Study of Morphological Features of Carcinoma of Breast in Relation to ER/PR and Her2/neu Status

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Abstract
Introduction: Breast cancer in India is the most common cancer among women in the urban areas and ranks second in the rural population. In this study our aim is to correlate the morphological features of breast carcinoma with hormone receptor status.

Objectives: To study the morphological features of carcinoma of breast in relation to ER/PR and Her2/neu status.

Materials and Methods: A prospective study conducted from 2016 to 2017 in the Department of Pathology, M.G.M medical college and M.Y Hospital, Indore. 50 cases of carcinoma breast were studied for morphological features and their relation to hormone receptor status.

Results: In present study total 50 patients ranging from 20 to 80 years of age, with 32 (64%) premenopausal and 18 (36%) post menopausal females. Right breast, was most frequently involved (64% cases). Most common size of tumour ranged between 2 to 5cm. Most common histological type of breast carcinoma was invasive ductal carcinoma NOS (not otherwise specified) (90.0%). Both premenopausal and postmenopausal cases showed triple negative as the most common pattern. Among the invasive ductal carcinoma cases, triple negative was the most common pattern. Most common tumour grade in the present study group was grade II and triple negative was the most common pattern in this group.

Conclusion: The breast cancer cases if diagnosed at earlier stage have more favourable prognosis. Increasing the awareness in the public and good programs for early detection of the disease will go a long way in reducing breast cancer.

Keywords: Breast carcinoma, Immunohistochemistry, Morphology and Triple markers.
Introduction
Breast carcinoma is the most common cancer among women in the urban Indian population second only to cervical cancer in the rural population based on cancer registry data.\(^1 - 3\). According to the World Health Organisation (WHO), approximately 70% of breast cancers occur in women with none of the known risk factors. Only about 5% of breast cancers are inherited. The number of global cancer deaths is projected to increase by 45% from 2007-2030 (from 7.9 million to 11.5 million deaths), influenced in part by an increasing and aging global population.\(^3\) The prognosis and treatment of an individual patient is determined by staging and determination of pathologic features such as receptor status and tumour grade.\(^4\)

Materials and Methods
This study was carried out in between the year 2016 to 2017 taking 50 consecutive cases. The study was done as per standard ethics. All the cases histopathologically diagnosed as carcinoma were included in the study. The clinical details like age, sex, duration of symptoms, laterality, size of the tumour, axillary lymph node status and imaging findings like MRI were recorded in each case. After carrying out the detailed gross examination, all tissues were fixed in 10% buffered formalin. Multiple sections were taken from the tumour and its margins and all the lymph nodes. Histopathological study of the specimen was done by Haematoxylin and Eosin staining and as per standard protocol. Grading of the tumour was done by modified Bloom Richardson grading system. Immunohistochemistry (IHC) for ER, PR and Her-2/neu was performed on representative blocks of paraffin embedded tissue in each case. 3 - 4 micron thick sections were submitted for IHC staining.

Results
The age of the patients ranged from 20 to 88 years. A total of 50 patients presented with unilateral breast involvement in which 32 (64%) had carcinoma in the right breast and 18 (34%) with left breast carcinoma. The most common histologic type of breast carcinoma was Invasive Ductal carcinoma (NOS). 45 patients out of total 50 (75%) had IDC (NOS) type. 74% (37 patients out of 50) presented with lymph node metastasis. 13 out of 50 patients (26.0%) had tumour size less than or equal to 4 cms. Majority of tumours were predominantly of histopathological grade 2. By Immunohisto-chemistry 20% were ER+/PR+, 05% were Her2/neu positive and 70% were triple negatives. In present study it is observed that grade 1 tumours are 80% triple negative, ER and PR positive with almost equal number of cases being HER2+. In grade 2 tumours are 63.6% triple negative, 9.0% HER2 + and 27.7% ER / PR positive. In grade 3 tumours are 85.7 % triple negative and 14.2% HER2 positive.

Table 1: Laterality

<table>
<thead>
<tr>
<th>Site</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right Breast</td>
<td>32</td>
<td>64</td>
</tr>
<tr>
<td>Left Breast</td>
<td>18</td>
<td>34</td>
</tr>
<tr>
<td>Bilateral Breasts</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

Graph 1: Distribution of Site of Carcinoma

Table 2: Histologic Types of Breast Carcinoma

<table>
<thead>
<tr>
<th>Histologic Types</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive ductal carcinoma (NOS)</td>
<td>45</td>
<td>90</td>
</tr>
<tr>
<td>mucinous carcinoma</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>lobular carcinoma</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Infiltrating papillary carcinoma</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>
Table 3: Histologic Grade Wise Distribution (SBR) of Breast Cases

<table>
<thead>
<tr>
<th>Histologic Grade</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>Grade 2</td>
<td>33</td>
<td>66</td>
</tr>
<tr>
<td>Grade 3</td>
<td>07</td>
<td>14</td>
</tr>
<tr>
<td>No Grade</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

Majority of the patients presented with Grade 2 (72%)
Figure 3: PR positivity 3+ in 100% of tumour cell nuclei (Anti-PR- poly horseradish peroxidase- DAB chromogen, x40)

Figure 4: HER2 / neu 3+ in 100% of tumour cells with complete membrane staining (Anti-HER2/ neu- poly horseradish peroxidase- DAB chromogen, x40)

Discussion
Breast cancer is a heterogeneous group of tumors and is the most common malignant tumour of the female malignancies. In the present study 50 modified radical mastectomy specimens received for breast cancer were evaluated by light microscopy to determine the histologic type and immunohistochemistry was done to find out the ER,PR and HER2/neu status of the tumour. Correlation between these markers and tumour histopathology was done. In the present study the peak was from 40-50 years of age, followed by 50-60 years of age. F. De Waard et al. from their study have concluded that after 60 years of age, the age specific breast cancer risk is on the increase due to postmenopausal hormonal stimulus. Mudduwa had 85.7% postmenopausal women and 14.3% premenopausal females in her study. In the present study most common subtype was IDC (NOS) followed by mucinous and lobular carcinoma. Priti Lal et al., Michael Stierer et al. Mehrdal Nadji et al. also had similar results. In the present study grade 2 was most common followed by grade 1 and grade 3. TB Pathak et al. also had similar results. In the present study lymph node metastasis were present in 74% (37 patients out of 50) cases. Lakmini K.B.Mudduwa. also had similar results. Mudduwa in her study found no statistically significant correlation between lymph node status and ER, PR scoring. In the present study there were no ER negative/PR positive tumours. Mehrdad Nadji et al. also had no ER-/PR + tumours in their study.

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 2 tumors showed ER, PR positivity as compared to grade 1 tumors. 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.

Conflict of Interests
There was no conflict of interests with respect to all authors.

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References


