Original Article

Expression of Estrogen Receptor, Progesterone Receptor and HER-2/Neu among Bangladeshi Women with Invasive Breast Cancer at a Tertiary Care Hospital

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Abstract

Background: Now-a-days determination of estrogen receptor (ER), progesterone receptor (PR) and HER-2/neu expression pattern by immunohistochemistry in invasive breast cancer have become the standard procedure for breast cancer management. **Objective**: To see the expression pattern of estrogen receptor, progesterone receptor and HER-2/neu in Bangladeshi women with invasive breast carcinoma. **Materials and Methods**: This retrospective study was performed in 67 cases of invasive breast cancer. Estrogen receptor (ER), progesterone receptor (PR) and HER-2/neu expression pattern were assessed by immunohistochemistry using monoclonal antibodies for detecting estrogen and progesterone receptors, and polyclonal antibody for detecting HER-2/neu. **Results**: All the cases were graded according to Nottingham Modification of Bloom-Richardson system. Of those, Grade I tumours were 14 (20.89%), Grade II tumors were 45 (67.16%) and Grade III tumors were 8 (11.95%). Both ER and PR positive reactivity were the same and it was found 50 (74.63%) and HER-2/neu reactivity patterns were found negative in 45 (67.16%) cases and positive in 22 (32.84%) cases. **Conclusion**: ER, PR and HER-2/neu expression do not correlate with each other, so it is recommended that each test should be independently determined by immunohistochemistry in all cases of invasive breast cancer. All equivocal cases of HER-2/neu (score 2+) should be analysed by FISH technique to find out the percentage of real score.

Key words: *Immunohistochemistry (IHC); Estrogen receptor (ER); Progesterone receptor (PR); HER-2/neu*

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Introduction

Carcinoma of the breast is the commonest malignancy of females all over the world and second leading cause of death due to cancer among females. Several histopathological features have prognostic significance in breast cancer like cancer subtypes, tumour grade, estrogen and progesterone receptor status, HER-2/neu expression, proliferation marker (Ki 67) and DNA content.[1] Analysis of estrogen receptor (ER) and progesterone receptor (PR) status has become the standard procedure for patient's care in breast cancer treatment. Particularly estrogen receptor (ER) content carcinoma of the breast is the commonest malignancy correlated more with prolonged disease-free survival of females all over the world and has increased response to endocrine therapy.[2] Biopsy specimen of breast cancer should

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be evaluated for hormone receptor status. If any of these two receptors expression is found, a response to hormonal therapy is expected. The more the estrogen or progesterone receptors present on those cells the more chance to result on effective hormonal therapy. The goal of therapy is to starve the breast cancer cells of the hormone they thrive on, which is estrogen.[3] Analysis of PR expression is generally reported with ER expression. PR status is independently associated with disease-free and overall survival. ER positive/ PR positive tumours have better prognosis than ER positive/PR negative tumours. But ER positive/ PR negative and ER negative/PR positive tumours have better prognosis than ER negative/PR negative tumours.[4] HER-2/neu oncogene encodes an 185kDa transmembrane protein and is expressed at low levels in a variety of normal epithelium including breast duct epithelium. HER-2/neu is overexpressed and amplified in 20−30% of invasive breast cancers. In approximately 90% of the cases, protein overexpression reflects amplification of the HER-2/neu gene located on chromosome 17q21.[5] HER-2/neu overexpression is associated with increased disease recurrence, metastasis and shortens survival. The overexpression of HER-2/neu protein and amplification of the HER-2/neu gene is also associated with poor prognostic tumour characteristics such as high histological grade, high proliferative index, negative or lower ER expression and p53 mutation. HER-2/neu status along with ER/PR status are considered together to give any adjuvant systemic therapy.[6] HER-2/neu testing should be routinely performed in patients with invasive breast cancer. Several techniques are available for the assessment of HER-2/neu status in patients with breast cancer. IHC is the most commonly practiced method. Another method is fluorescence in situ hybridization (FISH) used to assess gene amplification. FISH should be reserved for weakly positive (2+) cases stained by IHC.[6] In western world ER, PR and HER-2/neu overexpression status has been routinely practiced as an essential part in histopathology of breast cancer patients. In Bangladesh ER/PR and HER-2/neu pattern had been performed only in prescribed cases by medical and surgical oncologists. This work has been planned to explore the pattern of hormone receptors and HER-2/neu expression by immunohistochemistry in invasive breast cancer in Bangladeshi women.

Materials and Methods

This was a retrospective study and performed at the Department of Pathology, Enam Medical College & Hospital (EMCH), Savar, Dhaka during the period of January 2017 to December 2017. Only histopathologically diagnosed cases of invasive carcinoma of breast that were advised for determination of hormone receptor status and HER-2/neu reactivity by IHC were included in this study. Mastectomy specimen and lumpectomy specimen were received in the laboratory. Routine tissue processing was done. Paraffin blocks were made and sections were taken for routine hematoxylin and eosin (H&E) stain and for immunohistochemistry (IHC) blocks were sent to different specialized laboratories and collect the report. Routinely stained sections were examined under a microscope and histological diagnosis was made. All cases were classified according to WHO proposed classification.[7] In cases of invasive ductal carcinoma, NOS, grading of tumour was performed by the Nottingham Modification of Bloom-Richardson system.[8] All the specialized laboratories use Allred Score system[9] for immunohistochemical assessment of the hormone receptor status of breast carcinoma.

Results

A total of 67 cases of invasive breast cancer were included in this study. Average age of the patients was 42.57 years. Age distribution ranged from 22 to 65 years with a mean±SD of age 42.57±9.81 years. The median age was 42 years. The patients are divided into five age groups as shown in Table I.

Table I: Distribution of patients according to age

Age in years	Number of cases	Percentage
21 to 30	8	11.94
31 to 40	24	35.82
41 to 50	24	35.82
51 to 60	9	13.44
61 to 70	2	2.98
Total	67	100

All the 67 cases were diagnosed histopathologically as

invasive ductal carcinoma, NOS. Tumour sizes were grouped into three subgroups as shown in Table II.

Table II: Tumour numbers according to size

Tumour size	Number of cases	Percentage
<2 cm	8	11.94%
2−5 cm	47	70.15%
>5 cm	12	17.91%

According to Nottingham Modification of Bloom-Richardson system, 67 cases of invasive ductal carcinoma, NOS were graded into Grade I, Grade II and Grade III. Grade I tumours were 14 (20.89%), Grade II tumours were 45 (67.16%) and Grade III tumours were 8 (11.95%) (Fig 1).
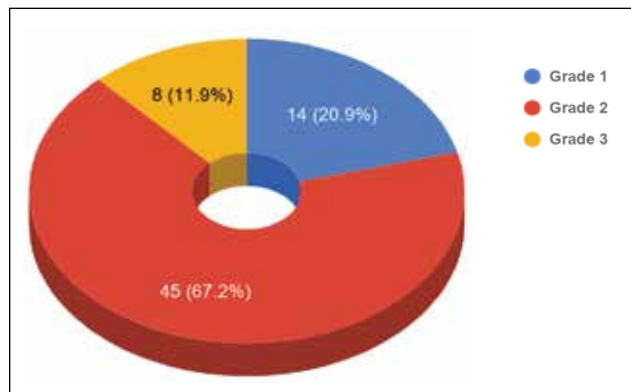

Fig 1. Number of tumours based on grading

Hormone receptor status

According to Allred Score criteria, both ER and PR positive reactivity were the same in 50 (74.63%) cases. The patterns of ER and PR expression status are shown in Table III.

Table III: Status of ER and PR in 67 cases of invasive ductal carcinoma

Receptor	Number of cases	Percentage
ER (+)	50	74.63
PR (+)	50	74.63
ER (+)/PR (+)	39	58.2
ER (+)/PR (-)	12	17.91
ER (-)/PR (+)	12	17.91
ER (-)/PR (-)	5	7.46

ER= estrogen receptor; PR= progesterone receptor

HER-2/neu reactivity patterns

HER-2/neu reactivity patterns were found negative (score 0, 1+, 2+), in 45 (67.16%) cases and positive (score 3+) in 22 (32.84%) cases (Fig 2).
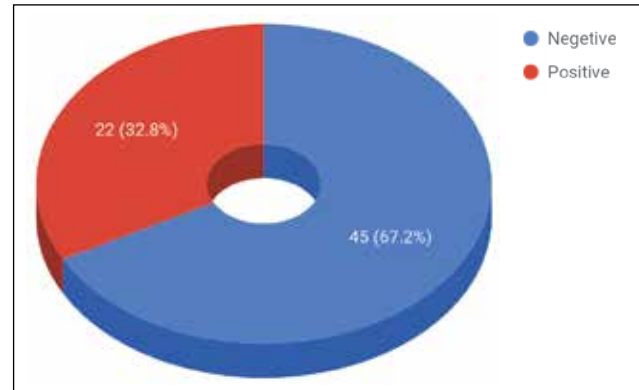

Fig 2. Percentage of HER-2/neu reactivity pattern

Low grade tumours had more tendency of having positive reactivity for estrogen receptor and Grade I tumours showed 100% positive reactivity (Table IV).

Table IV: Relationship between ER expression and tumour grade

Tumour grade	ER (+)	ER (−)	Total
Grade 1	14 (100%)	0 (0%)	14
Grade 2	32 (71.11%)	13 (28.89%)	45
Grade 3	4 (45.45%)	4 (54.55%)	8
Total	50	17	67

Discussion

This retrospective study was performed to see estrogen receptor, progesterone receptor status and HER-2/neu expression pattern in invasive breast carcinoma. A total of 67 cases of invasive breast carcinoma were included in this study. All the cases were invasive ductal carcinoma, NOS. All of them were Bangladeshi and the mean age of the patients was 42.5 years. Naeem et al[1] mentioned in their study the mean age of breast cancer 48.3 years in Pakistani women. According to Ayadi et al[10] the mean age of breast cancer in Tunisian women is 51.5 years while Huang et al[11] mentioned the mean age 50 years in Belgium women. So, the mean age of breast cancer in this study is less than the mean age found by other

investigators. It requires further careful examination to determine the nature of the predisposing factors. Estrogen receptor (ER), progesterone receptor (PR) and HER-2/neu status vary from country to country. In the present study, individual positive reactivity of ER and PR were same which was 74.63% and HER-2/neu overexpression was 32.84%.

Percentage of PR positive reactivity in the present study is less than the study of Ahmed et al[12] who showed 77.5% PR positive cases. Our study showed higher PR positivity than the studies of Narita et al[13], Ivkvic-Kapicl et al[6], Huang et al[11], Thompson et al[14], Farzami et al[15], Nadji et al[2], Ratnatunga & Liyanapathirana[16] and Azizun-Nisa et al[17] who showed 73.6%, 66%, 64.2%, 62%, 61.5%, 55%, 50% and 25.3% PR positivity respectively. The percentage of HER-2/neu overexpression is lower than the studies of Kumar et al[18], Narita et al[13] and Benohr et al[19] who showed HER-2/neu overexpression as 46.37%, 37.3% and 34.0% respectively. But the percentage of HER-2/neu overexpression in our study is more than the studies of Azizun-Nisa et al[17], Farzami et al[15], Ivkvic-Kapicl et al[6], Ayadi et al[10], Ratnatunga and Liyanapathirana[16] and Huang et al[11] who found HER-2/neu overexpression 24.7%, 21.7%, 20%, 18.1%, 14.6% and 10.9% respectively. In this study correlation between estrogen receptors and progesterone receptors expression status was evaluated. Fifty (74.63%) cases of ER positive tumours were associated with PR positivity. In the previous studies most of the investigators (Ayadi et al[10], Ratnatunga & Liyanapathirana[16], Farzami et al[15] and Huang et al[11]) found that estrogen and progesterone receptor status significantly associated with low grade tumours. In this study 100% of Grade I tumours and 71.11% of Grade II tumours showed positive reactivity for estrogen receptor (ER). In the case of progesterone receptor, tumour grade did not correlate with positive reactivity which was dissimilar to the observations of other investigators. This discrepancy may be due to a smaller number of higher-grade tumours included in the present study.

The issue of breast cancer care development is certainly related with a number of diagnostic approaches in which immunohistochemical determination of ER, PR and HER-2/neu play a certain role. Presently surgical oncologists in Bangladesh face major challenges due to lack of information about hormone receptors and HER-2/neu expression status. As ER, PR and HER-2/neu expressions do not correlate with each other, it is recommended that each test should be independently determined by immunohistochemistry in all cases of invasive breast cancer. All equivocal cases of HER-2/neu (score 2+) should be analysed by FISH technique to find out the percentage of real score.

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