma breast

The ER and PR expression in the present study is as follows; ER+/PR+ tumors were 29.2%, ER+/PR- were 2.4%, ER-/PR+ were 2.4% and ER-/PR- were 65.8%. The expression of both ER and PR receptors was seen in 83.3% of grade 1 tumors, 66.6% in stage I and stage II tumors, 41.6% in metastatic lymph nodes less than 4 in number in the present study. One case of tubular

carcinoma and one case of mucinous carcinoma was ER+ and PR +. Significant association of ER, PR expression was not seen with size of the tumor and age of presentation. ER+/PR+ expression documented in the studies by Vinod Raina et al.,² Menaka DS. Lokuhetty⁴ and Lobna Ayadi et al.¹ was 53.7%, 31.7%, 55.8% respectively.

In the present study out of 41 cases of infiltrating duct cell carcinoma 5 cases (12.1%) showed HER2/neu over expression. Twenty six cases (63.4%) showed negative expression and 10 cases (24.3%) showed equivocal expression. HER2/neu negative expression was seen in age greater than 45 years 11/16 (68.75%), tumor size greater than 2 cm; 15/16 (93.75%), grade 1 tumors 12/16 (75%), positive lymph nodes 8/16 (50%), number of lymph nodes more than 4; 4/16 (25%) and stage II, stage III tumors being 15/16 (97.75%). HER2/neu over expression is seen in two cases of medullary carcinoma, two cases of tubular carcinoma and three cases of metaplastic carcinoma. HER 2/neu expression was inversely related to expression of ER and PR. In four cases with ER+ and PR+ the HER2/neu expression is equivocal which needs confirmation by FISH which was not possible in our institute. The HER2/neu over expression in various studies was Menaka DS. Lokuhetty et al.⁴ was 14.5%, Lobna Ayadi et al.¹ was 18% and Lakmini KB. Mudduwa et al.⁵ was 19.1%.

The combined expression of ER/PR and HER2/neu in the present study was as follows; ER+/PR+/HER2 -ve: 9/31 (29.0%), ER-/PR-/HER2/neu +ve: 5/31 (16.12%), ER-/PR-/HER2-ve (Triple negative): 17/31 (54.83%). In the study by Mohd Shafi Moona et al.⁸ triple positive was seen in 15% of cases and triple negative in 15% of cases. The observations in various studies were Lakmini KB. Mudduwa et al.⁵ ER-/PR-/HER2/neu+; 69.2%, Adedayo et al.⁹ ER+/PR+/HER2/neu-; 68.9%, ER-/PR-/HER2/neu+; 7.5%, triple negative in 13.4% of cases. In the study by Lobna Ayadi et al.¹ the ER-/PR-/HER2/neu+ was 33.3% and triple negative in 21.9% of cases. Aye Thike et al.¹⁰ reported triple negative cases as 13% in their study.

On analyzing these triple negative cases 38.7% were seen in age greater than 45 years, 51.6% with tumor size greater than 2 cm, 29% cases showing lymph node metastasis. In 55.5% of cases with positive nodes more than 4 lymph nodes involved. Thirty nine percent tumors were grade 1 and 51.6% of tumors were in stage II and stage III disease. The molecular subtypes in the present study were luminal type A constituted 26.8%, Basal like 41.4% and HER2/neu type was 12.1%.

Estrogen receptor negative and triple negative breast carcinoma carry poor prognosis and are not amenable to hormone therapy. It is observed in literature that Indian patients with carcinoma breast have a higher tendency to have these with negative expression, which is also observed in the present study. Suraj Manjunath et al.¹¹ in

his study has documented the probable reasons for occurrence of such tumors with variable biological behavior. He suggested that the patients in India are about one decade younger than that of the west, which contributes to high ER negativity as younger patients tend to have more ER negative and more triple negative tumors. In India the patients often present at advanced stage of breast carcinoma, in which ER negativity is likely to be higher.

CONCLUSION

Infiltrating duct cell carcinoma (NOS) type was the commonest type of carcinoma breast in our institute with significant group occurring in less than 45 years of age. 95 % of women were multipara with two or more children. ER and PR positive expression was seen in grade 1 tumors and negative expression was seen with tumor size more than 2cm, positive lymph nodes and higher stage of disease. HER2/neu negative expression was seen in the post-menopausal age group, tumor size more than 2 cm, positive lymph nodes and higher stage of disease indicating bad prognosis. HER2/neu expression was inversely related to ER and PR expression. HER2/neu expression was seen in 50% of medullary carcinoma which is rare. Triple negative cases were seen in 54.8% cases of infiltrating duct cell carcinoma indicating bad prognosis.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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DOI: 10.5455/2320-6012.ijrms20150129

Cite this article as: Urmila Devi P, Prasad U, Bhagya Lakshmi A, Santa Rao G. A study of correlation of expression of ER, PR and HER2/neu receptor status with clinico-pathological parameters in breast carcinoma at a tertiary care centre. Int J Res Med Sci 2015;3:165-73.