Original Research Paper

Pathology

CLINICO-PATHOLOGICAL STUDY OF BREAST CARCINOMAS WITH ER, ER STATUS- A 2 YEAR RETROSPECTIVE STUDY

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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. The 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 descriptive study was conducted in Department of Pathology, Kilpauk Medical College, Chennai for a period of 2 years. A total of 73 cases were studied and IHC was done for 55 cases. 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 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 descriptive study of breast carcinomas conducted in Department of Pathology, Kilpauk Medical College, from the Department of Surgery between July 2008 and September 2010.

A total of 73 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.

Exclusion criteria :

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

ER, PR study was done for 55 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 histokinette. 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

0	-	No nuclear staining
1	-	< 1% nuclear staining
2	-	1 - 10% nuclear staining
3	-	11 - 33% nuclear staining
4	-	34 - 66% nuclear staining
5	-	67 - 100% nuclear staining

Score for staining intensity

0	-	No staining
1	-	Weak staining
2	-	Moderate staining
3	-	Strong 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 28 years old and the oldest patient was 80 years old. Maximum number of cases were seen in 41-50 years age group. Mean age was 50.18 years. 80% of the cases were more than 40 years. Majority of cases 56.2% were postmenopausal. 65.2% of cases were of TNM stage 2. Of the 55 cases 41.1% had lymph node stage N1,

34.2% had lymph node stage N2 and 24.7% had lymph node stage N3.

Maximum number of cases are Bloom and Richardson grade 2.

TABLE 1:HISTOLOGICAL GRADEWISE DISTRIBUTION OF BREAST CARCINOMAS

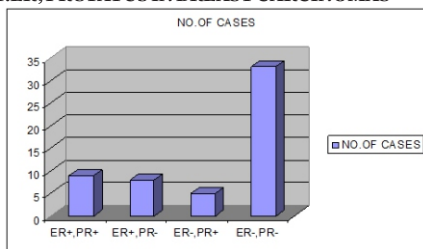| S.NO.	GRADE	CASES	
		NUMBER	%
1	1	7	9.6
2	2	53	72.6
3	3	13	17.8

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

TABLE 2:CORRELATION OF CLINICAL STAGING WITH NPI SCORE

STAGE	GOOD PROGNOSIS	MODERATE PROGNOSIS	POOR PROGNOSIS
1	2	4	NIL
2	2	38	9
3	1	4	13
4	NIL	NIL	NIL

Table 2 shows correlation between clinical staging and NPI score. There is statistically significant correlation between the two variables with a **p value of 0.001.** Majority of poor prognosis cases are of grade 3.

CHART 1:ER, PR STATUS IN BREAST CARCINOMAS

**TABLE 3:CORRELATION OF HISTOLOGICAL GRADING WITH ER, PR STATUS**

S.NO	GRADE	NO.OF CASES	ER/PR + CASES
1	1	7	6
2	2	40	16
3	3	8	2

There is a statistically significant correlation between the two variables with a **p value of 0.01.**

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.

Figure 1 MRM SPECIMEN SHOWING A GROWTH MEASURING 5x4cm
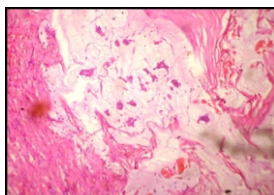
Figure 2 MUCINOUS CARCINOMA BREAST SHOWING TUMOR CELLS FLOATING IN POOLS OF EXTRACELLULAR MUCIN
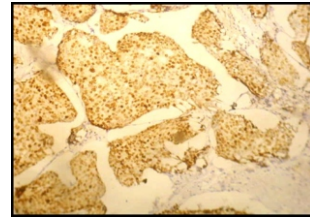
Figure 3 IHC SHOWING ER NUCLEAR POSITIVITY IN LOW POWER

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.

AGE DISTRIBUTION:
The mean age of patients included in our study was 50.18years. 80.9% of the cases were more than 40years of age. Maximum number of cases were in the age group of 41-50years.

This is less than the observation made by RhodesDT 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).

MENSTRUAL STATUS:
56.2% 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).

HORMONE RECEPTOR STATUS IN BREAST CARCINOMAS:
The hormone receptor status of breast carcinoma can predict the response to adjuvant endocrine therapy.

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 Lakmini K.B.Mudduwa the prevalence 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 40% of the cases were either ER or PR positive and 60% of the cases are negative for both the receptors. ER is positive in 30.9% of the cases and PR is positive in 25.5% of the cases.

These results are not in concordance with the studies conducted in western population.

But 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 oestrogens and a correspondingly low expression of steroid receptors, which is reflected in their tumours. There appears to be a variation in steroid receptor positivity in the Asian population (16).

CORRELATION OF HORMONE RECEPTOR POSITIVITY WITH OTHER PROGNOSTIC VARIABLES:

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

73 cases of mastectomy specimens were received and clinical staging, histological grading and NPI score were analysed for these cases. 55 cases were selected at random and ER, PR status was analysed using Quick score.

Greater than 80% of the cases were 40 years and above and majority were postmenopausal. Maximum number of cases were stage 2 and grade 2 with majority having no lymph node metastases.

ER was positive in 30.9% and PR in 25.5%, as the prevalence of hormone receptor positive breast cancers is less in the study population of Asian women compared with western world. 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.

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