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Breast cancer in young women: A retrospective study from tertiary care center of north India

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Abstract

Aim: Breast cancer is the most common cause of cancer in women worldwide. They have more aggressive clinical behaviour with poor outcomes in younger patients. The aim of this study was to evaluate the impact of age on prognosis of breast cancer in women above and under 40 years of age. **Material and Methods:** Medical record of 415 patients with invasive breast cancer were analysed from January 2011 to December 2014 in our department. The last was done in December 2015. All cases diagnosed with breast cancer stages I to IV were evaluated, and grouped on the basis of age [less than 40 and above 40 years]. Baseline categorical variables were analysed using the Chi-square test or Fisher's exact test. Non categorical variable were analysed using t-test. **Result:** A total of 372 patients were reviewed because 42 patients defaulted. The median age at the time of diagnosis was 44.6 years (range 23 to 90 years). Metastasis to distant organs were more in women with age <40. Tumour relapse occurred in 131 cases, among which 84 cases died, 35 patients (26.31%) in less than 40 group vs. 49 patients (20.50%) in above 40 groups. The estimated median OS in the two groups are 32 and 41 months respectively. **Conclusion:** The biological behaviour of breast cancer in younger age group has been shown to be associated with aggressive nature and has a worse clinical outcome as compared to that in older group.

Key words: Breast cancer, metastasis, poor prognosis, young age

Introduction

Breast cancer is the most common cause of cancer in women worldwide. Especially it is a disease of postmenopausal and elderly age group, approximately 5.6% of breast cancer patients are ≤40 years.[1] They are characterized by less hormone sensitivity, higher human epidermal growth factor receptor 2 expressions, aggressive clinical behavior with poor outcomes as compared to the elderly group.[2,3]

Aim

The aim of this study was to evaluate the impact of age as an adverse factor in the presentation, recurrence, and prognosis of breast cancer in women above and under 40 years of age.

Materials and Methods

We analyzed medical records of 415 patients diagnosed with invasive breast cancer from January 2011 to December 2014 in our hospital. A total of 42 patients were excluded as they did not turn up for any treatment. Finally, 372 patients were analyzed. The last follow-up of all patients was done in December 2015. All cases diagnosed with breast cancer Stages I–IV were evaluated. The patients were then grouped on the basis of age <40 and above 40 years of age, both groups were compared regarding the clinical presentation and the modality of treatment they received. Additional exclusion criteria were any therapy before diagnosis (surgery/radiotherapy/chemotherapy), previous history of malignancy and history of any other medical illness, which would otherwise limit the survival of the patient in the absence of malignancy. All patients underwent standard treatment modalities (neoadjuvant or adjuvant chemotherapy, radiotherapy, chemoradiation, and/or surgery: modified radical mastectomy, breast conservation surgery, toilet mastectomy depending on the stage of presentation [Table 1].

Statistical analysis

Overall survival (OS) was defined as the time period from diagnosis to death from any cause. Disease-free survival (DFS) was defined as the time period from diagnosis to the first locoregional or distant recurrence. The patients who did not experience any event/death or were lost to follow-up were censored for survival analysis. Baseline categorical variables were analyzed using Chi-square and Fischer's exact tests. Non-categorical variable was analyzed using t-test. DFS and OS curves were calculated using the Kaplan-Meier method. Log-Rank test was used to calculate OS and DFS. $P < 0.05$ was considered statistically significant.

Results

A total of 372 patients were reviewed. The median age at the time of diagnosis was 44.6 years (range 23–90 years) [Table 1]. Out of which 133 were <40 years (33.07%). A total of 353 patients were diagnosed with Stages II and III (125 in under 40 group and 228 in above 40 years age group). 66.16% of patients <40 group belong to Stage III as compared to 54.4% of patients in above 40 group ($P = 0.029$, significant). A total of 12 patients presented with metastasis at the time of diagnosis (4 and 8 patients, respectively) in two groups. In <40 group 96 patients (72.18%) presented with T3/T4 as compared to 150 patients (62.76%) in above 40 years age group.($P = 0.086$, not significant) 101 patients (75.93%) had positive axillary lymph nodes at presentation in <40 years group as compared to 130 patients (54.39%) in above 40 group ($P = 0.027$, significant).

About 52.63% of patients received neoadjuvant chemotherapy in <40 years group versus 46.86% in above 40 years group. Estrogen receptor (ER) positivity present in two groups is 39.84% versus 55.23%, respectively ($P = 0.005$, significant). Patients positive for progesterone receptors (PR) receptors in two groups are 38.54% versus 44.76% ($P = 0.001$, significant). However, 46.61% of patients were triple negative in <40 years age group versus 32.21% in above 40 years age group ($P = 0.007$, significant).

Table 1: Characteristics of 373 breast cancer patients: Comparison between two groups

	<40	>40	P
Patients number	133	239	
Stage III (%)			
Yes	88 (66.16)	130 (54.4)	0.029
No	45 (33.84)	109 (45.6)	
T status (%)			
T1	6 (4.5)	4 (1.67)	0.792
T2	31 (23.3)	85 (35.56)	
T3	60 (45.11)	75 (31.38)	
T4	36 (27.06)	75 (31.38)	
Nodal status (%)			
N0	32 (24.06)	87 (36.4)	0.659
N1	74 (55.63)	93 (38.91)	
N2	26 (19.54)	57 (23.84)	
N3	1 (0.75)	2 (8.36)	
Nodal positive (%)			
Yes	101 (75.93)	154 (64.43)	0.027
No	32 (24.06)	85 (35.57)	
Metastasis (%)			
M0	129 (90.97)	231 (95.82)	1
M1	4 (9.03)	8 (4.18)	
Surgery (%)			
MRM	126 (94.73)	226 (94.56)	1
BCS	2 (1.5)	3 (1.25)	
Toilet mastectomy	3 (2.25)	4 (1.67)	
None	2 (1.5)	6 (2.5)	
Chemotherapy (%)			
Neoadjuvant	70 (52.63)	112 (46.86)	0.23
Adjuvant	59 (44.37)	124 (51.88)	
Palliative	4 (3.0)	3 (1.25)	
Type of chemotherapy (%)			
Anthracycline based	58 (43.6)	121 (50.62)	0.21
Taxane based	73 (54.88)	115 (48.11)	
Others	2 (1.50)	03 (1.25)	
Margin status (%)			
Positive	16 (12)	29 (12.13)	0.874
Negative	102 (76.7)	182 (76.15)	
Not specified	15 (11.3)	28 (11.71)	
Grade (%)			
I	9 (6.76)	24 (10.04)	0.846
II	44 (33.08)	73 (30.54)	
III	31 (23.3)	62 (25.94)	
NS	49 (36.84)	80 (33.47)	
LVI (%)			
Positive	67 (50.37)	107 (44.765)	0.14
Negative	46 (34.58)	85 (35.56)	
Not specified	20 (15.03)	47 (19.66)	
ER status (%)			
Positive	53 (39.84)	132 (55.23)	0.005
Negative	80 (60.16)	107 (44.76)	
PR status			
Positive	37 (27.81)	107 (44.76)	0.001
Negative	96 (72.18)	132 (55.23)	
HER2/neu (%)			
Positive	28 (21.05)	52 (21.75)	0.89
Negative	105 (78.94)	187 (78.24)	
Metastasis			
Yes	55 (41.35)	76 (31.8)	0.07
No	78 (58.64)	163 (68.2)	

Contd...

Table 1: Contd...

	<40	>40	P
Primary site metastasis (%)			
Brain	4 (5.12)	7 (7)	1
Liver	5 (6.41)	10 (10)	1
Lung	18 (23.07)	18 (18)	0.069
Bone	27 (34.61)	33 (33)	0.1
Locoregional	18 (23.07)	25 (25)	0.4
Others	6 (7.69)	7 (7)	0.09
Subsequent metastasis (%)			
Brain	15 (57.69)	9 (32.14)	0.007
Liver	3 (11.53)	4 (14.28)	0.71
Lung	2 (7.69)	8 (28.57)	0.45
Bone	5 (19.23)	4 (14.28)	0.291
Locoregional	0	1 (3.57)	NA
Others	1 (3.84)	2 (7.14)	1

MRM=Modified radical mastectomy, BCS=Breast conservation surgery, NA=Not available, LVI=Lymphovascular invasion, ER=Estrogen receptor, PR=Progesterone receptors, HER2=Human epidermal growth factor receptor 2

41.35% patients developed metastasis/locoregional recurrence in less 40 years age group during follow-up versus 31.8% patients in above 40 years age group ($P = 0.07$, not significant). However, metastasis in triple-negative breast cancer in two groups is almost same 43.85% versus 43.18%, respectively.

There was 78 primary metastasis in <40 years group versus 128 in above 40 years age group. A number of subsequent metastasis in two groups is 26 and 25, respectively. The majority of patients had metastasis in different sites. In total, 55 patients developed metastasis/recurrence in less 40 group versus 76 patients in above 40 groups ($P = 0.071$).

Metastasis to distant organs was more in a patient of younger age group. 14.28% of patients, <40 years had metastasis to brain versus 6.69% of women above 40 years ($P = 0.025$, significant). It has been found that the no of subsequent brain metastasis in two groups are 57.69% versus 32.14% respectively ($P = 0.007$, significant), primary lung metastasis in two groups is 23.07% versus 18% respectively ($P = 0.069$, not significant) Within a median follow-up period of 26.5 months (2–63 months), tumor relapse occurred in 131 cases, among which 84 cases died, 35 patients (26.31%) in under 40 group versus 49 patients (20.50%) in above 40 group.

Mean DFS was 24.06 versus 20.33, and median DFS was 15 versus 14 ($P = 0.28$, not significant) in <40 and above 40 age group, respectively. The estimated mean OS for the two groups is 38.5 and 40.6 months. The estimated median OS in the two groups is 32 and 41 months, respectively [Figure 1].

Discussion

Breast cancer in young age is very aggressive and has a worse clinical outcome as compared to that in the older group.[3,4] Poor outcome in young age is due to an advanced presentation at diagnosis (larger T size and axillary lymph node positivity), a higher grade of differentiation, presence of lymphovascular invasion, lower ER/PR expression, presence of triple negativity.[5-7] In a study by Gajdos *et al*. demonstrated that patients younger than 36 years had larger tumors, more nodal involvement (50% vs. 37%) and were more likely to be diagnosed with Stage II or III cancer (60% vs. 43%).[7] In
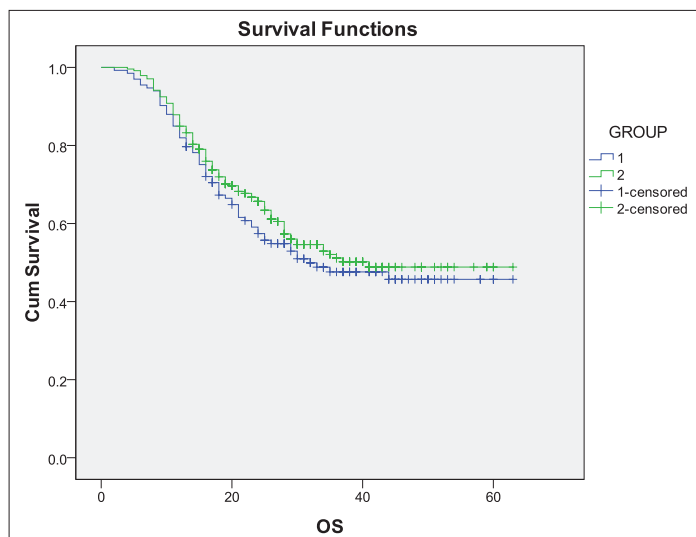
Figure 1: Kaplan–Meier for survival analysis

this present study, also 66.16% patients in under forty group belong to stage III as compared to 54.4% patients in above 40 group (P = 0.029, significant).

Younger age group has been shown to be associated with an increased incidence of ER/PR negativity compared to older patients.[6,8] This study also demonstrated that patients positive for ER and PR receptors in below 40 years age group were 39.84% and 27.81% respectively versus 55.23% and 44.76% respectively in above 40 years age group. In a study by Carvalho *et al.* demonstrated that triple negative tumors have also been found to be over-represented in young women with breast cancer, with rates close to 26%.[8] In this study, also 46.61% of patients were triple negative in below 40 years age group versus 32.21% in above 40 years age group.

In this study, locoregional recurrence in the two groups is 13.53% versus 6.27%, respectively. The analyses of NSABP group trials had also shown that young age is an independent predictor of locoregional recurrence in breast cancer.[9] A study by Bharat *et al.* estimated the risk of breast cancer recurrence for women diagnosed below the age of 40 to be 1.53 (95% confidence interval, 1.37–1.74) times higher than in those diagnosed above 40 years.[4]

This has been seen that the survival in the young age group is also inferior as compared to older age group.[3,4,9,10] In this study, the median DFS was 15 versus 14 (P = 0.28, not significant) in two arms, which may be contributed because of aggressive use of chemotherapy in young age group, especially taxane-based. Gnerlich *et al.* also showed that young women <40 years had a higher breast cancer mortality rate (18.3% vs. 12.1%, P = 0.001) than those older than 40 years.[10] In this study, the percentage of expired and lost to follow-up patients is also more in younger age group 49.31% versus 43.90%.

This study also has a limitation as it is a retrospective study with small sample size. Furthermore, the median follow-up is also very less. The cohort presented in the tertiary center is not the representative of the general population as a whole. In addition, patients came from distant places being a tertiary center; therefore, the percentage of loss to follow-up is high. A larger sample size with a long follow-up may reveal the significant differences between the two groups.

Conclusion

Many poor prognostic factors have been associated with young age patients with breast cancer as shown by many studies in English Literature as well as above retrospective study from our center, so aggressive management is required to reduce morbidity, mortality, and metastasis in breast cancer presenting at a young age.

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Conflicts of interest

There are no conflicts of interest.

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