EFFECT OF AGE ON PROGNOSIS IN DIFFERENT MOLECULAR SUBTYPES OF FEMALE BREAST CARCINOMA

Naveed Sharif¹, Sajjad Ahmad¹, Muhammad Mumtaz Khan¹, Ahmareen Khalid², Sadaf Alam¹, Sara Ziaullah¹, Sabeen Nasir¹, Fozia Rauf¹

¹Peshawar Medical College, Riphah International University Islamabad and ²Pakistan Institute of Medical Sciences, Islamabad, Pakistan

ABSTRACT

Background: Breast carcinoma is one of the ten commonest worldwide malignancies. The objective of the current study was to correlate the significance of prognostic markers and molecular subtypes with patients' age in carcinoma of female breast.

Material & Methods: A descriptive study was conducted at Department of Pathology, Peshawar Medical College, Peshawar and Pakistan Institute of Medical Sciences, Islamabad. Sixty mastectomy specimens were selected using a non-probability sampling method from 1st January, 2012 to 31st December, 2013. Histological type, tumor size, tumor grade and lymph node status were determined. Estrogen receptor (ER), progesterone receptor (PR) and Her-2/neu expression were evaluated immunohistochemically.

Results: Among these 60 patients, the mean age was 50.5±14.4 years. There were 26 (43.3%) patients with age more than 50 years while 24 (40%) were between 40 and 50 years. Ten (16.7%) patients had age less than 40 years. Luminal A molecular subtype was observed in 50% in age groups 40 to 50 and above 50 years. The age group above 50 years had more cases of luminal B (58%) and non-luminal (42%) types. Triple negative molecular subtype is more common in age group between 40 and 50 years i.e. 57.1%.

Conclusions: It was concluded that age is an important factor in determining the aggressiveness of female breast cancer along with other markers like, ER, PR and HER2/neu receptor status.

KEY WORDS: Invasive ductal carcinoma; Estrogen receptor; Progesterone receptor


INTRODUCTION

Breast carcinoma is one of the ten commonest worldwide malignancies. Every year more than one million women are diagnosed with breast malignancies. Approximately 14% of female cancer deaths are due to this disease.¹ It is the most common (25%) of all female malignancies in Pakistan.²

The breast carcinoma incidence peaks among women in their forties in Asian countries as compared to United States and Europe where it commonly involves women in their sixties.³

The variables which influence the prognosis and management of breast cancer include histological type, grade and stage of the tumor, along with ER, PR and Her-2/neu status.⁴ These biomarkers provide guidelines for treatment, its associated outcomes and about aggressiveness of the lesion. Their combined expression also represents surrogates for the four major molecular subtypes: Luminal A, Luminal B, HER2 positive (Non-Luminal), and triple negative (or basal-like).⁵ These molecular types have significant correlation with prognosis and response to chemotherapy of the disease.⁶

Studies have shown that breast cancer at a younger age showed more aggressive biological behavior and more unfavorable prognosis as compared with older patients.⁷

The objective of the current study was to correlate the significance of tumor size, lymph node involvement, histological grade and molecular subtypes with patients’ age in carcinoma of female breast.
MATERIAL AND METHODS

A retrospective descriptive study was carried out at the Department of Pathology, Peshawar Medical College, Peshawar and Pakistan Institute of Medical Sciences, Islamabad from 1st January 2011 to 31st December 2013.

Mastectomy specimens of female patients from its affiliated teaching hospitals, belonging to Khyber Pakhtunkhwa province with diagnosed breast carcinoma were included. Patients who had received neo-adjuvant chemotherapy before mastectomy were excluded. The sample size was 60. Patients were grouped as below 40, 40 to 50 and above 50 years. Samples were received in 10% buffered formalin. Tumor size was measured on gross examination and classified as < 2 cm, 2 – 5 cm and > 5 cm. Representative sections of the tumor and lymph nodes were submitted for paraffin embedding after formalin fixation; 3-4 µm thick sections of the tissue were made and stained with hematoxylin and eosin (H&E) for subsequent microscopy. Histological typing of the tumor and detection of lymph node metastases were performed. Histological tumor grading was done using modified Bloom and Richardson scoring system.2 Lymph nodes were grouped as 1-3, 4-9 and >9 according to number of lymph nodes showing metastases. The parameters were recorded according to TNM staging for breast carcinoma. Representative sections with tumor and the adjacent normal breast tissue (internal control) were processed for ER, PR and HER-2/neu immunohistochemical staining. ER and PR positivity were assessed by using H-scoring system taking nuclear staining with a score >50% as positive. For HER-2/neu staining, a score 3+ was taken as positive.9,10

Molecular Types    | Immunohistochemical Stain Reaction |
-------------------|----------------------------------|
Luminal A         | ER+ /PR+ HER2-                   |
Luminal B         | ER+ /PR+ HER2+                   |
Non luminal       | ER- PR- HER2+                    |
Triple Negative    | ER- PR- HER2-                    |

Data was entered in SPSS version 19.0 and statistical analysis was done to determine frequency of ER, PR and other morphological prognostic parameters along with different molecular subtypes.

RESULTS

During this study a total of 60 mastectomy specimens of female breast cancer were included. Morphologically all the cancers were invasive ductal carcinoma (NOS). The mean age was 50.5 ±14.4 ranging from 21 to 85 years. There were 26 (43.3%) patients with age more than 50 years while 24 (40%) were between 40 and 50 years. Ten (16.7%) patients had age less than 40 years. The right breast was more commonly involved (58%). The tumor size ranged from 1 cm to 26 cm. Four (6.7%) cases were multifocal. ER and PR were positive in 29 (48.3%) and 21 (35%) cases respectively while HER-2/neu was positive in 17 (28.3%). (Fig. 1)
Luminal A molecular subtype was observed 50% in age group between 40 and 50 and above 50 years each. The age group above 50 years had more cases of luminal B and non-luminal types i.e. 58% and 42% respectively. Triple negative molecular subtype was more common in the age group between 40 and 50 years i.e. 57.1%. (Table 2)

Table 2: Age with molecular subtypes of breast cancer.

<table>
<thead>
<tr>
<th>Age of patients in years</th>
<th>Luminal A n=20</th>
<th>Luminal B n=12</th>
<th>Non luminal n=14</th>
<th>Triple Negative n=14</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>0 (0.0)</td>
<td>3 (25%)</td>
<td>4 (28.6%)</td>
<td>3 (21.4%)</td>
</tr>
<tr>
<td>40-50</td>
<td>10 (50%)</td>
<td>2 (16.7%)</td>
<td>4 (28.6%)</td>
<td>8 (57.1%)</td>
</tr>
<tr>
<td>&gt;50</td>
<td>10 (50%)</td>
<td>7 (58.3%)</td>
<td>6 (42.9%)</td>
<td>3 (21.4%)</td>
</tr>
</tbody>
</table>

**DISCUSSION**

The present study comprised of referred cases from allied teaching hospitals of Peshawar Medical College for which hormonal and Her-2/neu receptors were requested by the clinicians.

A large number of studies show 20% to 38% regional variations of this disease in Pakistan including Khyber Pakhtunkhwa Province.11,12

The present study was designed to determine the association of patients’ age with histologic grade, tumor size, lymph node metastases, reactivity pattern of estrogen receptor (ER), progesterone receptor (PR) and HER-2/neu in invasive ductal carcinoma NOS of female breast in district Peshawar of Khyber Pakhtunkhwa.

In this study, all the cases belonged to histological type invasive ductal carcinoma NOS which is most commonly observed throughout the world.13

In our study the HER2/neu receptor was positive in 28.3% cases which is slightly higher than other studies from Northern America (22.2%)14 and Europe (13.0%)15. Her2/neu positivity in our study is almost identical to other regional studies conducted by Mostafa et al,16 Pinjawani et al17 and Keyhani et al18. The overall ER expression was positive in 29 (48.3%) cases which is lower than the findings of studies by Anderson et al19 and Chung et al20 i.e. 64.9% and 61% respectively. Our findings were different from other national studies by Kamil et al21 (32%) and Sharif et al22 (74%). Similarly, our findings of positive PR expression i.e., 21 cases (35%) was less than other international studies by Aprino et al23 (57%) and Chung et al24 (51.9%). Regarding studies in Pakistan, our findings were almost similar to Kam-

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CONCLUSION

It was concluded that age is an important factor in determining the aggressiveness of female breast cancer along with other markers like, ER, PR and HER2/neu receptor status.

REFERENCES


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CONFLICT OF INTEREST
Authors declare no conflict of interest.

GRANT SUPPORT AND FINANCIAL DISCLOSURE
None declared.