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Original Research Article

A retrospective, epidemiological study on the pattern of distribution of phenotypic subgroups among patients of breast cancer in a tertiary care level hospital of West Bengal, India

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ABSTRACT

Background: The burden of breast cancer is increasing worldwide and it is second most cause of mortality in India. Epidemiologic data regarding different phenotypic subgroups in Indian women is scarce. The present study aimed to find out the epidemiological distribution of different phenotypic subgroups in the patients suffering from breast cancer.
Methods: This was a retrospective, observational study conducted at the Department of Radiotherapy, Burdwan Medical College and Hospital, West Bengal, India between July 2012 and June 2017. Women diagnosed with biopsy proven breast carcinoma who had been attending radiation oncology outdoor patients department (OPD) were included in the study. The data of the patients regarding age at presentation, grade of tumor, Ki 67 status, hormone receptor status, and their phenotypic subgroup classification were retrieved from hospital record.
Results: A total of 280 women patients were included in the study, of these, 105 were premenopausal and 175 were postmenopausal. Locally advanced breast cancer (60.0%) was most prevalent breast cancer among them. Majority of the patients had grade III tumor and higher expression of Ki-67 index at the time of presentation (53.92% and 68.21%, respectively). Infiltrating Ductal carcinoma is the most prevalent histopathological sub-type in both premenopausal and postmenopausal women. Hormone receptor positivity in premenopausal women was comparatively higher than postmenopausal women. Whereas human epidermal growth factor receptor 2 negative cancer was comparatively higher in postmenopausal women (66.98%). The most prevalent phenotypic subgroup among premenopausal and postmenopausal group was luminal B (38.09%) and luminal A (36.57%), respectively.
Conclusions: Overall findings suggest that majority of patients were diagnosed with high grade and high Ki67 index which showed lack of awareness in these patients about this disease. Use of prognostic factors and predictive markers can be helpful to diagnose breast cancer at early life.

Keywords: HER2-neu, Ki67, Hormone receptor positivity, Premenopausal

INTRODUCTION

Breast cancer is the most frequently diagnosed cancer among females and the leading cause of mortality. The burden of cancer is increasing worldwide and incidence is rising in India. The incidence rate of breast cancer varies in different regions with multiple risk factors. Several risk factors are associated with development of breast cancer which could be differed by age, diverse cultures, geographical variations, family history, diets and habits.[1-3] Complications including fertility, conception and breast feeding are more prone to develop breast cancer in premenopausal women.[4] Menopausal status is another prognostic factor which may not responsible to cause

cancer, but it increases risk in woman who experiences menopause after age 55. Although this risk is even greater in woman began menstruating before age 12. In India, reasons for varying incidence of breast cancer are not well understood.

Traditional prognostic factors including tumor size, lymph-node involvement, vascular invasion, and predictive markers including expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) play pivotal role in determining the stages and/or severity of the breast cancer.[5] However, these factors are not enough to define the prognosis and treatment initiation.

Gene expression profiling studies have identified four phenotypic subgroups of breast cancer including luminal A, luminal B, HER2 overexpressing, and triple negative.[6,7] Epidemiologic data regarding different phenotypic subgroups in Indian women is scarce. Therefore, the present study aimed to find out the epidemiological distribution of different phenotypic subgroups in the patients suffering from breast cancer.

METHODS

This was a retrospective, observational, single-institutional, epidemiological study conducted at the Department of Radiotherapy, Burdwan Medical College and Hospital, West Bengal, India from July 2012 to June 2017. The study was approved by Institutional Ethics Committee and study procedure was in accordance with the principles of the Declaration of Helsinki.

Women diagnosed with biopsy proven breast carcinoma who had been attending radiation oncology outdoor patient's department (OPD) were included in the study. The menopausal status was identified and patients were divided into two groups pre-menopausal and post-menopausal. The data of histopathological examination (HPE) subtype, stage at presentation, grade of tumor, Ki 67 status, and their phenotypic subgroup classification were retrieved from hospital record. The expression status of estrogen receptor (ER)/ progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2-neu) amplified by fluorescence in situ hybridization (FISH) was also analyzed. All numerical variables were expressed as number and percentage.

RESULTS

A total of 280 women patients were included in the study, of these, 105 were premenopausal and 175 were postmenopausal. Overall, locally advanced breast cancer (60.0%) was most prevalent breast cancer, followed by breast cancer with visceral metastasis (15.35%), breast cancer with skeletal metastasis (14.28%) and early breast cancer (10.35%). More than 50% of women had grade III tumor. Majority of the patients (68.21%) showed high Ki-67 index. The receptor positivity of ER, PR, and HER2-neu were observed in 51.78%, 48.57% and 32.50% of the patients (Table 1).

Table 1: Baseline characteristic and demographic data of all patients.

Parameters	Total (n=280)
Menopausal status	
Premenopausal	105 (37.50)
Postmenopausal	175 (62.50)
Stage of presentation	
Locally advanced breast cancer	168 (60.0)
Breast cancer with visceral metastasis	43 (15.35)
Breast cancer with skeletal metastasis	40 (14.28)
Early breast cancer	29 (10.35)
Tumor grade	
Grade III	151 (53.92)
Grade II	100 (35.71)
Grade I	29 (10.35)
Ki-67 index	
High	191 (68.21)
Low	89 (31.79)
Receptor positivity	
Estrogen receptor	
Positive	145 (51.78)
Negative	135 (48.21)
Progesterone receptor	
Positive	136 (48.57)
Negative	144 (51.42)
HER2-neu	
Positive	91 (32.50)
Negative	173 (61.78)
Amplified	16 (5.71)

Data shown as n (%).
HER2- neu, human epidermal growth factor receptor 2; TNBC, triple negative breast cancer.

Among overall population, majority of patients had luminal-A subgroup (32.14%), followed by triple negative breast carcinoma (27.50%), luminal B (26.07%) and HER2-neu overexpressing subgroup (14.28%) (Figure 1).

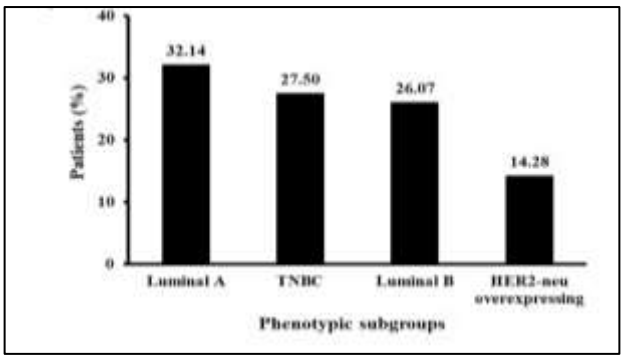

Figure 1: Phenotypic subgroups of overall population, majority of patients.

The most prevalent breast carcinoma in premenopausal and postmenopausal group was infiltrating ductal carcinoma (87.62% and 97.71%, respectively), followed by lobular carcinoma (8.57% and 2.29%, respectively). In both premenopausal and postmenopausal groups, majority of the patients showed grade III tumor (57.14% and 52.0%, respectively). Patients with locally advanced breast cancer were higher in premenopausal (68.57%) and postmenopausal (54.86%) group. Expression of high Ki67 index was comparatively higher in premenopausal group (76.19%) than postmenopausal group (36.57%). A total of 54.29% and 50.29% of patients from premenopausal group and 53.33% and 45.71% of patients from postmenopausal group diagnosed with positive ER and PR, respectively. The HER2-neu was overexpressed in 54.29% of the patients in premenopausal group and 50.29% of the patients in postmenopausal group (Table 2).

Table 2: Baseline characteristic and demographic data.

Parameters	Pre-menopausal (n=105)	Post-menopausal (n=175)
Carcinoma types		
Infiltrating ductal carcinoma	92 (87.62)	171 (97.71)
Lobular carcinoma	9 (8.57)	4 (2.29)
Mucinous carcinoma	4 (3.81)	0
Tumor grade		
Grade III	60 (57.14)	91 (52.0)
Stage of presentation		
Locally advanced breast cancer	72 (68.57)	96 (54.86)
Breast cancer with metastasis	24 (22.85)	59 (33.71)
Early breast cancer	9 (8.57)	20 (11.43)
Ki67 index		
High	80 (76.19)	64 (36.57)
Low	25 (23.80)	111 (63.42)
Receptor positivity		
Estrogen receptor		
Positive	57 (54.29)	88 (50.29)
Negative	48 (45.71)	87 (49.71)
Progesterone receptor		
Positive	56 (53.33)	80 (45.71)
Negative	49 (46.66)	95 (54.28)
HER2-neu		
Positive	44 (41.90)	47 (26.86)
Negative	57 (54.29)	117 (66.98)
Amplified	4 (3.81)	11 (6.86)

Data shown as n (%).
HER2- neu, human epidermal growth factor receptor 2; HPE, histopathological examination; TNBC, triple negative breast cancer.

The most prevalent phenotypic subgroup among premenopausal group was luminal B (38.09%), followed by TNBC (30.48%), luminal-A (23.81%) and HER2-neu overexpressing subgroup (7.62 %). In postmenopausal group, luminal A was most common phenotypic subgroup (36.57%) followed by, TNBC (25.14%), luminal-B and HER2-neu overexpressing subgroup (18.29% each) (Figure 2).

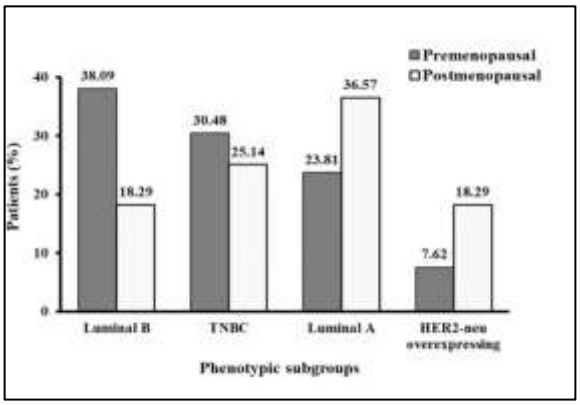

Figure 1: Phenotypic subgroup of premenopausal group and postmenopausal group.

DISCUSSION

Breast cancer is the leading cause of cancer-related death. Several risk factors including early menarche, late menopause, genetic and epigenetic reasons, family history of breast cancer, race and ethnicity, having dense breast tissue, drinking alcohol, and being overweight or obese are involved in the development of breast cancer.[8,9]

The present study was conducted on patients with breast cancer attending a tertiary care hospital in West Bengal, India, to evaluate epidemiological distribution of different phenotypic subgroups. The key findings suggest that infiltrating ductal carcinoma was the common histopathological sub-type in pre-menopausal and post-menopausal patients. Premenopausal women had more aggressive disease biology (76.19% presented with high Ki-67 index). The luminal A sub-group was comparatively more common in post-menopausal women (36.57%). A total of 27.14% patients found triple negative carcinoma of breast and 30.48% patients had triple negative among pre-menopausal sub-group. While majority of the patients (66.98%) from postmenopausal group were HER2-neu negative.

A total of 280 patients present with breast cancer, of these, 105 were premenopausal and 175 were postmenopausal at diagnosis. The risk of developing breast cancer was 25% higher in postmenopausal women. This is in accordance with previous epidemiological studies where the prevalence of breast cancer was higher in postmenopausal women.[10,11] As reported in most of the previous studies, majority of the patients (53.92%) were diagnosed at high-grade carcinomas with higher

Ki67 expression (≥14%).[12] This reflects that the population lacked awareness of the disease and worse the disease condition.

Tumor markers include ER, PR, and HER2 have been widely used to study etiology, prognosis and treatment of breast cancer subtypes. Anderson et al. and Leung et al. reported that hormone receptor negative cancer was prevalently observed in premenopausal women compared to postmenopausal women, while ER positive and PR positive breast cancer was more commonly associated with postmenopausal age.[13,14] Contradictory to the previous studies it was found that hormone receptor positive cancer was more common in premenopausal women (ER, 54.29%; PR, 53.33%). Whereas HER2-neu negative cancer was comparatively higher in postmenopausal women (66.98%). However, comparative study done by Surakasula et al showed majority of postmenopausal patients were PR positive, whereas the majority of premenopausal patients were ER positive.[15]

Based on gene expression profiling, breast cancer can be categorized into luminal A, luminal B, HER2 overexpressing, and basal-like or triple negative.[16] Ozmen et al reported breast cancer in large number of population (n=13240) in Turkey. The most prevalent molecular subtype among these patients was luminal A (62%) followed by luminal B (15%), HER-2 Group (8.5%) and triple negative (15%).[17] This may be due to relation of patient's age with the tumor progression. As patient age increased chances of developing luminal A molecular subtype also increased (p=0.006). In line with this, present study reported that luminal A was most common phenotypic subgroup in overall population (31.79%) and comparatively higher in postmenopausal women (36.57%).

Triple negative carcinoma accounted for 27.14% of the present study population which was in line with previous studies from North and South India, where the percentages were 18% and 31.5% respectively.[11,18,19]

Among the different forms of breast cancer observed in the present study, the most prominent histopathological type was infiltrating ductal carcinoma, accounting to 87.62% of the study population. This was supported by another study that highlighted infiltrating ductal carcinoma was the most common form of breast cancer, representing about 85 of total cases in which 39 were premenopausal and 46 were postmenopausal women, which agrees with the previous reported studies.[15,20,21] In contrast, a study from New Delhi observed that invasive ductal carcinoma was the most common type (88%), followed by infiltrating lobular carcinoma (3.7%).[22]

CONCLUSION

Infiltrating ductal carcinoma is the most prevalent histopathological sub-type in both premenopausal and postmenopausal women and majority of patients were diagnosed with high grade and high Ki67 index which showed lack of awareness in these patients about this disease. Overall findings suggest that prognostic factors and predictive markers can play a vital role in determining the severity of breast cancer.

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