CLINICAL CHARACTERISTICS OF BREAST CANCER PATIENTS IN YOUNGER VERSUS OLDER AGE GROUPS AT A TERTIARY CARE CENTER: A RETROSPECTIVE ANALYSIS

Astha Parmar[1], Hemendra Mishra[2*], Rajesh Patidar[3], Vikas Asati[4], Arth Shah[5], Anirudh Singh[6], Archit Jain[7], Prakash Chitalkar[8]

[1]Senior Resident, Department of Medical Oncology, Sri Aurobindo Institute of Medical Sciences, Indore. Email: asthaparmar201@gmail.com
[2*]Assistant Professor, Department of Medical Oncology, Sri Aurobindo Institute of Medical Sciences, Indore.
[3]Professor, Department of Medical Oncology, Sri Aurobindo Institute of Medical Sciences, Indore.
[4]Professor, Department of Medical Oncology, Sri Aurobindo Institute of Medical Sciences, Indore.
[5]Senior Resident, Department of Medical Oncology, Sri Aurobindo Institute of Medical Sciences, Indore.
[6]Senior Resident, Department of Medical Oncology, Sri Aurobindo Institute of Medical Sciences, Indore.
[7]Senior Resident, Department of Medical Oncology, Sri Aurobindo Institute of Medical Sciences, Indore.
[8]Professor, Department of Medical Oncology, Sri Aurobindo Institute of Medical Sciences, Indore.

*Corresponding Author: Hemendra Mishra
*Assistant Professor, Department of Medical Oncology, Sri Aurobindo Institute of Medical Sciences, Indore, Email: mishra.hemendra.usha@gmail.com

Abstract
Background
Breast cancer is the most common malignancy affecting women worldwide and in India. Younger women are often reported to present with more aggressive disease characteristics and worse prognostic factors.
Objectives
This study aims to compare the clinicopathological characteristics of breast cancer in younger women (≤40 years) versus older women (>40 years) at a tertiary care center in India.
Methods
We conducted a retrospective analysis of 784 breast cancer patients treated between January 2018 and December 2024. Patients were categorized into two groups based on age and compared for clinicopathological features, including stage, receptor status, histological type, and treatment patterns.
Results
Of the total patients, 161 (20.53%) were ≤40 years old, with a median age of 36 years, while 623 were >40 years with a median age of 52 years. Younger patients had a higher incidence of advanced stage at presentation (stage II & III: 70.80% vs. 66.45%) and higher rates of PR positivity (51% vs. 43.33%). The HER2 negative expression rate was slightly higher in younger patients. A significant proportion of younger women also had triple-negative breast cancer.

Conclusion

Breast cancer in young Indian women demonstrates distinct clinicopathological features, including higher tumour stage and more aggressive biological behaviour. Awareness of these characteristics is essential for early diagnosis and tailoring of treatment strategies to improve outcomes in this population.

Introduction

Breast cancer is the most commonly diagnosed cancer among females worldwide, accounting for 23.8% of all female cancer cases in 2022, per GLOBOCAN.[1] In India, it is also the most prevalent cancer in women.[2] Incidence rates vary across metropolitan, urban, and rural areas.

Studies from Western countries and LMICs show that young patients are more likely to present with advanced, aggressive disease.[3-5] Prognosis is influenced by age, sex, stage, histology, grade, hormone and HER2 status, and treatment. Multiple large-scale Indian studies have explored breast cancer clinicopathology. We analyzed institutional data to assess age-based differences in clinicopathological features in our patient population.

Material & Methods

Retrospective review of a prospectively maintained database of all patients of breast cancer treated between January 2018 and December 2024 was done. All patients were staged as per AJCC staging-seventh edition[6] and managed according to standard guidelines and departmental protocols.

The minimum 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 age and sex. Patients with incomplete documentation of stage and histological type were excluded.

Patients were divided into two groups younger than 40 years and those older than 40 years. Groups were compared for clinicopathologic features.

The parameters taken for the study were age, sex, stage at the time of presentation, histological type, estrogen receptor (ER) status, progesterone receptor (PR) status, HER2/neu status, site of metastasis for stage 4 diseases, parity, and significant family history. Mammography was performed in all cases with the exception of ulcerated breast cancers, where ultrasound breast and axilla were performed for local imaging. Technetium 99m methylene diphosphonate (99mTc-MDP) bone scan was performed in locally advanced, metastatic cases in early breast cancer with raised alkaline phosphatase levels in liver function tests or having symptoms of bony metastasis. Contrast-enhanced computerized tomography (CECT) or whole body positron emission tomography (PET) scan was performed for metastatic workup. MRI of the brain, plain plus contrast, was performed in only those with signs of brain metastasis or suspicious lesion found in PET scan or CECT scans. The immunohistochemistry (IHC) method was used to determine ER, PR, and HER2/neu status on either pre-operative biopsy or post-operative tissue using the standard method of sectioning paraffin-embedded tissue and staining with monoclonal antibodies for ER, PR, and HER2/neu. Nuclear staining of more than 1% was definition for ER and PR positivity. ALLRED scores were also used for determining hormone receptor positivity.

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. The patients with any first- or second-degree

family member with a history of related cancers such as carcinoma ovary/ fallopian tube were labeled as significant family history.

Results

A total of 784 patients with breast cancer presented to our center over the 7-year review period. The median age at diagnosis was 36 (range 24 years to 40 years) years, 161 patients (20.53%) were younger than 40 years at presentation. The median age at diagnosis for patients aged >40 years is 52 years (range 41 years to 91 years)

We analyzed the distribution of estrogen-related breast cancer risk factors as these factors may affect both the pathogenesis of breast cancer and the expression level of hormone receptors. We found that the age of menarche was significantly earlier ($p < 0.001$) in the young (<40 years) patients compared to older (>40 years) patients.

As to biomarker expression levels, there were significant differences in progesterone receptor (PR) and HER2 expression levels in breast cancer tissues of different age groups (Table 1). The PR positive expression rate was higher in young (<40 years) patients compared with older (>40 year) patients (51%. vs. 43.33%, $p < 0.001$; Table 1). In addition, the HER2 negative expression rate was higher in the young age group compared with the older age group (59%. vs. 54.89%, $P > 0.05$); Table 1).

The diagnosis of all patients was confirmed microscopically, 66.45% were diagnosed in stage II & III in older patients as compared to 70.80% in young patients (Table 1).

Table 1: characteristics feature of breast cancer patients

Variables		Group I (≤40Years of age) (n=161)	Group II (>40 years of age) (n=623)
Age median (Mean±SD) (yrs)		36 (range 24 – 40 years) 32.64±7.92	52 (range 41 – 91 years) 63.56±10.24
Menopause	Yes	3	334
	No	158	289
Site	Right	91	342
	Left	68	277
	Bilateral	2	4
Estrogen Receptors (ER)	Positive	87	342
	Negative	70	270
Progestrogen Receptors (PR)	Positive	82	270
	Negative	75	341
HER2Neu	Low	8	31
	Equivocal	0	5
	Positive	50	222
	Positive (fish)	0	5
	Negative	95	342
	Negative (fish)	3	6
TNBC	No	43	206
	Yes	33	88
Stage	I	3	12
	II	59	213
	III	55	201
	IV	21	121
Treatment	MRM	97	362
	BCS	12	26
	Lumpectomy	0	4
Metastasis site	Bone	7	29
	Brain	3	21
	Lungs	10	18
	Liver	3	18
	Multiorgan	9	60

Discussion

The age at which women present with breast cancer varies between countries, but breast cancer generally is thought to be more aggressive in younger women. The median age of breast cancer presentation is much younger in many Asian countries.[7-9] The young patients (<40 years) accounted for 20.53% of all breast cancer cases. These differences may be related to race, social background factors, dietary habits, economic development levels, among others.[10-12]

First, we found a lower ER-positive expression rate in young patients compared with older patients, but the PR positive expression rate was significantly increased in young breast cancer patients, which differed from the results of western population. To date, most studies from western developed countries have shown that the positive expression rate of ER and PR was lower in young patients.[13,14] Second, As PR-positive expression reflects complete estrogen signaling pathways[15,16] and patients with ER+/PR+ double positive expression seem to have better prognosis in the clinic.[17,18] Therefore, we analyzed both ER and PR expression and found that the ER+/PR+ double positive rate of young patients was higher than in older patients, which was also a rare phenomenon. Third, in our study we found that the HER2 negative expression rate in young patients was higher than that of older patients. This contradicts most previous research that has found that breast cancer cells of young patients are more likely to show HER2 positive expression.[19,20] The above results indicated the possibility that the pathogenesis mechanism of young female breast cancer in India may differ from other ethnic populations in western world.

In terms of treatment options, we compared the two age groups in terms of four aspects: surgery, chemotherapy, radiotherapy and endocrine therapy. First, in the choice of surgical approach, the proportion receiving breast-conserving surgery and sentinel lymph node biopsy, was higher in young patients, which was consistent with our previous research.[21] Previous studies that showed young patients have a greater desire to preserve breasts, and are more accepting of advanced operation methods, compared to older patients.[22]

In this study, we observed that the young women with BC reported with an adverse clinicopathological characteristics, including advance tumor stage, more lymphovascular invasion, and more distant metastases compared with older women. Similar to our data, the study conducted by Foo et al of 843 women with BC from Singapore showed that young patients had a higher tumor grade and vascular invasion compared with older women ($p=0.012$ and $p=0.034$).[23] Telfah et al[24] from Jordan also reported similar results and found that young BC patients had larger tumors ($p=0.02$), increased lymphovascular invasion ($p=0.05$), and higher tumor grade ($p=0.0001$) compared with the disease arising in older patients. In addition, Maggard et al[25] from the USA found that young patients were more likely to present with more advanced tumor grades and tumor stages than their older counterparts ($p<0.0001$ and $p<0.0001$). Similarly, Bharat et al[26] from the USA reported that the young patients with BC in their cohort presented at an advance tumor stage with a higher grade and more lymphovascular invasion compared with aged patients ($p<0.05$, $p<0.01$ and $p<0.05$ respectively).

Our findings of significantly high rates of triple negative BC in young women as compared to their older counterparts are in accordance with the previous published research.

Younger people are coming in bigger numbers with breast cancer probably due to impact of health education campaigns. Multi-disciplinary studies are necessary within geographical regions to characterize the biology of young person's breast cancer and of course to derive effective therapies.

Conclusion

In conclusion, although young women's breast cancer has distinct clinicopathological characteristics, it may be different with regards to poor prognostic outcomes which is particularly ascribed to more aggressive histopathological features such as higher tumor grade and lymphovascular invasion and less conducive hormonal receptor status when compared to the cases diagnosed in older women. Healthcare professionals should keep the aggressive nature of BC in young patients in their mind while dealing with the breast abnormalities in this age group.

Conflict of Interest Declaration

The author(s) declare(s) that there is no conflict of interest.

References

1. Cancer Today [Internet]. [cited 2024 Feb 4]. Available from: https://gco.iarc.who.int/today/.
2. Sathishkumar K, Chaturvedi M, Das P, Stephen S, Mathur P. Cancer incidence estimates for 2022 & projection for 2025: Result from National Cancer Registry Programme, India. Indian J Med Res. Oct-Nov 2022;156:598-607.
3. Fredholm H, Magnusson K, Lindstrom LS, et al. Long-term outcome in young women with breast cancer: A population-based study. Breast Cancer Res Treat. 2016;160:131–143.
4. Brandt J, Garne Tengrup I, et al. Age at diagnosis in relation to survival following breast cancer: A cohort study. World J Surg Oncol. 2015;13:33.
5. Chen HL, Zhou MQ, Tian W, et al. Effect of age on breast cancer patient prognoses: A population-based study using the SEER 18 database. PloS One. 2016;11:e0165409
6. Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A, editors. AJCC cancer staging manual (7th ed). New York, NY: Springer; 2010.
7. Akarolo-Anthony SN, Ogundiran TO, Adebamowo CA. Emerging breast cancer epidemic: Evidence from Africa. Breast Cancer Res. 2010;12:S8.
8. Jazayeri SB, Saadat S, Ramezani R, et al. Incidence of primary breast cancer in Iran: Ten-year national cancer registry data report. Cancer Epidemiol. 2015;39:519–527.
9. El Saghir NS, Khalil MK, Eid T, et al. Trends in epidemiology and management of breast cancer in developing Arab countries: A literature and registry analysis. Int J Surg. 2007;5:225–233.
10. Vostakolaei FA, Broeders MM, Rostami N, van Dijck JAM, Feuth T, Kiemeney LLM, et al. Age at diagnosis and breast cancer survival in Iran. Int J Breast Cancer. 2012; 2012: 517976.
11. Morrison DH, Rahardja D, King E, Peng Y, Sarode VR. Tumor biomarker expression relative to age and molecular subtypes of invasive breast cancer. Brit J Cancer. 2012; 107: 1–6.
12. Lin CH, Chuang PY, Chiang CJ, Lu YS, Cheng AL, Kuo WH, et al. Distinct clinicopathological features and prognosis of emerging young-female breast cancer in an East Asian country: a nationwide cancer registry-based study. The Oncologist. 2014; 19: 583–591.
13. Johnson RH, Hu P, Fan C, Anders CK. Gene expression in "young adult type" breast cancer: a retrospective analysis. Oncotarget. 2015; 6: 13688–13702.
14. Gnerlich JL, Deshpande AD, Jeffe DB, Sweet A, White N, Margenthaler JA. Elevated breast cancer mortality in women younger than age 40 years compared with older women is attributed to poorer survival in early-stage disease. J Am Coll Surg. 2009; 208: 341–347.
15. Petz LN, Ziegler YS, Schultz JR, Kim H, Kemper JK, Nardulli AM. Differential regulation of the human progesterone receptor gene through an estrogen response element half site and sp1 sites. J Steroid Biochem Mol Biol. 2004; 88: 113–122.
16. Schultz JR, Petz LN, Nardulli AM. Estrogen receptor alpha and Sp1 regulate progesterone receptor gene expression. Mol Cell Endocrinol. 2003; 201: 165–175.
17. Ravdin PM, Green S, Dorr TM, McGuire WL, Fabian C, Pugh RP, et al. Prognostic significance of progesterone receptor levels in estrogen receptor-positive patients with

metastatic breast cancer treated with tamoxifen: Result of a prospective Southwest Oncology Group study. J Clin Oncol. 1992; 10: 1284–1291.

18. Osborne CK. Steroid hormone receptors in breast cancer management. Breast Cancer Res Treat. 1998; 51: 227–238.

19. Kheirelseid EH, Boggs JM, Curran C, Glynn RW, Dooley C, Sweeney KJ, et al. Younger age as a prognostic indicator in breast cancer: A cohort study. BMC Cancer. 2011; 11:383. doi: 10.1186/1471-2407- 11-383.

20. Pronzato P, Mustacchi G, De Matteis A, Di Costanzo F, Rulli E, Floriani I, et al. Biological characteristics and medical treatment of breast cancer in young women-A featured population: results from the NORA study. Int J Breast Cancer. 2011; 2011: 534256.

21. Wang K, Ren Y, Huang R, He JJ, Feng WL, Kong YN, et al. Application of intraoperative frozen section examination in the management of female breast cancer in China: a nationwide, multicenter 10-year epidemiological study. World J Surg Oncol. 2014; 12:225.

22. Morrow M, White J, Moughan J, Owen J, Pajack T, Sylyester J, et al. Factors predicting the use of breast-conserving therapy in stage I and II breast carcinoma. J Clin Oncol. 2001; 19: 2254–2262.

23. Foo CS, Su D, Chong CK, et al. Breast cancer in young Asian women: Study on survival. ANZ Journal of Surgery 2005; 75: 566–572.

24. Telfah, A, Obeidat M, Swailmeen A, et al. Breast Cancers in Young Women: A Retrospective Study at King Hussein Medical Center. Journal of the Royal Medical Services 2015; 22: 62–68.

25. Maggard MA, O'Connel JB, Lane KE, et al. Do young breast cancer patients have worse outcomes? J Surg Res 2003; 113: 109–113.

26. Bharat A, Aft RL, Gao F, Margenthaler JA.. Patient and tumor characteristics associated with increased mortality in young women (<40 years) with breast cancer. J Surg Oncol 2009; 100: 248–251.