International Journal of Applied Research

Dr. Mahesh C Patil
MD Pathology, Associate
Professor, Department of
Pathology, Vishwabharti
Medical College, Kurnool,
Andhra Pradesh, India

Dr. Saurabh Shrivastava
MD Pathology, Consultant
Pathologist, Sunrise Diagnostic
Lab, Gwalior, Madhya
Pradesh, India

Hormone receptor (ER, PR) status in breast carcinoma – correlation with clinicopathological prognostic parameters

Dr. Mahesh C Patil and Dr. Saurabh Shrivastava

Abstract
Background: Breast is one of the most common cause of death in women. Earlier diagnosis and treatment with appropriate therapy based on hormonal status leads to a reduction in mortality rate. Aim of this study is to assess the hormone receptor status in breast carcinomas and to compare them with other clinical and pathological parameters.
Materials and Methods: This retrospective study was conducted in Department of Pathology, Vishwabharti Medical College, Kurnool, A.P. for a period of 2 years. A total of 52 cases were studied and IHC were done. ER, PR status of patients were studied and compared with other parameters.
Results: Majority of cases were in postmenopausal women. Clinical stage 2 and histological grade 2 cases were more in number. There was significant correlation between clinical staging and NPI sore and between tumor grade and ER, PR status.
Conclusion: ER, PR status has significant correlation with histological grading but does not have significant correlation with clinical staging. So, irrespective staging and other clinical parameters hormonal studies should be conducted in all cases to reduce mortality and recurrences.

Keywords: Carcinoma breast, grading, staging

Introduction
Breast cancer is common worldwide and has relatively high morbidity and mortality although a large proportion of breast carcinomas are detected by systematic screening by self examination of breast and mammography. In India most of the patients present with palpable cancer and even with lymph node metastasis at the time of their first visit. Stratification of patients according to nodal status and results of estrogen and progesterone receptor (ER, PR) status has assumed a great therapeutic importance. Breast carcinoma has a major impact on the health of women. Cancer of the breast is the most common cancer among women in many regions in India and has overtaken cancer cervix [1].
Prognosis is related to a variety of clinical, pathological and molecular features which includes stage of the carcinoma, histologic type, grade and lymph node metastasis.
Estrogen and progesterone receptors have, with increasing importance, influenced the management of this malignancy [2]. With an established positive correlation of ER and PR with the degree of tumour differentiation, determination of ER and PR status on breast biopsy specimens, prior to therapeutic intervention is advocated as a standard practice [3].
This study is aimed at assessing the hormone receptor status in breast carcinomas and to correlate this reactivity pattern with histologic grade, tumor stage and lymph node metastasis.

Materials and Methods
This is a retrospective study of breast carcinomas conducted in Department of Pathology, Vishwabharti Medical College, Kurnool, A.P. between January 2017 and December 2018. A total of 52 mastectomy specimens were received. A detailed history regarding age, parity, socio economic status, family history and menstrual history were reviewed in all cases.

Inclusion criteria: All female patients who underwent mastectomy irrespective of age and proved to be malignant histologically were included for study.

Correspondence
Dr. Saurabh Shrivastava
MD Pathology, Consultant
Pathologist, Sunrise Diagnostic
Lab, Gwalior, Madhya
Pradesh, India

Exclusion criteria: Excision and incision biopsies, proven to be malignant histologically, were not included in the study.

ER, PR study was done for all 52 cases. All the mastectomy specimens received were properly sliced and fixed in 10% formalin for 18 – 24 hours. Detailed gross examination pertaining to over all size of the specimen, nipple and areola, margin status and nodal status were carefully studied. Histological grading was done by modified Bloom and Richardson scoring system. Representative samples are taken from tumour, margins, nipple and areola and lymph nodes. The tissues were processed in various grades of alcohol and xylene using automated prcessor. Paraffin blocks were prepared and sections of 5micron thickness were cut in microtome using disposable blades and stained with hematoxylin and eosin. Suitable blocks were chosen for IHC. Sections for Immunohistochemistry were also cut in microtome using disposable blades. Slides coated with chrome alum were used. Sections were subjected to antigen retrieval using pressure cooker technique using citrate retrieval solution (pH 6) and then treated by Horse Radish Peroxidase (HRP) polymer techniques.

Scoring system - Scoring done by Quick Score System

Score for proportion staining	Score for staining intensity
0 - No nuclear staining	0 - No staining
1 - < 1% nuclear staining	1 - Weak staining
2 - 1 - 10% nuclear staining	2 - Moderate staining
3 - 11 - 33% nuclear staining	3 - Strong staining
4 - 34 - 66% nuclear staining	
5 - 67 - 100% nuclear staining	

Scores are summed to give a maximum score of 8.

Nottingham Prognostic Index was calculated based on the formula

NPI=0.2x tumor size (in cm)+ lymph node stage(1-3)+ histological grade (1-3) and graded as

NPI Score Prognosis

<3.4 good prognosis

3.4 - 5.4 moderate prognosis

>5.4 poor prognosis

Results

The youngest patient was 32 years old and the oldest patient was 76 years old. Maximum number of cases were seen in 51-60 years age group. Mean age was 57.1 years. 82% of the cases were more than 40 years. Majority of cases 51.8% were postmenopausal. 53.8% of cases were of TNM stage 2. Of the 52 cases 24 (46.1%) had lymph node stage N1, 15 (28.8%) had lymph node stage N2 and 13 (25.1%) had lymph node stage N3. Maximum number of cases are Bloom and Richardson grade 2.

Table 1: Histological gradewise distribution of breast carcinomas

Grade	Number of Cases	Percentages (%)
I	08	15.4
II	35	67.3
III	09	17.3
Total	52	100

Majority of cases (63%) were having moderate prognosis as per NPI score.

Table 2: Correlation of clinical staging with NPI Score

Stages	Good Prognosis	Moderate Prognosis	Poor Prognosis	Percentages (%) out of 52 cases
I	04	05	NIL	17.3
II	03	21	04	53.8
III	01	03	11	28.8
IV	NIL	NIL	NIL	0.00
Total	08 (15.3%)	29 (55.8%)	15(28.9%)	100

There is statistically significant correlation between the two variables. Majority of poor prognosis cases are of grade 3.

Table 3: ER, PR status in breast carcinomas

ER / PR status	Number of cases	Percentages (%)
ER+ / PR+	12	23.1
ER +/PR-	07	13.5
ER- /PR+	04	7.7
ER-/PR-	29	55.7
Total	52	100

Table 4: Correlation of histological grading with ER, PR Status

Histological Grade	Number of cases	ER/PR + cases	Percentages (%)
I	08	06	75.0
II	35	15	42.8
III	09	02	22.2

There is a statistically significant correlation between the two variables. Percentage of ER, PR positivity decreases with increase in tumor size. There is no significant correlation between ER, PR status and clinical stage, lymph node status and NPI score.

Discussion

Incidence of breast carcinoma is increasing in India. Prognosis is related to a variety of clinical, pathological and molecular features which include stage of the carcinoma, histologic type, grade and lymph node metastasis. Estrogen and progesterone receptors, have with increasing importance, influenced the management of this malignancy. Rhodes DT *et al.*, who found more than 75% of the cases were above 50years and the mean age was 64 years [14]. But usually in Asian countries breast carcinoma occurs a decade earlier. Our results are in concordance with the study conducted by Lakmini. K.B. Mudduwa in which mean age was 52.5 years and 85.7% of the patients were more than 40years [11].

51.8% of the patients were postmenopausal women. This is in concordance with the study conducted by Louis. W.C. Chow *et al.*, in which 52% of the women were postmenopausal [15] and Col V Dutta *et al.*, in which 59% of the cases were postmenopausal women [16].

In a study conducted by Priti Lal *et al.* at NewYork with 3655 breast carcinomas, ER was positive in 71.6% and PR in 47.4% [13]. Mehedad Nadji *et al.* found in Miami with 5993 breast cancers that ER was positive in 75% of the cases and PR in 55% of the cases [21]. Li CI *et al.* from Seattle conducted a study between 1992 to 1998 and found ER positivity in 77.5% and PR positivity in 67.7% [5]. These are some of the studies conducted in western population. According to Lakhmini K.B. Mudduwa the prevelance of hormone receptor positive breast cancer in Asian countries has found to be lower than western world where more than 50% tumors express hormone receptors [11]. However the number of studies performed on this topic is much less in the Asian communities compared with the western world. Ljiljana Hulpic *et al.* conducted a study in Croatia with 242 cases and found ER positivity in 37.5%, PR positivity in 40.6% of the cases [4]. Azizun Nisa *et al.* studied 150 cases in Karachi and found that ER and PR was positive in 32.7% and 25.3% of the cases respectively [20]. In a study conducted by Desai SB *et al.* in India of 798 cases ER was positive in 32.6% of the tumors and PR was positive in 46.1% of the cases [6]. Col V Dutta *et al.* conducted a study in Army Hospital and Research centre in New Delhi and found that out of 75 cases, 24% were ER positive and 30% were PR positive [16]. In this study 44.2% of the cases were either ER or PR positive and 56.8% of the cases are negative for both the receptors. ER is positive in 36.5% of the cases and PR is positive in 30.7% of the cases.

The results of our study are in concordance with studies conducted in Asian population and one study of western population. The overall positivity rate for ER and PR is lower possibly because of the difference in techniques of evaluation [17], high tumour grades and majority being menopausal women in our study. Nulliparity, late age at first birth, early age at menarche, higher body mass index and the use of hormone replacement therapy have all been associated with increased risk of developing an ER + tumour but with a decreased risk of developing an ER- tumour. Young patients have high levels of circulating oestroges and a correspondingly low expression of steroid receptors, which is reflected in their tumours. Were appears to be a variation in steroid receptor positivity in the Asian population [16].

In this study there is a statistically significant association between ER, PR status and histological grade. Hormone receptor expression decreases with increasing tumor size but no statistically significant association between the two variables. No significant of ER, PR status with clinical staging, lymph node metastasis and NPI score noted. Lakmini. K.B. Mudduwa has found a significant inverse relation ship with the grade and ER, PR expression in his study. His study also shows no significant association of hormone receptor status with tumor size and lymph node metastases [11]. Ana Lucia Amaral Eisenberg *et al.* in Brazil also has established a significant correlation between ER, PR status and histological grade [8].

Col. V. Dutta in India observed that the reactivity for steroid receptor decreases with increasing grade but no significant association with other variables like lymph node metastases,

tumor size [16]. Ljiljana Hupic has found no statistically significant association between ER, PR status and NPI score in concordance with our study but in contrast to this study there is a significant association with lymph node metastases [4]. Kenneth McCarty and Rosemary. R. Millis *et al.* have also obtained similar results of association between ER, PR status and histological grade but no association with other prognostic variables [18, 19].

This study shows results of association between ER, PR status and other prognostic variables comparable to most of the studies conducted especially in Asian population.

Conclusion
Hormone receptor status was identified as an independent predictor of outcome in women with breast carcinoma. Data from clinical trials with long follow-up may shed light on whether and how the benefit of hormonal and other treatment varies with hormone receptor status. There was a statistically significant association between hormone receptor expression and histological grade but not with other prognostic factors. Presence of hormone receptors correlates well with response to hormone therapy. There is a significant decrease in mortality and tumor recurrences with hormone therapy. So, determination of ER, PR status is essential in all cases irrespective of clinical staging and lymph node metastasis.

References
1. Murthy NS, Chaudhry K, Nadayil D. Changing trends in incidence of breast cancer: Indian scenario. 2009; 46(1):73-74.
2. Rampaul RS, Pinder SE, Elston CW *et al*. Prognostic and predictive factors in primary breast cancer and their role in patient management: we Nottingham Breast Team. Eur J Surg Oncol. 2001; 27(3):229-38.
3. Mori I, Yang Q, Kakudo K *et al*. Predictive and prognostic markers for invasive breast cancer. Pathol Int. 2002; 52(3):186-94.
4. Ljiljana Hlupic, Jasminka Jakic-Razumovic, Jadranka Boz¡ikov *et al*. Prognostic Value of Different Factors in Breast Carcinoma. Tumori. 2004; 90:112-19.
5. Li CI, Daling JR, Malone KE. Incidence of invasive breast cancer by hormone receptor status from 1992 to 1998. J Clin Oncol. 2003; 1;21(1):28-34.
6. Desai SB, Moonim MT, Gill AK *et al*. Hormone receptor status of breast cancer in India: a study of 798 tumours. we Breast. 2000; 9(5):267-70.
7. Cubilla AL, Wooddruff JM *et al*. Primary carcinoid tumor of the breast: A report of eight patients. Am Jour of Surg Pathol. 1977; 1:283-92.
8. Ana Lucia Amaral Eisenberg, Sergio Koifman *et al*. Hormone Receptors: Association with Prognostic Factors for Breast Cancer. Revista Brasileira de Cancerologia. 2001; 47(1):49-58.
9. Jirström1 K, Rydén1 L, Anagnostaki L *et al*. Pathology parameters and adjuvant tamoxifen response in a randomised premenopausal breast cancer trial. J Clin Pathol. 2005; 58:1135-1142.
10. Elizabeth M Hammond H, Daniel Hayes F, Mitch Dowsett *et al*. American Society of Clinical Oncology/College of American Pathologists Guideline Recommendations for Immunohistochemical Testing of Estrogen and Progesterone Receptors in Breast Cancer. Jour of Clin Oncol. 2010; 201:1-15.

11. Lakhmini Mudduwa KB. Quick score of hormone receptor status of breast carcinoma: Correlation with other clinicopathological prognostic parameters. Indian Jour of Pathology and Microbiology. 2009; 52(2):159-63.

12. Osborne CK, Yochmowitz MG, Knight WA *et al*. The value of estrogen and progesterone receptors in the treatment of breast cancer. Cancer. 1980; 46:2884-88.

13. Priti Lal, Lee Tan K, Beiyun Chen. Correlation of HER-2 Status with Estrogenand Progesterone Receptors and Histologic Features in 3,655 Invasive Breast Carcinomas. Am J Clin Pathol. 2005; 123:541-46.

14. Deborah Rhodes J. Identifying and Counseling Women at Increased Risk for Breast Cancer. Mayo Clin Proc. 2002; 77(4)355-61.

15. Louis WC, Chow Pei Ho. Hormonal receptor determination of 1,052 Chinese breast cancers. Journal of Surgical Oncology. 2000; 75(3):172-75.

16. Col V, Dutta SM, Brig GS, Chopra SM, Lt Col K, Sahai *et al*. Hormone Receptors, Her- 2/Neu and Chromosomal Aberrations in Breast Cancer. MJAFI. 2008; 64:11-15.

17. DM Barnes, Harris WH, Smith P *et al*. Immunohistochemical determination of oestrogen receptor: comparison of different methods of assessment of staining and correlation with clinical outcome of breast cancer patients. Brifish Journal of Cancer. 1996; 74:1445-51.

18. Kenneth S, McCarty Jr., Womas Barton K, Bernard Fetter F *et al*. Correlation of Estrogen and Progesterone Receptors with Histologic Differentiation in Mammary Carcinoma. Cancer. 1980; 46:2851-58.

19. Rosemary Millis R. Correlation of hormone receptors with pathological features in human breast cancer. Cancer. 1980; 46:2869-71.

20. Azizun-Nisa, Yasmin Bhurgri, Farrukh Raza *et al*. Comparison of ER, PR & HER-2/neu (C-erb B 2) Reactivity Pattern with Histologic Grade, Tumor Size and Lymph NodeStatus in Breast Cancer. Asian Pacific J Cancer Prev. 2008; 9:553-56.

21. Mehrdad Nadji, Carmen Gomez-Fernandez, Par Vin Ganjei-Azar *et al*. Immunohistochemistry of Estrogen and Progesterone Receptors Reconsidered Experience With 5,993 Breast Cancers. Am J Clin Pathol. 2005; 123:21-27.