ORIGINAL ARTICLE

CORRELATION OF HORMONAL RECEPTOR AND Her-2/neu EXPRESSION IN BREAST CANCER: A STUDY AT TERTIARY CARE HOSPITAL IN SOUTH GUJARAT

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ABSTRACT

Introduction: Breast cancer is the most common cancer in women and leading cause of cancer death in women. In India its incidence is rapidly rising. Present study was aimed to study pattern of expression of Hormone receptor and Her-2/neu in invasive breast carcinoma and to correlate ER PR status and Her-2/neu expression with various Clinicopathological aspects.

Method: The present study was carried out in the Department of Pathology, Government Medical Collage, Surat, from the period of January 2011 to December 2011. Routine H&E staining for histological diagnosis and IHC analysis for ER, PR and Her-2/neu was carried out in all cases.

Result: This study includes total 58 cases of breast malignancies. 94.82% cases of invasive duct carcinoma. The age of patients ranged from 35 to 73 years of age. Majority of tumors are grade 2 (43.10%) followed by grade 3 (29.31%). ER, PR and Her-2/neu expression was seen in 48.27%, 37.93% and 27.58% respectively. Triple negative cases comprised of 25.86% in our study. Significant correlation was observed between hormonal receptor status and Her-2/neu expression.

Conclusion: Our study of ER, PR and Her-2/neu in breast carcinoma by IHC method indicates higher rates of positive expression correlated with various clinicopathological aspects. Higher number of grade 1 tumor showed ER, PR positivity as compared to grade 3 tumors. Inverse relationship was observed between Her-2/neu expression and ER, PR receptor status. Her-2/neu expression was increased with size and high grade of tumor. Her-2/neu expression did not show any significant correlation with age.

Key words: Breast carcinoma, Her-2/neu, ER/PR.

INTRODUCTION

Breast cancer is the most common cancer in women in developed countries, and 12% breast cancer occur in women between 20-34 yrs.[1] In India, Breast Cancer is second to cancer of the Cervix among women, but is considered the leading Cancer in certain metros such as Mumbai and Bangalore. It is estimated that approximately 80,000 cases occur annually; the age adjusted incidence rates varying between 16 and 25/ 100,000 population.[2] Several histopathological features have prognostic significance in breast carcinoma which includes histologic subtype, Grade, lymph node status, ER/PR status, Growth factor and its receptors, proliferation activity and DNA content, oncogenes and tumor suppressor genes.[3]

Now a day, in the treatment of breast carcinoma, conservative and reconstructive surgery is more popular. ER PR and Her2/neu immunostaining is very useful tool for rapid diagnosis and for treatment point of view. Determination of ER PR status on biopsy specimen prior to therapeutic intervention is advocated as standard practice.[4]

Our study was aimed, 1) to study pattern of expression of Hormone receptor and Her2/neu in invasive breast carcinoma. 2) to correlate ER PR status and Her-2/neu expression with various Clinicopathological aspects.

This study was carried at New Civil Hospital, situated in Surat city of South Gujarat. Our Hospital is major tertiary care centre in south Gujarat. Most of the patients are referred for tertiary care from South Gujarat region and adjoining states.

MATERIAL AND METHOD

The present study was carried out in the Department of Pathology, Government Medical Collage affiliated with New Civil Hospital, Surat, from the period of January

2011 to December 2011. This study has been done as per standard ethics & by maintaining confidentiality of reports. Detailed gross examination of all received MRM specimen was carried out for tumor size and nodal metastasis. All tissues were fixed in 10% buffered formalin for not more than 24 hours. Representative tumor tissue was submitted for processing and H&E stain for routine histological diagnosis according to modified Bloom Richardson grading system of WHO.

IHC for ER, PR and Her-2/neu were performed on representative blocks of paraffin embedded tissue. 4 µm thick sections were submitted for IHC Staining. Sections were taken on slides previously coated with poly L lysine. Antigen retrieval was done by HIER method using Citrate buffer at PH 2.5 for ER/PR and PH 6 for HER-2/neu. The normal epithelial component served as internal control for ER/PR. IDC with known HER-2/neu over expression was used as external positive control for each lot of staining.

The ER and PR results were screened and interpreted as positive when more than 1% of tumor cells showed positive nuclear staining. For interpretation of HER-2/neu staining following method was used.
Score 0: No staining is observed or membrane staining is observed in <10% of the tumor cells.
Score 1+: Faint/barely perceptible membrane staining is detected in >10% of tumor cells. The cells exhibit incomplete membrane staining.
Score 2+: A weak to moderate complete membrane staining is observed in >10% of tumor cells.
Score 3+: Strongly Positive A strong complete membrane staining is observed in >30% of tumor cells.
Score 3+ was considered as positive immunostaining for HER-2/neu.

RESULT

Total 58 cases of invasive duct carcinoma were observed in our study. The age of patients ranged from 35 to 73 years of age. Most of the patients were presented with >40 years of age (84.81%). Most common age group involved was 41-50 years (41.37%).

Table 1: Distribution of patients according to age group

Age Group	Cases (%)
21-30	0 (0)
31-40	9 (15.51)
41-50	24 (41.37)
51-60	13 (22.41)
61-70	11 (18.96)
71-80	1 (2)
Total	58 (100)

Majority of the tumors in our study were grade 2(43.10%) followed by grade 3 (29.31%). In our study 76.47% of grade 3 tumors show lymph node metastasis. ER and PR positivity was seen more frequently in grade 1 and 2 than grade3.

Table 2: Clinico-pathological feature and receptor status

Histopathological Features		No. (%)
Subtype	IDC	55 (94.82)
	Medullary Carcinoma	2 (3.44)
	Mucinous Carcinoma	1 (1.72)
Her2/neu Status	Positive	16 (27.58)
	Negative	42 (72.72)
ER	Positive	28 (48.27)
	Negative	30 (51.73)
PR	Positive	22 (37.93)
	Negative	36 (62.04)
Tumor Grade	1	16 (27.58)
	2	25 (43.10)
	3	17 (29.31)
Tumor Size	< 2 cm	5 (8.62)
	>2 cm	53 (91.38)
Lymph Node Status	Positive	31 (53.44)
	Negative	27 (46.56)
Age	≤40	9 (15.51)
	>41	49 (84.49)

In our study Her-2/neu positivity was correlated with grade of tumor. Grade 1 tumors was negative for Her-2/neu, 28% of grade 2 and 52.94% of grade 3 tumors were positive for Her-2/neu.

In our study two case of medullary carcinoma were seen which were negative for ER, PR and Her-2/neu.

Table 3: Hormonal receptor status and Her-2/neu expression according to size of tumor

Tumor size	Cases	ER+	PR+	Her-2/neu+
<2 cm	5	5(100%)	4(80%)	0(0%)
2-5 cm	37	17(45.94%)	12(32.43%)	11(29.72%)
>5 cm	15	6(40%)	6(40%)	5(31.33%)

Table 4: IHC positivity according to histological grade

Grade	Cases	ER+	PR+	Her2Neu+
1	16	8(50%)	7(43.75%)	0(0%)
2	25	14(56%)	10(40%)	7(28%)
3	17	6(35.29%)	5(29.41%)	9(52.94%)

DISCUSSION:

Present study comprised of 58 cases of primary breast carcinoma. 91.38% of cases showed more than 2cm tumor size. Similar results were observed by Azizun Nisa et al, Moses Embroise et al and Mona Rashed et al in their study,[5,6,7] while study from western country, Adendaya et al showed 71.4% cases with ≤ 2cm size, this could be due to early cancer detection programs.[8]

Our study showed 48.27% of cases with positive ER status while, 37.93% PR positive status. The study by Munjal et al showed 41.41% positivity for ER and PR, Shet T et al showed similar result, Azizun Nisa et al showed 32.7% and 25.3% positivity respectively.[4, 9, 5]

Significant inverse association was found between hormonal receptor and histology grade. Greater percentage of grade 1 tumors shows ER, PR positivity while compared to grade 3 tumors. The findings in study by Azizun Nisa et al showed similar results.[5]

Hormones receptors in this study were found as follow: ER+/PR+(36.20%), ER+/PR- (12.06%), ER-/PR+(1.72%) and ER-/PR-(48.27%). Study by Hussain G A et al and Maha Arafah also showed similar result in their study.[10,11]

Her-2/neu positivity in our study was 27.58%. Study by Haung HJ et al showed 17.7% positivity, Lal P et al showed 26.89% and Moses Embroise et al showed 27.10% positivity respectively in their study which are correlated with our study [12,13,6] . While few study like Vaidhyanathan et al found 43.2%, Munjal el al found 40.2% positivity respectively in their study.[14, 4]

In our study Her-2/neu receptor revealed a significant inverse association with hormone receptor status. We found that ER and PR expression was increased in Her-2/neu negative tumors compared to Her-2/neu positive tumors. Similar results were found in study by Mona Rashed et al, Maha Arafah, Huang HJ et al and MS Al-Ahwal et al.[7,11,12,15] There was no significant correlation was observed between lymph node status with ER,PR and Her-2/neu expression in present study. Studies by Azizun Nisa et al, Haung HJ et al and Muhmmad Azam et al showed similar results. [5,12,16]

The results in our study do not show any correlation between age and Her-2/neu expression. Study by Vaidyanathan et al also shows similar result. [14]

The triple negative breast carcinoma is characterized by lack of ER, PR and Her-2/neu expression. Our study showed 25.86% cases with Negative ER, PR and Her-2/neu status. Study by Patil et al showed 19.9%, Moses Embroise et al showed 25% of triple negative cases respectively.[17, 6]

In our study Her-2/neu positivity was expressed 0%, 28% and 52.94% in grade 1,2 and 3 respectively. Similar results were observed by Azizun Nisa et al and Moses Embroise et al.[5,6]

Significant association between increasing tumor size and Her-2/neu expression were seen in our study. Tumors larger than 5 cm size have higher rates of Her-2/neu expression (31.33%) than those of 2 to 5 cm size tumors (29.27%). Similar result was observed by Nidal M Almasri et al in their study.[18]

CONCLUSION

In present study of ER, PR and Her-2/neu expression in breast carcinoma by IHC method indicates higher rates of positive expression correlated with various clinicopathological aspects. Higher number of grade 1 tumors showed ER, PR positivity as compared to grade 3 tumors. Inverse relationship was observed between Her-2/neu expression and ER, PR receptor status. Her-2/neu expression was increased with size and high grade of tumor. ER, PR status and Her-2/neu expression did not show any significant correlation with lymph node status. Her-2/neu expression did not show any significant correlation with age.

Abbreviations

MRM – Modified Radical Mastectomy
H&E – Haematoxylin and eosin
ER – Estrogen Receptor
PR – Progesterone Receptor
WHO – World Health Organization
HIER – Heat Induced Epitope Retrival
IHC – Immunohistochemistry
IDC – Invasive Duct Carcinoma

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