

# Study of comparative patterns of breast cancer stages and positive hormone (ER/PR/HER2-neu) status

## Abstract

A cross-sectional study was carried out at the Institute of Nuclear Medicine and Oncology, Lahore (INMOL) during July to August 2017 for the determination of comparative patterns of distribution of four stages that is commonly assessed in breast carcinoma, and to estimate a patient response to endocrine therapy for better clinical outcomes. Name, age, sex, other relevant data, history and examination findings and results of histopathology and other investigations were recorded. Total of 53 breast cancer patients were evaluated for this study. The patients were categorized stage wise and the hormone receptor (ER/PR/HER2-neu) status was analyzed. The age of patients ranged from 16 to 84 years. 35.84% patients had carcinoma of right breast, 26.41% were diagnosed as stage III, and 69.41% of stage II and 3.77% patients were as stage IV. Those diagnosed with ER+ were 11.32%, HER2-neu+ were 4, ER+/PR+ were 16.98%, ER+/HER2-neu+ were 3.77%, 1.88% was PR+/HER2-neu+ and ER+/PR+/HER2-neu+ had 43.39%. There were 3.77% cases each for grade I and IV, 30.18% grade II and 252.83% cases of grade III. Breast carcinoma is still a common problem presenting at a young to middle age group with invasive ductal carcinoma being the commonest variant with a high grade and a late stage presentation due to lack of screening and awareness programs. Therefore, Public health awareness needs to be directed towards the societal influences that impact breast carcinoma development.

**Keywords:** carcinoma, breast, chemotherapy, imaging, estrogen

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**Tanveer Ahmed Khan,<sup>1</sup> Sobia Noreen<sup>2</sup>**

<sup>1</sup>Rashid Latif College of Pharmacy, Pakistan

<sup>2</sup>Hajvery University, Pakistan

**Correspondence:** Tanveer Ahmed Khan, Rashid Latif College of Pharmacy, Lahore, Pakistan, Tel +923202882884, Email tanveerahmedkhan754@gmail.com

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## Introduction

Breast cancer refers to several types of neoplasm arising from breast tissue, the most common being adenocarcinoma of the cells lining the terminal duct lobular unit. Breast cancer is the most prevalent cancer in women all around the globe, and is the second leading cause of cancer deaths in women. However, the prognosis is good if detected early. The overall 5-year relative survival is 88% in women.<sup>1,2</sup> Risk of breast cancer increases with lifetime estrogen exposure. The majority of breast cancers are hormone sensitive, meaning that they express estrogen receptors and proliferate in response to estrogen stimulation. Endocrine therapies that inhibit estrogen production are effective in treating hormone-sensitive breast cancer.<sup>3,4</sup> Approximately 5-10% of breast cancers are hereditary, meaning that there is a known genetic mutation causing increased cancer risk in the patient's family.<sup>5</sup> Hereditary breast and ovarian cancer (HBOC) syndrome is caused by mutations in two genes, *BRCA1* and *BRCA2*. The genes code for a DNA repair pathway that is important for protecting against mutations. The loss of either gene confers a high risk of breast cancer, as well as other cancers.<sup>6</sup> There are different and multiple steps in the diagnostic approach including screening, imaging (ultrasound and/or mammography), biopsy, pathological diagnosis and staging.<sup>7</sup>

Cytotoxic chemotherapy, endocrine therapy, or radiation therapy may be used post-surgery to prevent relapse. Either whole or partial breast irradiation may be used. Adjuvant radiation therapy is applied post-mastectomy to prevent recurrence. Since most recurrence of early-stage breast cancer occurs locally, partial irradiation at the tumour site has similar mortality benefits as whole breast irradiation. However, new evidence suggests an increased risk of local and

auxiliary recurrence with partial irradiation. Radiation of metastatic disease (e.g. bone or brain metastases) is also used.<sup>6-8</sup> Cytotoxic drugs, such as Cyclophosphamide, methotrexate, doxorubicin, and paclitaxel, are used in hormone receptor-negative or HER2-positive breast cancers. They can either be given pre-surgery as neo-adjuvant to shrink the tumour or post-surgery as adjuvant to prevent relapse. The objective of current study was to determination of comparative patterns of distribution of four stages that is commonly assessed in breast carcinoma, and to estimate a patient response to endocrine therapy for better clinical outcomes.

## Materials and methods

A cross-sectional study was carried out at the Institute of Nuclear Medicine and Oncology, Lahore (INMOL), the leading hospital dealing with cancer related diseases in Punjab province of Pakistan, consisting of 53 patients during the months of July to August 2017. The proforma was designed to collect information regarding various parameters associated with breast cancer directly by patient counseling. Records of patients having primary or recurrent ductal, lobular and other types of breast carcinoma were evaluated for hormone receptor status. The pathology reports were reviewed for patient's demographics, site of tumour, histological type of carcinoma, grade and stage of carcinoma at diagnosis, hormonal status, nodal status, treatment strategy, additional associated conditions and adverse drug reactions (ADRs) due to chemotherapy. Inclusion criteria included all those patients with breast carcinoma who gave positive diagnostic tests for hormone receptors status i.e. immune-histochemical test. Data of estrogen, progesterone and human epidermal growth factor receptor 2 expression status was analyzed. Exclusion criteria included those

patients who refused to undergo assessment and treatment in the unit, those who left against medical advice after a provisional diagnosis was made and those patients who refused to provide informed consent for their treatment and inclusion in the study. Those patients having metastasis in breast with primary tumour outside breast were excluded from the study. Data was summarized on statistical package for social sciences software version 22.0.

## Results

The most common age group was 45-54 years with 16 cases (30.18%), then 55-64 years with 15 cases (28.30%). This shows that breast carcinoma is high between 45 to 60 years of age and found least below 40 years in Pakistan (Figure 1). There were 45.2% patients identified to have positive hormone receptor status. Besides, 35.84% patients had carcinoma of the right breast. Those diagnosed with ER-positive status were 11.32%, HER2-neu over-expression 7.54%, ER/PR receptor-positivity (or luminal A) 16.98% and 3.77% were ER/HER2-neu positive, 1.88% was PR/HER2-neu positive and 1.88% was triple positive while none of them showed positivity for HER2, 23 patients were positive for all the three receptors. These cases were diagnosed at different grades including 22.64% of G1 (low grade), 39.62% of G2 (intermediate grade), 26.41% of G3 (high grade) and 11.32% of G4 (undifferentiated). Combined chemotherapy and radiotherapy was prescribed in 52% cases, only chemotherapy in 18% and chemotherapy and hormones in 9 patients. Mastectomy and auxiliary clearance was done in 60% patients. Chemotherapy with Fluorouracil, Adriamycin and Cyclophosphamide (FAC) was recommended to 62.2% patients, while Taxol, Adriamycin and Cyclophosphamide (TAC) to 33.5%. Fluorouracil, Epirubicin, Cyclophosphamide (FEC) was prescribed in 0.06%, Tamoxifen to 0.01% and herceptin to 0.09%. About 66% patient were diagnosed as Stage III, 26.41% as Stage II and 3.77% patients were as Stage IV and 3.77 as Stage I as well. Infiltrating ductal carcinoma with nonspecific features was the commonest type, found in 82.6% out of a total of 53. Other types included 4.35% cases of infiltrating ductal carcinomas of papillary type, 2.17% of mucinous type and 2.17% of medullary type, 6.52% of invasive lobular carcinoma and 1.88% case of mixed lobular and ductal carcinoma. Two patients presented with metastasis in the breast having primary tumor elsewhere. One of these patients had choriocarcinoma and the other had non-hodgkin's lymphoma. These patients were excluded from the study. Some other information which was recorded from patients was as follow.

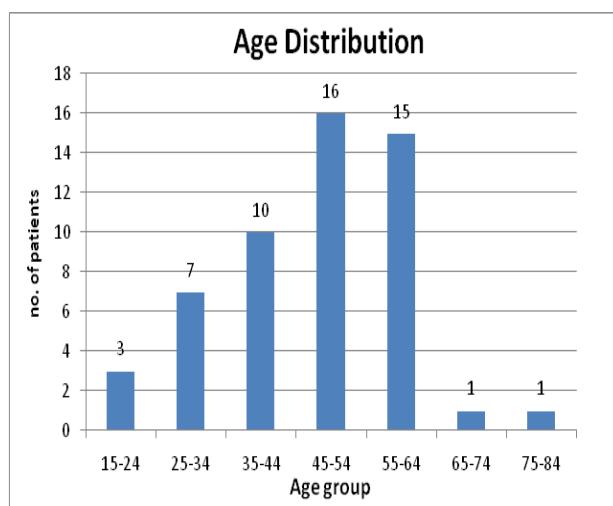


Figure 1 Breast carcinoma among different age groups.

## Discussion

This study was conducted to see the pattern of breast cancer and its various aspects in the local setting. An important point to note in this data is the late (stage II, III and IV) presentation of our breast cancer women. As advanced stage (stage IV) is considered incurable and without treatment the survival is limited (2.7 years or less).<sup>9,10</sup> Every effort should be made to diagnose breast cancer at an early stage. Our data is in sharp contrast to the international literature, where only 10% or fewer women will have a metastatic stage (i.e. stage IV) of breast cancer at presentation.<sup>10</sup> One of the most important parameters in breast cancer management and patient survival is the hormone status and responsiveness of tumour to hormone. In developed countries, many studies have been carried out to evaluate the hormone receptors and HER2-neu status. In US, numerous studies have been used to demonstrate and evaluate differences in hormone receptor status and histology by race and ethnicity among women.<sup>11,12</sup> In young women, risk profile is worse than in older women. It was seen that young women with breast tumours had a tendency to have larger tumour sizes, more positive lymph nodal status, more negative hormone receptors status, higher tumour grades at diagnosis than the older women.<sup>13</sup> The results of the study showed that women of the middle age group (30-59 years) are at a higher risk of developing breast cancer in the local setup. A high proportion of breast cancer patients, 71% of the cases at INMOL have reported at stage II and III. Such late presentation of the disease is an important aspect of this study. It points to the alarming situation due to the rising trend of breast cancer incidence in Pakistan. The public awareness of this disease may help in early detection of breast cancer, decreasing the mortality and ultimately increasing the probability of survival. If breast cancer is detected at an early stage, it is curable and may be treated better. Therefore, women must be made well acquainted with the symptoms of the problems of breast cancer. Special programs like seminars, lectures and screening programs may be arranged to educate the women in this regard.

In the present study, the most common histopathological type found was infiltrating ductal carcinoma. Many other International studies conducted in USA, Malaysia, Germany and India have shown that breast cancer is detected more commonly in the earlier stages due to better screening programs.<sup>14,15</sup> Variations in the incidence of breast cancer among multicultural populations suggest different etiological factors including genetics, environment, reproductive experience, endogenous and exogenous hormones in women, immune status, host vulnerability, Cultural dynamics, socio-demographic differences, and behavioral characteristics across population. No author reported any other type of cancer to be more common than this one. Hunter (2000) in his study has also found infiltrating ductal carcinoma to be more common than lobular carcinoma. Stages in which disease presented included 2(4.35%) cases of stage I, 16(34.78%) stage II, 20(43.47%) stage III, and 08(17.39%) cases of stage IV disease. Thus patients presented most commonly in stage III(42.2%) and IV(17.7%) collectively constituting almost 60% of the total cases, which means that the disease is still presenting at a late stage and thus making curative treatment difficult. The studied histological types of breast tumour greatly differed in their clinical presentations, and the differences found in their hormone receptor status and grading point to their markedly different etiologies. This reveals the following facts; about half of the patients had positive hormonal status, luminal A IHC subtype was more prevalent among patients compared to other subtypes. Both sides of the body were equally involved in this study; 35% cases of the right breast and 64% of the left side.

Treatment also depends on the histopathological stage, grade and

the breast cancer cells with ER, PR or HER2-neu receptors on their surface. Most of the patients were receiving FAC/CAF, TAC, and FEC with anti-oestrogens for treating their positive hormonal status, and patients with HER2-neu were recommended treatment with herceptin. Similar findings were reported by Aryandono et al.<sup>16</sup> and Hisham et al.<sup>17</sup> As far as association of age with ER expression is concerned most reports in the literature show an association between the expression of ER and age in breast carcinoma while other studies have reported otherwise.<sup>18</sup> This study did not show statistically significant expression for grade-II tumours but the trend was more for grade-II tumours for ER/PR expression compared to grade-I tumours which may need to be verified in larger sample study. In the present sample size only a very small number of grade I tumours were available. Considering the fact that grade-I tumours are less commonly seen, these results point towards an important fact of conducting a larger sample review. The present study has clearly shown that breast cancer presents in the middle age group at an advance stage (II, III and IV) in the local setup. These facts may indicate that the disease in this area is probably more aggressive and that there may be social and economic reasons and lack of awareness due to which patients do not come up for medical consultation in early stages of the disease. Public health awareness needs to be directed towards the societal influences that impact breast carcinoma development.

## Conclusion

Further research should be carried out to understand the various trends and relationships between different variables associated with breast cancer for better prognosis of breast cancer patients in order to obtain better clinical outcomes with improved survival. Breast carcinoma is still a common problem presenting at a young to middle age group with invasive ductal carcinoma being the commonest variant with a high grade and a late stage presentation due to lack of screening and awareness programs. Public health awareness needs to be directed towards the societal influences that impact breast carcinoma development.

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## Conflict of interest

Author declares that there is no conflict of interest.

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