Original Research Article

Clinico-pathological study of locally advanced breast cancer and their hormone receptor analysis

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ABSTRACT

Background: Breast carcinoma is one of the most common malignant tumor of women. Determination of estrogen receptors (ER) and progesterone receptors (PR) status, prior to therapeutic intervention has become standard practice. Survival and response to hormone therapy are most favorable among women who are receptor positive. The aim of this study is to assess the hormone receptor status in locally advanced breast carcinomas and correlate this reactivity pattern with tumor stage, clinical stage and lymph node metastasis. Objective of the study was to co-relate the locally advanced breast cancer and their hormone receptor analysis.

Methods: Patients who visited Department of General Surgery, Hamidia Hospital, Bhopal were assessed clinically, radiologically and histopathologically and then ER and PR study was done, for a total of 50 cases were done.

Results: In our study majority of the cases were locally advanced breast cancer (50%) which may be due to the low socio economic status, late presentation, pain tolerance, illiteracy and availability of the resources. Majority of cases were in postmenopausal, clinical stage 3 and histological grade 2. ER positivity 50% and PR positivity 44% and it was found that hormone receptor positivity was high in locally advanced breast cancers 63.5%.

Conclusions: Hormone receptor analysis should be an integral part of initial workup of carcinoma breast, as the percentage of hormone receptor positivity is increasing in our population in locally advanced breast cancer. So locally advanced breast cancer can be diagnosed at an early stage by screening and conducting breast awareness programs.

Keywords: Locally advanced breast cancer, Estrogen receptors, Progesterone receptors

INTRODUCTION

Breast carcinoma is the most common malignant tumor and has a major effect on the health care of women in the world. It is the leading cause of death due to carcinoma in women. Breast cancer is ranked number one among Indian females with age adjusted rate as high as 25.8 per 100,000 women and mortality 12.7 per 100,000 women.[1] In India most of the patients present with palpable cancer and even with lymph node metastasis at the time of their first visit. Determination of estrogen receptors (ER) and progesterone receptors (PR) status on breast biopsy specimens, prior to therapeutic intervention has become standard practice. Survival and response to hormone therapy are most favorable among women who are receptor positive.

The aim of this study is to assess the hormone receptor status in locally advanced breast carcinomas and correlate this reactivity pattern with tumor stage, clinical stage and lymph node metastasis. It is particularly important to address this disease in developing nations, where over 70% of all cancer cases will occur by 2020.

METHODS

Patients diagnosed as carcinoma breast, admitted in the Department of General Surgery, Hamidia Hospital, Bhopal

during the period from August 2017 to August 2019 were studied. Clinical data were obtained from patients' history, clinical examination, hospital records and requisition forms received in the department.

Inclusion criteria

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

Exclusion criteria

Male patients suffering from breast cancer were not included for study.

Patients who visited Department of General surgery, Hamidia Hospital, Bhopal were assessed by using clinical, imaging and histopathological methods and then ER and PR study was done. All the 50 mastectomy specimens received were properly sliced and fixed in 10% formalin for 18-24 hours. Detailed gross examination pertaining to overall size of the specimen, nipple and areola, margin status and nodal status were carefully studied. Histological grading was done by modified Bloom and Richards scoring system.

Representative samples are taken from tumor, margins, nipple and areola and lymph nodes. The tissues were processed in various grades of alcohol and xylol using automated Histokinette. Paraffin blocks were prepared and sections of 5 micron thickness were cut in microtome using disposable blades and stained with hematoxylin and eosin. Suitable blocks were chosen for immunohistochemistry (IHC).

Sections for IHC were also cut in microtome using disposable blades. Slides coated with chrome alum were used. Sections subjected to antigen retrieval using pressure cooker technique citrate retrieval solution (pH 6) and then treated by horse radish peroxidase (HRP) polymer techniques.

Scoring system

Scoring was done by quick score system. Scores for proportion staining were- 1: no nuclear staining, 2: <1% nuclear staining, 3: 1-10% nuclear staining, 4: 11-33% nuclear staining, 5: 34-66% nuclear staining and 6: 67-100% nuclear staining.

Scores for staining intensity

The scores for staining intensity were- 1: no staining, 2: weak staining, 3: moderate staining and 4: strong staining.

Scores are summed to give a maximum score of 8. The final reaction product by increasing the sensitivity of antigen-antibody reaction.[3]

The sample size was determined based on duration of the study, which was from August 2017 to August 2019. All female patients who underwent Mastectomy irrespective of age and proved to have malignant cytology were included in the study. Hence a sample size of 50 cases was obtained. Sampling technique used was: convenient sampling. There were no limitations to the study. Statistical Method and tool used in the study was EPI info version 7.

Interpretation

Patients with tumor scoring less than 2 are regarded as ER and PR negative and may have a negligible chance to response to therapy and patients above quick score 2 and above 2 are regarded as positive and can be benefited from adjuvant endocrine therapy.

RESULTS

In our study majority of the patients were between the age group of 50-60 years with 35 cases constituting 70% of total cases, and the mean age was 51 years. The youngest case was of 31 years and the oldest was of 60 years. Majority were post-menopausal and were in low socio-economic group with 35 out of 50 cases constituting 70%. Majority of the cases, 25 cases (50%) were of grade 2, followed by 18 cases (38%) of grade 1. The least number of cases, 7 cases (14%) were of grade 3. Majority, 20 cases (40%) were of stage N2, followed by 15-30% cases of stage N1, 7-14% cases of stage N3 and 8-16% cases of stage N0. Majority of the cases 25-50% were locally advanced breast cancer.

Table 1: Correlation of age with ER/PR status.

Age (in years)	N	%	ER/PR+ cases
31-40	2	4	Nil
41-50	6	12	2
51-60	35	70	23
>60	7	14	5

Table 2: Correlation of menopausal status with ER/PR status.

Menopausal status	N	%	ER/PR+ cases
Premenopausal	15	30	5
Postmenopausal	35	70	25

Table 3: Correlation of socio-economic status with ER/PR status.

Socio-economic status	N	%	ER/PR+ cases
Lower	35	70	23
Middle	14	28	7
Higher	1	2%	Nil

Table 4: Correlation of lymph node stage with ER/PR status.

Lymph node stage	N	%	ER/PR+ cases
0	8	16	Nil
1	15	30	6
2	20	40	20
3	7	14	4

Table 5: Correlation of clinical stage with ER/PR status.

Clinical stage	N	%	ER/PR+ cases
1	3	6	1
2	20	40	12
3	25	50	16
4	2	4	1

Table 6: Correlation of locally advanced breast cancer with ER/PR status.

Locally advanced cancer	N	%	ER/PR+ cases
Early	20	40	7
Locally advanced	25	50	19
Advanced	2	4	2
Recurrent	3	6	2

Table 7: Correlation of grading with ER/PR status.

Grade	N	%	ER/PR+ cases
1	18	36	9
2	25	50	16
3	7	14	5

Table 8: Correlation of tumor stage with ER/PR status.

Tumor stage	N	%	ER/PR+ cases
1	3	6	1
2	20	40	8
3	8	16	4
4	19	38	17

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. ER and PR, have with increasing importance, influenced the management of this malignancy.

The mean age was found out to be 51 years and 70% of cases were between the age group 50-60 years. More than 80% of the cases were 40 years and maximum age of the patient was 75 years and minimum age was 32 years. This finding is similar to several other studies, in which it was found that more than 75% of the cases were above 50 years.[4] A similar study conducted in 2009 reported that the mean age was 52.5 years and 85.7% of the patients were more than 40 years.[5]

70% of cases were postmenopausal women. It is in concurrence with some recent studies conducted, in which, the post-menopausal age group was more common, some showing up to 70% while some others showing up to 59% case prevalence.[6,7]

In our study, carcinoma breast, especially locally advanced breast cancer was more common in lower socio economic group 35 cases of 50 cases (70%). The incidence is higher in lower economic class due to ignorance or negligence, illiteracy and low in higher socio economic class as they are educated, aware and more concerned.

In our study of 50 cases, 25 cases (50%) were locally advanced breast cancer, mostly belonging to the lower socio economic strata, as they present at a late stage of disease. This being in concurrence with a recent study in which 65% of the affected patients were from the low socio-economic class.[8]

From the total of 50 cases, 50% cases were ER positive and 44% cases were PR positive. 63.5% were locally advanced breast cancer with ER and PR positivity. In a study conducted by some authors, attempts were made to correlate ER and PR status along with various histological types of breast carcinoma in 333 patients.[9,10]

In that study, ER and PR were positive in 70-80% of the tumors and HER-2/neu expression was present in 15-20% of the tumors.

A population based study conducted in 2003 has documented the incidence of invasive carcinoma by hormone receptor status from 1992 to 1998.[9] It was found that hormone receptor positivity increased from 75.4% to 77.5% in United States with a rise in prevalence over the years. In a study conducted in 2005 at New York with 3655 breast carcinomas, ER was positive in 71.6% and PR in 47.4%.[11] These were some of the studies conducted in western population.

An Indian study conducted in 2000 documented the ER and PR status of breast carcinoma in 798 cases. The procedure was done by immuno-histo-chemical method.[12] Out of 798 tumors, 32.6% were ER positive and 46.1% were PR positive which was also in concordance with a study in Karachi.[13]

Another Indian study conducted in 2008 included 75 cases.[6] The author analyzed hormone receptors and HER-2/neu expression in breast carcinoma. In total of 75 tumors, 33% (25/75) cases expressed ER and PR or both, whereas 67% (50/75) were found out to be both the receptor negative. HER-2/neu over expression was seen in 58%

(43/75) of tumors. This study reveals that receptor negativity is higher in this subset of tumors when compared with western communities.

Table 9: Comparison of various studies.

Study (year)	ER+ (%)	PR+ (%)
Present study	50	44
Li et al[10]	77	67
Desai et al[12]	32	46
Dutta et al[7]	35	33
Aziz et al[8]	32	45
Lakmini et al[5]	45	48

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 in the developing countries because of the possibility of the difference in techniques of evaluation, high tumor grades, illiteracy, low socio-economic status, lack of awareness and ignorance or negligence by the patients.

CONCLUSION

Locally advanced breast cancer is one of the most common way of presentation in Asian population, especially those belonging to low socio economic status because of the poverty, illiteracy lack of awareness and habit of delaying treatment for various reasons. In our study, locally advanced breast cancer were constituting (50%) of the cases and the hormone receptor positivity was found to be (63.5%) in locally advanced breast cancer. It signifies that although, we are facing a disease which is locally advanced but high percentage of hormone receptor positivity can result in relatively better prognosis. Hence it can be concluded that hormone receptor analysis should be an integral part of initial work up of carcinoma breast and locally advanced breast cancer is no exception. The high trend of locally advanced breast cancer cases in our population can be diagnosed at an early stage by screening and conducting breast cancer awareness programs.

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