Section: Oncology

Original Research Article

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

Hemendra Mishra[1], Vikas Asati[2], Rajesh Patidar[3], Mahima Kharbanda[1], Archit Jain[1], Astha Parmar[1], Arth Shah[1], Anirudh Singh[1], Prakash Chitalkar[4]

[1]Senior Resident, Department of Medical Oncology, SAIMS (Sri Aurobindo Institute of Medical Sciences), Indore, Madhya Pradesh, India.
[2]Associate Professor, Department of Medical Oncology, SAIMS (Sri Aurobindo Institute of Medical Sciences), Indore, Madhya Pradesh, India.
[3]Professor, Department of Medical Oncology, SAIMS (Sri Aurobindo Institute of Medical Sciences), Indore, Madhya Pradesh, India.
[4]Professor & Head, Department of Medical Oncology, SAIMS (Sri Aurobindo Institute of Medical Sciences), Indore, Madhya Pradesh, India.

Received : 30/06/2024
Received in revised form : 19/07/2024
Accepted : 08/08/2024

Keywords:
Young female, BCS, MRM, Breast cancer, TNBC.

Corresponding Author:
Dr. Mahima Kharbanda,
Email: kharbanda.mahima@gmail.com

DOI: 10.47009/jamp.2024.6.4.162

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (4); 825-828

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

ISSN (O): 2687-5365; ISSN (P): 2753-6556

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

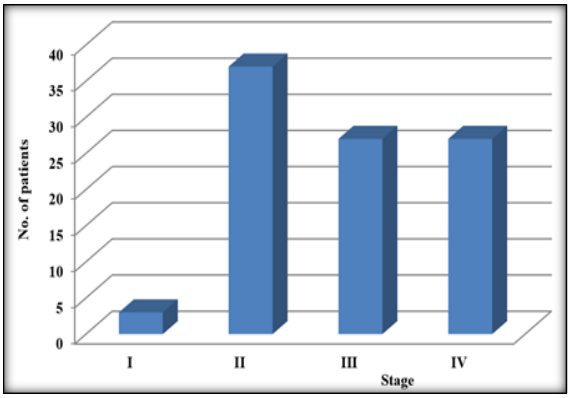

Figure 1: Distribution of patients according to different stages of breast cancer

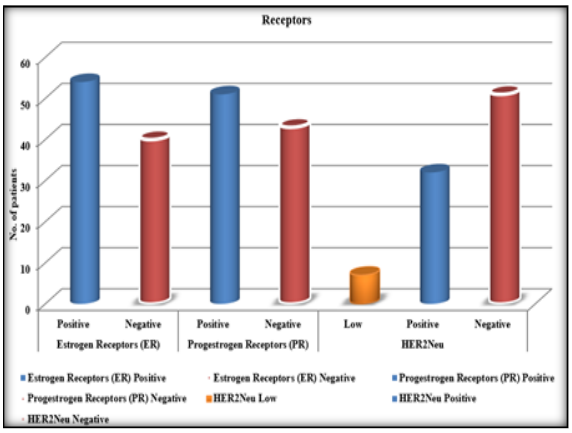

Figure 2: Distribution of patients according to various receptors

ISSN (O): 2687-5365; ISSN (P): 2753-6556

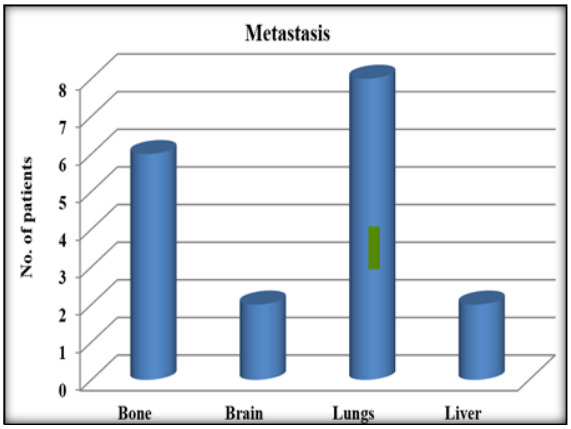

Figure 3: Distribution of patients according to metastasis site

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 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%). [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

ISSN (O): 2687-5365; ISSN (P): 2753-6556

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 be 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.

REFERENCES

1. Cancer Today [Internet]. [cited 2024 Feb 4]. Available from: https://gco.iarc.who.int/today/
2. Gupta A, Shridhar K, Dhillon PK. A review of breast cancer awareness among women in India: cancer literate or awareness deficit? Eur J Cancer 2015; 51: 2058–66.
3. Anders CK, Johnson R, Litton J, et al. Breast cancer before age 40 years. Semin Oncol 2009; 36:237-49.
4. Shah, A.N.; Carroll, K.J.; Gerratana, L.; Lin, C.; Davis, A.A.; Zhang, Q.; Jacob, S.; Finkelman, B.; Zhang, Y.; Qiang, W.; et al. Circulating tumor cells, circulating tumor DNA, and disease characteristics in young women with metastatic breast cancer. Breast Cancer Res. Treat. 2021, 187, 397–405.
5. Murphy, B.L.; Day, C.N.; Hoskin, T.L.; Habermann, E.B.; Boughey, J.C. Adolescents and Young Adults with Breast Cancer have More Aggressive Disease and Treatment Than Patients in Their Forties. Ann. Surg. Oncol. 2019; 26: 3920–30.
6. Pruessmann, J.; Pursche, T.; Hammersen, F.; Katalinic, A.; Fischer, D.; Waldmann, A. Conditional Disease-Free and Overall Survival of 1858 Young Women with Non-Metastatic Breast Cancer and with Participation in a Post-Therapeutic Rehab Programme according to Clinical Subtypes. Breast Care 2020; 16: 163–72.
7. Johnson, R.H.; Hu, P.; Fan, C.; Anders, C.K. Gene expression in "young adult type" breast cancer: A retrospective analysis. Oncotarget 2015; 6: 13688–702.
8. Fredholm, H.; Magnusson, K.; Lindström, L.S.; Garmo, H.; Fält, S.E.; Lindman, H.; Bergh, J.; Holmberg, L.; Pontén, F.; Frisell, J.; et al. Long-term outcome in young women with breast cancer: A population-based study. Breast Cancer Res. Treat. 2016; 160: 131–1.
9. Greenup, R.; Buchanan, A.; Lorizio, W.; Rhoads, K.; Chan, S.; Leedom, T.; King, R.; McLennan, J.; Crawford, B.; Marcom, P.K.; et al. Prevalence of BRCA Mutations Among Women with Triple-Negative Breast Cancer (TNBC) in a Genetic Counseling Cohort. Ann. Surg. Oncol. 2013; 20: 3254–58.
10. Fredholm, H.; Eaker, S.; Frisell, J.; Holmberg, L.; Fredriksson, I.; Lindman, H. Breast Cancer in Young Women: Poor Survival Despite Intensive Treatment. PLoS ONE 2009, 4, e7695.
11. Copson, E.; Eccles, B.; Maishman, T.; Gerty, S.; Stanton, L.; Cutress, R.I.; Altman, D.G.; Durcan, L.; Simmonds, P.; Lawrence, G.; et al. Prospective Observational Study of Breast Cancer Treatment Outcomes for UK Women Aged 18–40 Years at Diagnosis: The POSH Study. Gynecol. Oncol. 2013;105: 978–88.
12. Yeo, W.; Lee, H.-M.; Chan, A.; Chan, E.Y.; Chan, M.C.; Chan, K.-W.; Chan, S.W.; Cheung, F.-Y.; Cheung, P.S.; Choi, P.H.; et al. Risk factors and natural history of breast cancer in younger Chinese women. World J. Clin. Oncol. 2014; 5: 1097–1106.
13. Elizabeth J. Cathcart-Rake, Kathryn J. Ruddy, Archie Bleyer, and Rebecca H. Johnson. Breast Cancer in Adolescent and Young Adult Women Under the Age of 40 Years. American Society of Clinical Oncology.2021;17(6):314-17.
14. Chopra B, Kaur V, Singh K, Verma M, Singh S, Singh A. Age shift: breast cancer is occurring in younger age groups—is it true? Clin Cancer Investig J 2014; 3: 526–29.
15. Thangjam S, Laishram RS, Debnath K. Breast carcinoma in young females below the age of 40 years: a histopathological perspective. South Asian J Cancer 2014; 3: 97–100.
16. Sandhu D, Sandhu S, Karwasra R, Marwah S. Profile of breast cancer patients at a tertiary care hospital in north India. Indian J Cancer 2010; 47: 16–22.
17. Jyoti Bajpai, Pradeep Ventrapati, Shalaka Joshi, Tabassum Wadasadawala, Sushmita Rath and Rima Pathak. Unique challenges and outcomes of young women with breast cancers from a tertiary care cancer centre in India. The Breast. Dec. 2021; 60:177-84.
18. Kakarala M, Rozek L, Cote M, Liyanage S, Brenner DE. Breast cancer histology and receptor status characterization in Asian Indian and Pakistani women in the U.S.: a SEER analysis. BMC Cancer 2010; 10: 191.
19. Murthy NS, Agarwal UK, Chaudhry K, Saxena S. A study on time trends in incidence of breast cancer: Indian scenario. Eur J Cancer Care (Engl) 2007; 16: 185–6.
20. Anders CK, Hsu DS, Broadwater G et al. Young age at diagnosis correlates with worse prognosis and defines a subset of breast cancers with shared patterns of gene expression. J Clin Oncol 2008; 26: 3324–30.
21. Das ULK, Lokanatha D. Breast Cancer in Women of Younger than 35 Years: A Single Center Study. J Mol Biomark Diagn 2015; 6: 261.
22. S.P. Deshmukh, A.D. Mane, B.P. Zade, S.P. Sane. Breast Cancer in Young Women in India (Abstract). Annals of Oncology. 2012:265P.
23. Gogia A, Raina V, Deo S, Shukla N, Mohanti B. Triple negative breast cancer: An institutional analysis. Indian J Cancer 2014; 51: 163–66.
24. Sandhu GS, Erqou S, Patterson H, Mathew A. Prevalence of triple-negative breast cancer in India: systematic review and meta-analysis. J Global Oncol 2016; 2: 412–21.
25. Ghosh J, Gupta S, Desai S et al. Estrogen, progesterone and HER2 receptor expression in breast tumors of patients, and their usage of HER2-targeted therapy, in a tertiary care centre in India. Indian J Cancer 2011; 48: 391–6.
26. H. Keegan, M.C. DeRouen, D.J. Press, A.W. Kurian, C.A. Clarke Occurrence of breast cancer subtypes in adolescent and young adult women. Breast Cancer Res.2012; 14 (2): R55.

ISSN (O): 2687-5365; ISSN (P): 2753-6556