ORIGINAL ARTICLE

Aggressiveness of Breast Carcinoma in Young Pre-Menopausal Patients

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ABSTRACT

Background: Breast cancer is the most commonly diagnosed malignancy in female population.
Aim: To determine and compare the frequency of aggressiveness of breast cancer in pre and post-menopausal patients.
Study design: Cross sectional study
Place and duration of Study: Department of Histopathology, K.E. Medical University Lahore from 1st January 2016 to 31st December 2018.
Methodology: One hundred and fifty female patients diagnosed with breast cancer to assess the aggressiveness of breast cancer in young - premenopausal patients. Post-Surgical Modified Radical Mastectomy specimens were submitted and evaluated for grade, stage, involved lymph nodes, tumor size and metastasis.
Results: Sixty four percent of the tumors were left sided and the invasive ductal carcinoma was the most dominant histologic type (96%). Ninety two patients were premenopausal while 58 were post-menopausal. Nodal positivity in patients less than 40 years was more pronounced (74.2% versus 56.8%, p=0.029).
Conclusion: Young premenopausal patients represent high risk group for advanced breast cancer.
Key words: Breast Cancer, Young, Premenopausal, Post-menopausal, Invasive Ductal Carcinoma

INTRODUCTION

Breast cancer is the most common malignancy diagnosed in the female population. One in every eighth woman has risk of breast malignancy through her lifetime[1]. The Global Cancer survey reports that female breast cancer accounts for 23% of all diagnosed cancers[2]. The incidence of breast cancer peaks in reproductive years and wanes off after menopause[3].

The genetic makeup of a population is closely related to its ethnic background, and in Pakistan due to the protective effect of consanguineous marriages, the disease expression is different.[4] The trends of early marriages, multiparity, longer infant nursing and obesity, seen in our country, greatly influence the disease presentation as old age pregnancy, nulliparity, absent or decreased breast feeding and obesity are important risk modulators of breast malignancy identified in the West[1].

For malignant lesion, patient survival and treatment modalities depend greatly on its morphologic and biologic prognostic factors[1]. However, young age alone serves as an important independent clinical prognostic factor for patient outcome and survival. The younger women presented with higher tumor stage and grade and were seen to be estrogen and progesterone receptor negative[5-9].

There is a dire need to conduct this study to highlight the prognostic factors particularly menopausal status and age of occurrence of this killer disease, to compare the results with the already conducted studies and to render community aware of the early screening programs in order to improve the health status of the community.

MATERIALS AND METHODS

This cross-sectional analytical study conducted at the Department of Histopathology, K.E. Medical University Lahore with collaboration of Tertiary Care Hospital of Pakistan and 150 cases were enrolled. The sample size was calculated through 95% confidence level, 9% margin of error and taking expected percentage of young female patients i.e. 31.56%[8] with breast cancer. Patients with breast carcinoma (as per operational definition), Post pubertal female patients from 20 years to 80 years of age, Modified Radical Mastectomy (MRM) Specimens and Lumpectomy with Axillary clearance Specimens sent to Department of Pathology, KEMU were included in the study while Female patients below 20 years, and above 80 years of age or with Unfixed biopsies were excluded. All 150 patients undergoing histopathology of MRM
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specimens were enrolled after informed consent and ensuring their confidentiality. Their demographic features i.e. age, sex, address were noted. The biopsies received in the Pathology Department were formalin fixed and stained with haematoxylin and eosin stain. Pathological examination was be carried out by a single consultant histopathologist under light microscope. The patients were divided into two age groups, younger age group ranging from 20 years to 40 years of age and older age group addressing above 40 years old patients. The data was recorded and aggressiveness of breast carcinoma was obtained. All of the MRM biopsies diagnosed for carcinoma breast will be evaluated for patient's age, laterality, tumor type, tumor grade and tumor stage. Permission was obtained from Ethical Committee.

Each breast specimen was serially sectioned and later palpated for masses, then oriented and laterality determined by using axillary fat as lateral. Margins were inked and size of the tumor and its relation to each margin was recorded. The lymph nodes were examined, isolated and submitted. The description of specimen, tumor size in three dimensions, color consistency, necrosis and presence of any additional cysts, fibrosis and scars was noted. Representative sections were taken from each specimen for histopathologic evaluation. These sections were taken from nipple areola complex, skin above the tumor, multiple sections of tumor, resection margins, and all four quadrants for secondary lesions. An automatic tissue processor (Model RH-12 EP Sakura, Fine Technical Co. Ltd, Tokyo Japan) was used for further processing of tissue blocks and staining was performed. All the data was analyzed using SPSS-24.0, using Mean and standard deviation and Chi square were applied. P value ≤0.05 was considered significant.

RESULTS

The median age for carcinoma was 45 years. 62 (41.3%) patients ranged between 21 to 40 years of age, while 88 (58.7%) patients belonged to the older age group. Sixty one percent of the patients under study were premenopausal while 38.7% were post-menopausal. Around 72.2% tumors were aggressive, accounting for 109 cases. Aggressiveness of breast carcinoma was analyzed in younger and older age groups, and premenopausal and post-menopausal patients by assessing tumor grade, tumor size, involvement of lymph nodes, metastasis and tumor stage. Tumor grade distribution was also assessed in premenopausal and post-menopausal reproductive groups. Premenopausal patients strikingly showed high grade tumors than post menopausal women (70.7% vs 36.2%, p<0.001) [Table 1]

The tumor size was also evaluated according to reproductive groups. In Premenopausal patients, bigger tumor nodules were seen with T3 and T4 tumors collectively accounting for 60.9% of all pre-menopausal patients. However in older age groups the tumors were

less alarming, collectively making only 19% T3 and T4 tumors (60.9% versus 19%, p<0.001). In older patients the tumors were mostly smaller in size, constituting 72.4% T2 tumors and 8.6% T1 tumors (Table 2)

Notable involvement of lymph nodes was seen in pre-menopausal patients. Out of 92 patients, 68 (73.9%) showed nodal positivity, while in post-menopausal patients 48.3% showed nodal positivity (73.9% versus 48.3%, p=0.001). None of the patients in post-menopausal group showed involvement of more than 10 lymph nodes. While it was observed that analyzing the age of patients and tumor metastasis showed no statistically significant correlation (12.9% versus 4.5%, p=0.063), the metastasis of tumor showed a distinct behavior in the reproductive groups. In premenopausal patients tumor metastasis was seen in 13% patients while no patient in post-menopausal group showed seeding of tumor to distant sites(p=0.004) [Fig.1].

Table 1: Distribution of tumor grade in reproductive groups

Reproductive groups	Tumor Grade	
	Grade II	Grade III
Pre-menopausal (n=92)	27(29.3%)	65(70.7%)
Post- menopausal (n=58)	37(63.8%)	21(36.2%)

Table 2: Distribution of tumor size in reproductive groups

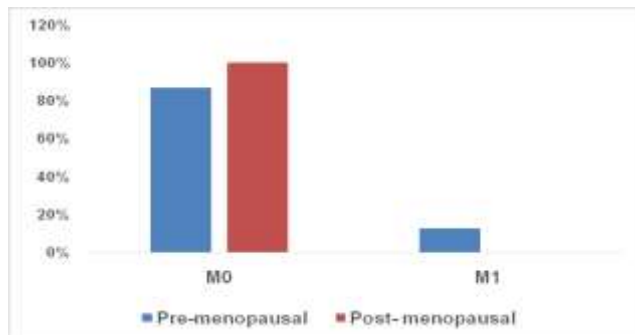| Reproductive groups	Tumor Size				Overall aggressive tumors
	T1, <2cm	T2, 2 to 5 cm	T3, >5cm	T4, skin ulceration	
Pre-menopausal (n=92)	-	36 (39.1%)	29 (31.5%)	27 (29.3%)	82 (89.1%)
Post-menopausal (n=58)	5 (8.6%)	42 (72.4%)	8 (13.8%)	3 (5.2%)	27 (46.6%)

Fig. 1: Distribution of Metastasis in reproductive groups

DISCUSSION

Breast cancer is the most common malignancy in females with a continual rise in its incidence. The disease is seen prominently in older women, however even the young females are not protected.[10] Hence strategies must be devised for detection at young age as young age itself is a worse prognostic factor for survival.[11]

A study conducted on 763 breast cancer patients in Nigeria concluded that 85% of young female patients presented with aggressive breast cancer and the invasive ductal carcinoma, (NOS type) remained the predominant histologic pattern (95%).[12] These findings are close to our study showing IDC 96% and aggressive tumors in young patients accounting for 93.5% of cases. Nigeria is a developing country with near similar socio-economic status as Pakistan and hence comparable public awareness and health facilities[13] These similarities can in part affect disease presentation and patient management in strategically different areas.

Ginsburg et al[14] demonstrated in his study that patients less than 36 years of age presented with locally advanced tumors, with sizable tumors and metastatic lymph nodes. The disparity is fairly prominent in tumor presentation, prognosis and mortality of young and old patients. These differences can be in part due to previous family history of breast cancer, use of contraceptives and early menarche in young patients.[15]

Screening mammography for breast tumors has demonstrated little efficacy in detection of early breast cancers. Hence younger patients tend to present with advanced cancers.[16]However targeted screening of young high risk females with positive family history can still be of aid in detection and management of these aggressive tumors[15].

Tumor metastasis to distant sites adversely affects prognosis and patient survival. Tumor metastasis is reported in higher proportions in young patients[17]. Comparable results are noted in our study and metastasis was seen in 12.9% of patients less than 40 years of age. Those above 40 years manifested with only 4.5% tumor metastasis. The results were also significant in premenopausal groups with 13% patients showing distant metastasis and none of the post-menopausal patient had distant tumor seeds (p=0.004)

The premenopausal patients presented with advanced aggressive tumors when compared to post-menopausal patients (89.1% versus 46.6%, p <0.001). Higher grade, larger tumor sizes, prominent lymph node involvement and Stage III and Stage IV tumors were seen characteristically in premenopausal patients. These results correspond well to findings in a study by Hartmann et al[18].

CONCLUSION

The premenopausal females present with advanced breast cancer that are grave in stage, grade and prognosis. Promotion of self-examination, frequent breast cancer awareness camps and free screening programs can assist in early detection and timely management of this morbid disease and encourage a healthful approach in general masses.
Conflict of interest: Nil

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