

PROGNOSIS OF BREAST CANCER IN VERY YOUNG AGE (LESS THAN 30 YEARS)

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Abstract

Purpose: Breast cancer diagnosed at a younger age has aggressive biology being triple negative and high grade and is associated with poor prognosis.

Materials and Methods: Retrospectively data of 121 patients age 30 years or younger registered during the year 2008 were reviewed. Data were extracted from the cancer registry department of the institute. Demographics studied were the age at diagnosis, gender, pregnancy or lactation association, family history of breast cancer, histopathological diagnosis, and stage of the disease, receptors, type of treatment, response, local recurrence, distant relapse, and survival.

Results: A total of 121 patients with age 30 years or less were included. An only a single patient was male. The age range was from 20 to 30 years; bilateral involvement was seen in a single patient. Almost half 50.4% ($n = 61$) patients had locally advanced disease at presentation. Pregnancy/lactation-associated breast cancer was seen in 29.8% ($n = 36$). The most common stage was Stage III (52.1%) and Stage II (33.9%). Invasive ductal carcinoma was the most common histology 94.2% ($n = 114$) of patients; triple negative was the most common molecular subtype present in 46.3% ($n = 56$). Chemotherapy was received by 92.6% ($n = 112$), 88.4% ($n = 107$) patients received radiation therapy. Modified radical mastectomy was performed in 57% ($n = 69$), breast conservation surgery in 35.5% ($n = 43$), follow-up period was 5 years, local recurrence was observed in 12.4% ($n = 15$) and cancer related deaths were 42.1% ($n = 51$).

Conclusions: Breast cancer in very young has very aggressive tumour biology, needs aggressive treatment with surgery, chemotherapy, radiation therapy and hormonal therapy.

Key words: Breast cancer, pregnancy-associated aggressive tumour biology, triplenegative, young

Introduction

Breast cancer is the most common type of cancer found in the female population. Breast cancer in young age is relatively uncommon accounting for 7% in women diagnosed at 40 years or younger.^[1] Young age (<35) is an independent risk factor for breast cancer-related deaths, they are at higher risk of death as compared to middle age women.^[2] Multiple studies from different centres and different countries show that breast cancer in young females presents as an aggressive disease which is difficult to manage and shows poor outcome in terms of survival when they are compared with the older patients.^[3,4] Younger patients <35 years, even with receptors positive

have 1.5-fold higher risks for mortality as compared to those above 35.^[5] Tumours in young females are usually node positive, locally advance with negative hormonal status. The reason for this unusual behaviour is yet to be found.^[6,7]

Our aim was to review the demographics, to see the incidence of brain metastasis, after complete treatment, and prognosis of breast cancer in very young females.

Materials and Methods

A total of 179 patients age 30 years or less were registered at our institute from January 2008 to December 2008, after exclusion of patients with incomplete data final sample size was 121. Medical records were reviewed for clinicians notes, medical reports, and treatment charts. Demographics studied were the age at diagnosis, gender,

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clinical presentation, pregnancy or lactation associated, family history of breast cancer in a first-degree relative and locally advanced disease (tumour size >5 cm, nipple retraction, skin involvement, inflammatory features) histopathological diagnosis, stage of the disease, receptors, type of treatment, response to neoadjuvant chemotherapy, local recurrence, distant relapse, disease-free and overall survival (OS). Patients were categorised into luminal subgroups according to the receptors (oestrogen receptor, progesterone receptor and her-2 neu receptor). Disease-free survival was calculated from the date of complete treatment till the locoregional recurrence, while OS was calculated from the date of diagnosis till the time to death. Neoadjuvant chemotherapy was offered to all patients with locally advanced disease, lymph node-positive disease and Stage IV disease, response to neoadjuvant chemotherapy was assessed clinically, radiological, pathologically as complete response (CR), partial response (PR) or no response (NR). 5 years survival was calculated using Kaplan–Meier survival curve. Data were analysed using SPSS version 19.

Results

The final sample size was 121; the age range was 20 years–30 years with a median age of 28 years. Demographic characteristics are summarised in Table 1. Female patients were 99.1% ($n = 120$); only a single patient was male. Locally advanced disease (tumour size >5 cm, skin involvement and clinically lymph nodes node-positive disease) was present in 50.4% ($n = 61$) patients, 76.8% ($n = 93$) patients had nodal metastasis at presentation while 28 (23.1%) of patients were node negative, pregnancy/lactation-associated breast cancer was found in 29.8% ($n = 36$). Left side involvement was seen in 53.7% ($n = 65$); only a single patient had bilateral disease at the time of presentation. Most patients presented in Stages III and II disease, 52.1% ($n = 63$) and 33.9% ($n = 41$), respectively, 10% ($n = 13$) of patients presented with Stage IV disease. Most common histological subtype was invasive ductal carcinoma, found in 94.2% ($n = 114$), other less common types were mucinous, invasive lobular, malignant phyllodes and ductal carcinoma *in situ*. Triple negative was the most common luminal subtype present in 46.3% ($n = 56$), followed by luminal A 29.8% ($n = 36$) and luminal B 16.5% ($n = 20$), her-2 neu overexpression was seen in 7.4% ($n = 9$) patients.

Table 1: Demographic characteristics

Characteristics	Frequency % (n)
Age group	
20–25 years	18.1 (22)
26–30 years	81.8 (99)
Gender	
Females	99.1 (120)
Male	0.8 (1)
Locally advanced	
Yes	50.4 (61)
No	49.6 (60)
Pregnancy/lactation associated	
Yes	29.8 (36)
No	70.2 (85)
Family history	
Present	11.6 (14)
Absent	88.4 (107)
Histology	
Invasive ductal carcinoma	94.2 (114)
Mucinous carcinoma	2.47 (3)
Malignant haloids	0.8 (1)
Invasive lobular carcinoma	1.65 (2)
Ductal carcinoma <i>in situ</i>	0.8 (1)
Molecular subtypes	
Luminal A	29.8 (36)
Luminal B	16.5 (20)
Triple negative	46.3 (56)
Her 2 neu type	7.4 (9)
Stage	
Stage 0	3.3 (4)
Stage I	0.8 (1)
Stage II	33.9 (41)
Stage III	52.1 (63)
Stage IV	9.1 (11)

Almost half of the patients 49.6% ($n = 60$) received neoadjuvant chemotherapy. CR was observed in 20% ($n = 12$) while 66.6% ($n = 40$) had PR and 5 patients showed NR to first-line chemotherapy.

Modified radical mastectomy was performed in 57% ($n = 69$), while 35.5% ($n = 43$) underwent breast conservation surgery, nine patients were not candidates for surgery as they had progressive Stage IV disease. 52 patients received chemotherapy in the adjuvant setting. Most of our patients 88.4% ($n = 107$) did receive radiation

therapy. Hormonal treatment in the form of tamoxifen was received by 45.5% ($n = 55$) of patients, targeted therapy in the form of trastuzumab was received by four patients only [Table 2]. Local relapse occurred in 12.4% ($n = 15$), while 33.8% ($n = 41$) developed distant relapse, 17.4% ($n = 21$) patients developed brain metastasis. After 5 years only 57.9% ($n = 70$) were alive, cancer related deaths were 42.1% ($n = 51$). 5 years OS was 57.9%. 5 years survival according to the stage at presentation is shown in Figure 1.

Discussion

Breast cancer in women of age 35 is different from breast cancer occurring at an older age (>40 years), it has aggressive tumour biology, high proliferative index, higher tumour grade, lack of oestrogen receptors and progesterone positivity, usually are poorly differentiated and carry poorer survival as compared to the older population.^[9] Most of our patients had invasive ductal carcinoma grade two or three, 46.3% of our patients were triple negative.

Table 2: Treatment details

Chemotherapy	Frequency % (n)
Neoadjuvant	49.6 (60)
Adjuvant	42.1 (52)
Surgery	
Modified radical mastectomy	57 (69)
Breast conservation surgery	35.5 (43)
No surgery	7.4 (9)
Radiation to breast	
Received	88.4 (107)
Not received	11.6 (14)
Hormonal Treatment	
Received	45.5 (55)
Not received	54.5 (66)
Targeted therapy (herceptin)	3.3 (4)
Locoregional recurrence	
Yes	12.4 (15)
No	87.6 (106)
Distant relapse	33.8 (41)
Brain mets	17.4 (21)
Outcome	
Alive	57.9 (70)
Dead	42.1 (51)

Due to the lack of screening programs in the developing countries presentation is often delayed,^[10] almost half of our patients (50.4%) were locally advanced at presentation. Due to unfavourable tumour biology younger women has low survival as compared to the elderly.^[11] 5 years OS in our study population was 57.9%.

The mean age at diagnosis is much younger in Asian countries as compared to western; the incidence is increasing with the passage of time.^[12] Pregnancy-associated breast cancer (PABC) is defined as breast cancer arising in pregnant women or lactation, 1 year after the delivery,^[13] it carries poorer prognosis due to delay in diagnosis as breast size increase and denser. PABC is very aggressive with her-2 neu overexpression, or triple negative with higher proliferative index.^[14] The interactions between pregnancy and breast cancer are complex and variable, may be increased hormonal levels promote proliferation of existing tumours,^[15] 29.8% of our patients presented with pregnancy or lactation-associated breast cancer, all presented with larger tumour size. Risk of breast cancer becomes 2 times in patients with family history of breast cancer, however, for PABC, the risk remains the same as for non PABC tumours according to Johansson *et al.*^[16] 11.6% of our patients have a positive family history of first-degree relative.

Triple negative breast cancer is an independent poor prognostic factor, this molecular subtype is more common

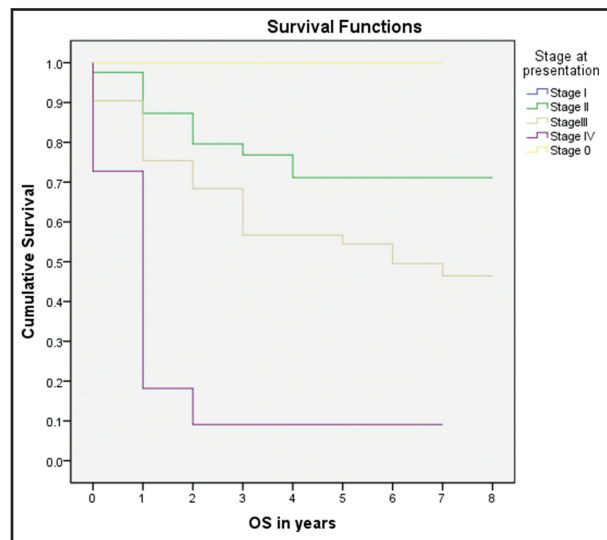


Figure 1: Kaplan–Meier showing 5 years overall survival according to stage

in the younger age group, therefore, two worst things combine together, risk of death becomes 2.7-folds when triple negative cancer arise in younger population,^[17] 46.3% of our patients were triple negative and only nine patients showed her-2 neu overexpression. Tang *et al.* carried out a retrospective review of 1360 Chinese women <40 years of age and studied the relationship between luminal B subtype and prognosis; they found increased risk of local recurrence and increase death risk in these patients.^[18] Younger patients also show a higher proportion of BRCA1 and BRCA 2 mutations.^[19]

Chemotherapy is the mainstay of treatment in invasive breast cancer, to achieve local as well as systemic control, inpatient with locally advanced disease, lymph node-positive patients and to downstage tumour size in patients who are candidates for breast conservation.^[20] Women who are <30 years who do not receive chemotherapy are at high risk of local and distant relapse. 60 patients in our study received neoadjuvant chemotherapy while 52 patients received chemotherapy after surgery.

Nearly 57% of our patients underwent modified radical mastectomy, while 35.5% underwent breast conservation surgery, Cao *et al.* compared local recurrence and survival rate in younger patients undergoing breast conservation or mastectomy and they observed that mastectomy offers no additional survival benefits compared to breast conservation.^[21] According to Bleyer *et al.* younger women carries poorer survival in all stages of the disease when compared to older women,^[22] they compared women age groups; 20–35 and 45–75 years old and for all the stages younger patients had decreased OS as compared to older patients.

Many studies have shown that age itself is a risk factor for poor prognosis, Brandit *et al.* studied age at diagnosis in relation to the survival in 4453 women of different age groups and observed that after follow-up period of 10 years women of age group <40 years with axillary lymph node-negative disease had poorer outcome.^[23] We also found a higher mortality rate in our population despite aggressive treatment. Andres *et al.* concluded that younger age at the time of diagnosis carries poorer prognosis.^[24] Assi *et al.* described breast cancer in younger age as very aggressive tumours with poor prognostic factors

and higher recurrence rate and distant relapse leading to worst prognosis.^[25]

Conclusions

The incidence of breast cancer in very young females (<30) is increasing over the years, tumour biology in this age group is aggressive, with poorer prognostic factors. Since half of our patients presented with advanced stage; therefore, we emphasize the need to increase awareness among the younger population to achieve better disease control.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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