



MOLECULAR PHENOTYPES OF BREAST CANCER BASED ON IHC

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ABSTRACT **Background:** Breast carcinoma is the most common malignancy of women globally and causes the majority of cancer deaths in women. The major factors underlying this increasing trend in developing countries are thought to be social changes that increase breast cancer risk - specifically, delayed childbearing, fewer pregnancies, and reduced breastfeeding - combined with a lack of access to optimal health care. The lifetime risk of breast cancer is 1 in 8 for women living to age 90 in the United States.^[1]

Objectives: To study ER, PR & HER-2/ Neu reactivity in the patient of breast carcinoma.

To analyzing the prevalence of molecular phenotypes in invasive breast carcinoma based on ER/HER-2 neu status .

Methods: A prospective study of 100 patients was done from July 2018 to June 2020 in Department of Pathology, GCSMCH & RC, Ahmedabad. The detailed clinical history and results of relevant investigations done were collected from hospital record.

Results: A 100 cases of radical mastectomies done for breast carcinoma were studied. Of these 100 cases, 98 were female and 2 were male. The patients age ranged from 25 to 83 years. Invasive Ductal Carcinoma with No Special Type was the most common histologic type observed in this study. ER, PR and Her2 status were assessed and ER positivity in 48% cases, PR positivity in 48% cases and Her2 positivity in 38% cases was seen. According to molecular subtypes, Luminal A was the most common subtype observed.

Conclusion: The survival of patients is linked to early detection, appropriate timely given treatment and genetic predisposition. Identification of Molecular phenotypes by IHC helps to guide the treatment and determine the prognosis. More aggressive multimodality treatment leads to improved clinical outcome, quality of life with significant decline in deaths due to breast carcinoma.

KEYWORDS : Invasive Ductal carcinoma, ER, PR, Her2.

INTRODUCTION:

Breast carcinoma is the most common malignant tumor and the leading cause of carcinoma death in women with a tremendous heterogeneity in its clinical behavior. Evaluation of breast lesions with imaging and histological sampling with core biopsy or FNAC are indicated to establish a definitive diagnosis. Nuclear Estrogen receptor (ER) expression should be evaluated in Invasive Breast Carcinoma because of its utility in predicting clinical benefit from hormonal therapy. Progesterone receptor (PR) expression tend to vary more than ER expression, and this helps account for the effectiveness of PR to further stratify ER-positive cases into prognostic categories. HER2 is a member of a family of growth factor receptors that regulate normal cell proliferation, development and survival. In 10-20% of IBCs, ERBB2 (HER2) gene is amplified, resulting in overexpression of the HER2 protein at the cell surface. There are number of HER2-targeted therapies available, some of which are used in combination with the first (and still standard) anti-HER2 biologic therapy, Herceptin. The classification system which relies on gene expression profiling is currently used divides breast cancers into four major types:

Luminal A. The majority are lower-grade ER-positive cancers that are HER2 negative.

Luminal B. The majority are higher-grade ER-positive cancers that may be HER2 positive.

HER2-enriched. The majority overexpress HER2 and do not express ER.

Basal-like. The majority by gene expression profiling resemble basally located myoepithelial cells and are ER-negative, HER2-negative.^[1]

MATERIALS AND METHODS:

A prospective study of 100 patients was done from July 2018 to June 2020 in Department of Pathology, GCSMCH & RC, Ahmedabad. Approval was taken from Institutional Ethical Committee before commencement of the present study. For prospective cases, on arrival to the department, the mastectomy and lymph node dissection specimen were received and subjected for adequate fixation using 10% neutral buffered formalin (NBF). Specimen was kept for fixation for 24

hours. These tissue bits were subjected for routine processing in an Automatic Tissue Processor and embedded in paraffin wax. Three to four micron thick sections were taken from paraffin embedded blocks and were stained using Hematoxylin and Eosin (H & E) for histopathological study. Additional sections were cut for immunohistochemistry (IHC) to detect ER, PR and HER2/neu overexpression.

RESULTS:

Of the 100 cases of breast carcinoma, 98 were females and 2 were males, and of these female most of the patients were postmenopausal (66%), and 32% were premenopausal. In present study, age ranged from 25 to 83 years and the mean age was 54.3±13.1 years. Majority of the cases (54%) had carcinoma in the Left breast and 46% had Right breast carcinoma. In present study, the predominant histologic type was Invasive Ductal Carcinoma, No special type (IDC,NST) consisting of 77 cases (77%) followed by 12 cases (12%) had invasive ductal carcinoma with ductal carcinoma in situ. In special subtype of carcinoma include one case of each medullary carcinoma, cribriform carcinoma and mucinous carcinoma. 48 cases (48%) tumor expressed estrogen (ER) and progesterone (PR) receptor each, whereas 38 tumors (38%) expressed HER-2. According to Molecular subtypes, maximum number of cases were Luminal A type tumors (36%) followed by triple negative tumors (26%).

Table 1: Final Histologic Types Of Breast Carcinoma

Histologic subtype	Number of patients	%
Invasive Ductal Carinoma with No Specific Type(NST)	77	77.0
Invasive Ductal Carinoma + Ductal carcinoma in situ (DCIS)	12	12.0
Invasive Ductal Carinoma with Lobular carcinoma in situ	01	1.0
Invasive Ductal Carinoma with Paget's disease of nipple	01	1.0
Invasive Ductal Carinoma with Medullary feature	03	3.0

Invasive Ductal Carcinoma with Ductal carcinoma in situ and Lobular carcinoma in situ	02	2.0
Invasive Ductal Carcinoma with Mucinous component	01	1.0
Medullary carcinoma	01	1.0
Cribriform carcinoma	01	1.0
Mucinous carcinoma	01	1.0
Total	100	100

Table 2: Molecular Subtype Of Breast Cancer Based On Er, Pr And Her2 Status

Molecular Subtypes	No. of patients	%
ER/PR+ve & HER2 + ve (Triple positive / Luminal B)	17	17.0
ER/PR-ve & HER2+ve (HER-2 positive)	21	21.0
ER/PR+ve & HER2-ve (Luminal A)	36	36.0
ER/PR-ve & HER2-ve (Triple negative/Basal like)	26	26.0
Total	100	100.0

Table 3: Comparative Analysis Of Molecular Types Of Breast Carcinoma With Various Studies

Authors	Luminal A (%)	Luminal B (%)	Her2 enriched (%)	Triple Negative (%)
Onitilo AA ^[16]	68.9	10.2	7.5	13.4
Shukla A et al ^[17]	26.66	10.0	24.44	32.22
Huang HJ ^[19]	66.4	30.9	45.6	13.8
A spitale ^[13]	73.2	13.8	5.6	7.4
Present study	36.0	17.0	21.0	26.0

DISCUSSION:

As the carcinoma of breast being the most common cancer among women of India and in many other regions of world, a constant research on predictive and prognostic markers of breast cancer are going on. The use of IHC has become the integral part of a complete and comprehensive histopathology report.

In the present study, the age range of presentation was 25-83 years with mean age 54.3 years. Majority of cases (58%) belonged to age group of 40 to 59 years followed by 60-69 years (18%). Similar observations made by Azizun-Nisa^[2], Ayadi L^[3] and Mudduwa^[4]. In present study majority of the females were postmenopausal (66.0%) and the result were concordance to the studies done by Mudduwa^[4] and Moradi^[5].

Incidence of male breast carcinoma in present study was 2%. Korde et al^[6] & Donegan WL et al^[7] noted incidence of male breast carcinoma in 1% patients. Sundriyal D^[8] noted in 1.03%. Ghosh J^[9] noted in 1.2%.

Majority of cases (74.0%) were between 2-5 cms in size followed by 20.0% cases were more than 5cms in size and 6.0% of cases measured less than 2cm in size on gross examination.

Table 1 shows final histological diagnosis of breast carcinoma. In present study, the predominant histologic type was Invasive Ductal Carcinoma, No special type (IDC,NST) consisting of 77 cases (77%) followed by 12 cases (12%) of invasive ductal carcinoma with ductal carcinoma in situ. In special subtype of carcinoma included one case each of medullary carcinoma, cribriform carcinoma and mucinous carcinoma. In studies conducted by Adedayo A^[16], Ghosh J^[9] and Azizun Nisa^[2], the predominant histologic type was Invasive Ductal Carcinoma, No special type comprising of 72.7 %, 95.4% and 85.3% respectively. Architecturally, the tumor cells may be arranged in cords, clusters, and trabeculae, and some tumors are characterized by a predominantly solid or syncytial infiltrative pattern with little associated stroma.

Immunohistochemical studied of breast carcinoma cases for ER status showed that 48% cases were ER positive. Several other studies done by Patnayak R^[14], Ahmad HG^[15], Shukla A et al^[17] and Bhagat vasudha M^[18], showed ER positivity in 47.6%, 43.8%, 49.1%, 48.27% and 41.1% cases of breast carcinoma respectively. Immunohistochemical studies of breast carcinoma cases for PR status showed that 48% cases. Several other studies done by Patnayak R^[14], Ayadi L^[3] and Shukla A et al^[17], showed PR positivity in 48.8%, 52.3%, 43.75%, and 41.1% cases of breast carcinoma respectively. Majority of our cases showed

negative HER2 status (62%) and these findings similar to the studies done by Ayadi L^[3], Shukla A et al^[17], Bhagat Vasudha M^[18], Patnayak R^[14] and Ahmad HG^[15] who demonstrated majority of the cases having negative HER2 status.

Table 2 shows molecular subtype of breast cancer based on ER, PR and Her2 status. Maximum number of cases were Luminal A type(ER/PR+HER2-) tumors followed by triple negative (ER/PR-HER2-). Table 3 shows comparative analysis of molecular types of breast carcinoma with various studies. In present study data were consistent with the studies done by Onitilo A et al^[16] and Shukla A et al^[17], in that ER and PR expression generally inversely correlated with HER2 overexpression. However, there is a substantial number of HER2 positive tumors which still expressed ER and or PR (Luminal B). In our study they comprise 17.0% of total cases.

CONCLUSION:

The prognosis and management of breast cancer is influenced by classic variables such as tumor size, histologic type and grade, status of lymphnode and hormone receptor status such as ER, PR and HER2/neu. The inter-relationship between ER, PR and HER2 has come to have an important role in the management of the breast cancer. Hence, immunohistochemical assessment of ER, PR & HER2 status should be incorporated as a routine investigation. This along with histopathological grading will help to guide the clinicians in making correct choice of treatment and disease free survival for the patient.

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