

A RETROSPECTIVE STUDY TO EVALUATE THE EPIDEMIOLOGICAL PROFILE OF BREAST CANCER IN YOUNG FEMALES AT A TERTIARY CARE CENTER IN CENTRAL INDIA

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Abstract

Background: Breast cancer in younger women remains poorly understood. There is a lack of age-specific clinical characteristics or outcome data for young women in low & middle income countries (LMIC), and most of the standard treatments used in this subpopulation currently were tested in older patients. We evaluated the epidemiological data of our institute to find out the demography and disease specific characteristics of the young patients presenting at our center. **Materials & Methods:** A hospital-based review of a prospectively maintained database of young patients (< 40 years of age) of breast cancer treated between January 2018 and December 2022 was done. The parameters taken for the study were histological type, stage at the time of presentation, estrogen receptor (ER) status, progesterone receptor (PR) status, HER2/neu status and site of metastasis. The collected data was entered into the Microsoft Excel sheet and was analyzed using IBM SPSS version 26.0. **Results:** On retrospective review of 494 patients, a total of ninety-four young female patients (<40 years of age) were evaluated in the study. The median age of patients present at our centre was 35 years (range 28-40 years). Out of 94 young patients, 35 patients were less than 35 years of age. The diagnosis of all patients was confirmed microscopically, 3% were stage I, 40% were stage II, 29% were stage III & 28% were diagnosed in stage IV. Fifty-seven percent patients were ER positive, 54 % were PR positive, 34% harbored Her2 Neu positivity, 54% were Her 2 Neu negative and around 8% were Her2 Neu Low (defined by Her2 1+ by IHC or Her2 2+ by IHC and FISH negative) (graph 2). Nine out of 94 patients (10%) had triple negative breast cancer (TNBC). Out of the 94 patients, 4 (4%) underwent breast conservative surgery (BCS) and 75% underwent modified radical mastectomy (MRM). Nineteen patients (21%) had metastases at presentation, the most common site being lung (44%) followed by skeletal metastases (33%). **Conclusion:** The shifting age demographics among breast cancer patients are a cause for serious concern. Young patients have an aggressive disease resulting in poorer outcomes. This necessitates breast cancer awareness, early diagnosis and prompt treatment.

INTRODUCTION

Breast cancer is the most common cancer detected worldwide in females, as per GLOBOCAN 2022. The number of new cases were 23.8% of the total cancer incidence in females.¹ In India, age adjusted incidence rate of breast cancer is lower

(25.8 per 100 000) than United Kingdom (95 per 100 000) but mortality is at par (12.7 vs 17.^[1] per 100 000).^[2] Breast cancer is the fourth leading cause of cancer death around the world.^[1] Of all the diagnosed breast cancer cases, 6.6% diagnosed in women less than 40 years of age, 2.4% in women

less than 35 years, and 0.65% in women less than 30 years.^[3]

Young women constitute a special population of breast cancer patients with distinct tumour pathology, prognosis, diagnostic evaluation, treatment decision-making, survivorship, and fertility considerations all of which are unique to this age group. Compared to older women, tumours in young women tend to be more aggressive, with a higher proportion of estrogen receptor (ER) negative, triple-negative, and HER 2 neu positive tumours.^[4] Younger age has been associated with tumour characteristics that confers a worse prognosis, which includes high grade, poor tumour differentiation, increased Ki-67 expression and more extensive lymph node involvement compared to women more than 50 years of age.^[5-8] Further, a larger proportion of young women with breast cancer carry pathogenic variants in cancer predisposition genes such as BRCA1/2.^[9] The other important factor is that young women are often not included in screening programs and are more likely to be diagnosed with advanced disease. Several studies have found worse clinical outcomes and late effects among these young women compared to older patients.¹⁰⁻¹²

Breast cancer in younger women remains poorly understood. There is a lack of age-specific clinical characteristics or outcome data for young women in low & middle income countries (LMIC) and most of the standard treatments used in this subpopulation currently were tested in older patients. We evaluated the epidemiological data of our institute to find out the demography and disease specific characteristics of the young patients presenting at our center.

MATERIALS AND METHODS

A hospital-based review of a prospectively maintained database of young patients (< 40 years of age) of breast cancer treated between January 2018 and December 2022 was done. All patients were staged as per American Joint Committee on Cancer (AJCC) staging and managed according to standard guidelines and departmental protocol.^[4]

The criteria for inclusion were the availability of information regarding clinical or pathological stage and histological type on biopsy or post-operative histopathology along with basic parameters such as below 40 years of age and sex. The parameters taken for the study were histological type, stage at the time of presentation, estrogen receptor (ER) status, progesterone receptor (PR) status, HER2/neu status and site of metastasis.

Sono-mammography of both breasts was performed in all cases with the exception of ulcerated breast cancers, where only ultrasound was performed. Contrast-enhanced computerized tomography (CECT) or whole-body positron emission tomography (PET) scan was performed for metastatic workup of eligible cases. Technetium

99m methylene diphosphonate (99mTc-MDP) bone scan was performed in cases where PET CT scan was not done as part of initial work up. In addition to this, Bone scan was done in early breast cancer cases with raised alkaline phosphatase levels or having symptoms of bony metastasis. Brain MRI (Magnetic Resonance Imaging) was performed in selected cases with signs and symptoms of brain metastasis. ER, PR, and HER2/neu status on either pre-operative biopsy or post-operative tissue was assessed by Immunohistochemistry (IHC).

Patients with HER2/neu score 3+ or fluorescence in situ hybridization (FISH) positive (more than six copies of HER2/neu gene or HER2/CEP17 ratio of more than 2) were defined as HER2 positive by the DAKO Hercept test. All patients with HER2/neu scores of 2+ were subjected to the FISH method for confirming HER2/neu amplification. Nuclear staining of more than 1% was definition for ER and PR positivity.

The patients with any first or second-degree relative with a history of carcinoma breast, carcinoma ovary/fallopian tube, carcinoma pancreas or carcinoma prostate were labelled as significant family history. Collected data was entered in Microsoft Excel sheet and was analyzed using IBM SPSS version 26.0.

RESULTS

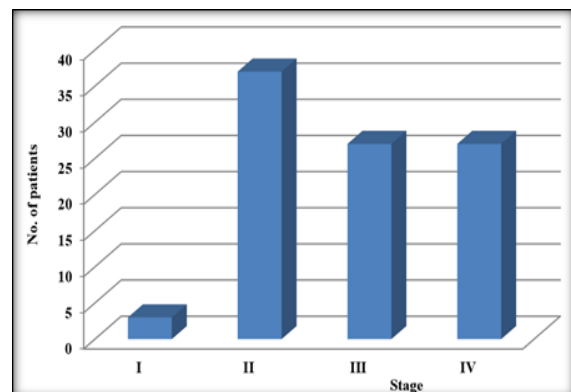


Figure 1: Distribution of patients according to different stages of breast cancer

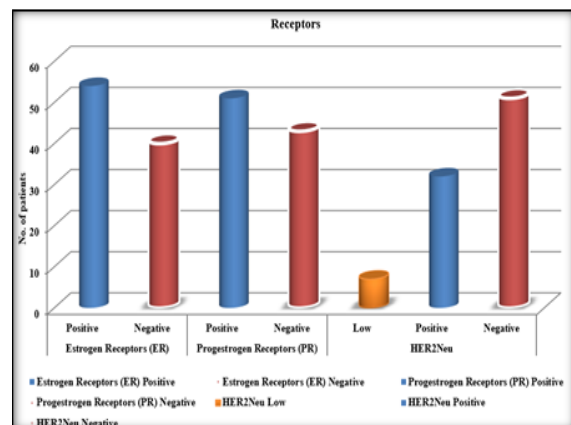


Figure 2: Distribution of patients according to various receptors

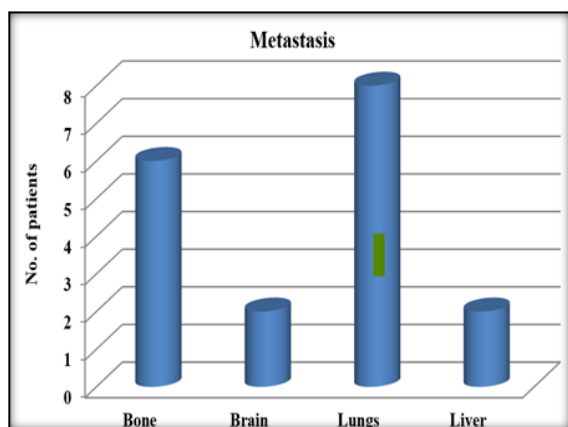


Figure 3: Distribution of patients according to metastasis site

On retrospective review of 494 patients, a total of ninety-four young patients (<40 years of age) were evaluated in the study. The median age of patients present at our centre was 35 years (range 28-40 years). Out of 94 young patients, 35 patients

belonged to less than 35 years of age. The diagnosis of all patients was confirmed microscopically, 3% were stage I, 40% were stage II, 29% were stage III & 28% were diagnosed in stage IV (Figure 1). Fifty-six percent (53 out of 94) patients were diagnosed with right breast cancer and 44% (41 out of 94) with left breast cancer. Fifty-seven percent patients were ER positive, 54% were PR positive, 34% harbored Her2 Neu positivity, 54% were Her2 Neu negative and around 8% were Her2 Neu Low (defined by Her2 1+ by IHC or Her2 2+ by IHC and FISH negative) (Graph 2). Nine out of 94 patients (10%) had triple negative breast cancer (TNBC). Out of the 94 patients, 4 (4%) underwent breast conservative surgery (BCS) and 75% underwent modified radical mastectomy (MRM). Nineteen patients (21%) had metastases at presentation, the most common site being lung (44%) followed by skeletal metastases (33%). [Table 1 & Figure 3]

Table 1: Characteristics feature of breast cancer patients below 40 years of age

Variables		No. of patients (N=94)	Percentage
Age (Mean±SD) (yrs)		35.06±8.86 (median 33 years)	
Site	Right	53	56.38%
	Left	41	43.62%
Estrogen Receptors (ER)	Positive	54	57.44%
	Negative	40	42.56%
Progesterone Receptors (PR)	Positive	51	54.25%
	Negative	43	45.75%
HER2Neu	Low	7	7.44%
	Positive	32	34.04%
	Negative	51	54.25%
TNBC		9	9.57%
Stage	I	3	3.19%
	II	37	39.36%
	III	27	28.72%
	IV	27	28.72%
Treatment	MRM	76	80.85%
	BCS	4	4.26%
Metastasis site (N=18)	Bone	6	33.33%
	Brain	2	11.11%
	Lungs	8	44.44%
	Liver	2	11.11%

DISCUSSION

Breast cancer is the most common cancer among adolescents and young adults (AYAs) of age 15-39 years at diagnosis, accounting for 30% of cancers among AYA women.^[13] AYA breast cancer is frequently familial, and approximately half of AYA women with breast cancer under the age of 30 years harbor a germline mutation in BRCA1, BRCA2, or TP53.^[14] Hormonal factors that increase breast cancer risk among AYAs include early menarche, oral contraceptives, anovulatory infertility, and late parity after the age of 30.^[15,16]

The median age of patients included in our study was 35 years (range 28-40 years), similar to studies from Mumbai and Delhi where the median age was 36 and 31 years respectively.^[17] The incidence of young breast cancer in India has been reported as

8% of all breast cancers.^[18] Contrary to their findings, a SEER data analysis showed a higher frequency of YBC (< 40 years) among Asian women compared to the Caucasian women, 16.2% vs 6.23% (p < 0.0001).^[19]

Early-onset breast cancer tends to be more aggressive with higher stage and grade at presentation.^[20] Our patients were distributed across all stage groups as follows: 3% were diagnosed in stage I, 40% in stage II, 29% in stage III & 28% were detected in stage IV. In a study done by Bajpai et al,^[17] comparable stage wise distribution of patients was noted except for stage IV disease (3.5%). Young females below 40 years have denser breast tissue which makes them less amenable to routine screening programs and likely to present with a palpable mass a larger and a nodal involvement at the time of presentation.^[21] Since

most of our patients were from rural areas, a lack of breast cancer awareness and delayed diagnosis may explain discrepancy.

Our study showed that 57% of the patients were ER positive and 54% were PR positive. Similar ER/PR rates were shown in a study done by Deshmukh et al,^[22] which was aimed to assess the prognostic factors in YBC. Thirty four percent of patient harbored Her 2 neu positivity, comparable to the findings in a study conducted by Gogia et al,^[23] Younger patients tend to be triple negative (TNBC) which is a significant poor prognostic factor.^[23] Prevalence of TNBC in India is considerably higher compared with that seen in Western populations as suggested by various meta-analysis studies.^[24,25] But this trend did not reflect in our study which showed lesser number of TNBC (10%) than various studies done across India.^[21-23] Our TNBC rates were in concordance with a study from California, where 10% of the breast cancers were TNBC.^[26]

Most of our patients preferred mastectomy over BCS and as a result of this, 94% of all procedures performed were MRM. However other Indian studies.^[20,23] have shown a higher number of patients opting BCS as compared to our results.

CONCLUSION

The shifting age demographics among breast cancer patients are a cause for serious concern. Young patients have an aggressive disease resulting in poorer outcomes. This necessitates breast cancer awareness, early diagnosis and prompt treatment.

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