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Original Research Article

Study of carcinoma breast in women under 40 years of age

Mrinalini Milind Borkar*, Abdul M. Quraishi, Gaurav Jannawar

Department of Surgery, Government Medical College, Nagpur, Maharashtra, India

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***Correspondence:**
Dr. Mrinalini Milind Borkar,
E-mail: mrinalborkar@yahoo.co.in

ABSTRACT

Background: Carcinoma breast is the commonest malignancy in females worldwide. Although a disease of postmenopausal age, occurrence in young age is a poor prognostic factor. Hence this study was undertaken to study clinical presentation, extent of disease, treatment modalities, histopathological typing and grading of carcinoma breast in females upto 40 years and to compare tumor characteristics between very young (≤30 years) and young (30- 40 years) patients.
Methods: This was a hospital based observational study conducted at Department of Surgery, GMC Nagpur, from July 2009 to November 2011. All cytologically or histologically proven cases of carcinoma breast in females ≤40 years of age giving consent were included. All the patients were evaluated by detailed clinical evaluation and investigated, treated with different modalities according to clinical stage and were followed up for a period of two months. Data was collected and tabulated into a master sheet and statistical tests were applied to test the significance of association.
Results: Mean age was 35.24 years (19-40 years), 12 patients being under 30 years (very young). Mean duration of presentation 3.08 months. Mean lump size was 5.32 cm, 56% had lump >5 cm. Only 1/3rd of patients had EOBC, 2/3rd had LOBC/LABC. FNAC was 87% sensitive, ER positivity was low. All patients received multimodality treatment, 84% underwent mastectomy and none underwent BCT. We report two deaths. Very young group showed more incidence of node positivity, advanced stage of the disease and positive margin of resected specimen than young age group but had no significant difference with respect to tumor size and histopathological characteristics. Nulliparity, breast feeding and protective effect of early age at 1st pregnancy when were independently tested in operable and advanced staged cancer groups no statistically significant association was found.
Conclusions: Carcinoma of breast in young females, although less common, is an aggressive disease. In India more patients present in advanced stage precluding BCT. Early diagnosis can improve outcome.

Keywords: Carcinoma breast in young age, Premenopausal

INTRODUCTION

Breast cancer is the most frequently diagnosed cancer among women worldwide in 140 out of 184 countries, according to the World Cancer Research Fund International.[1] In India, breast cancer is the second most common cause of cancer death preceded by cervical cancer.[2] Although the disease is common in post-menopausal age, increasing number of Indian women having breast cancer are found a decade younger in comparison to western women suggesting that breast cancer occurs at a younger pre-menopausal age in India.[3]

Breast cancer in young females is unique in the sense that breast cancer in young females is itself a poor prognosis factor because of greater incidence of advanced stage of

disease at presentation with high risk of recurrence.[4-10] This is because of low index of suspicion in young females, firm breasts hindering clinical and radiological interpretation also causing missing of small breast lumps. Incidence of Triple negative breast cancer (TNBC) is higher in young age. Early onset breast cancer not only has different molecular or etiological basis but also has psychological aspect too, as patient loses breast in sexually active phase of life when it is most desirous to have one.

Hence this study was undertaken to study clinical presentation, extent of disease, treatment modalities, histopathological typing and grading of carcinoma breast in females upto 40 years and to compare tumor characteristics between very young (≤30 years) and young (30-40 years) patients, to compare tumor characteristics between operable and advanced stage cancers.

METHODS

This was a hospital based observational study conducted at Department of Surgery, GMC Nagpur, from July 2009 to November 2011.

Inclusion criteria

All cytologically or histologically proven cases of carcinoma breast in females ≤40 years of age giving consent.

Exclusion criteria

Patients not giving consent or refusing treatment.

All the patients after admission in the wards were evaluated by detailed history and examination according to the standard proforma and investigated. Patients were treated with different modalities according to clinical stage. All the patients were followed up for a period of two months from starting of treatment. Data was collected and tabulated into a master sheet and statistical tests were applied to test the significance of association.

RESULTS

Total 57 patients below 40 years of age were included. Incidence of breast cancer in women upto 40 years of age was 21% as per hospital record.

Mean age of the study group was 35.24 years, with range from 19 years to 40 years. Majority of the patients fell in 35-40 years age group, amounting to 56% of the total patient load. 12 patients belonged to <30-year group (very young) and 45 patients were found in >30-year age group (young) (Table 1).

Duration of lump i.e. the period for which patient was having lump before coming for consultation ranged from 1 month to 6 months with an average of 3.08 months. Majority of patients presented within 3-4 months. Increase in duration of lump was associated with adverse presentation, out of 10 patients presenting after 5 months, 7 patients (70%) presented with advanced T stage, 5 patients had T4 lesions and 2 patients had T3 lesions.

Table 1: Age wise distribution of the patients.

Age group	Number of patients	Percentage
0-10 years	0	0
11- 20 years	1	1.75
20- 30 years	11	19.3
30- 40 years	46	56
Total	57	

Figure 1: Clinical photographs showing Paeu-de-orange.

Figure 2: Clinical photograph showing ulceration.

Lump in breast was the most common symptom. Right sided lumps were commoner in 35 (61.40%) patients. Other symptoms included pain in breast (11 patients), nipple discharge [10 patients, serous (8), bloodstained (2)], metastatic symptoms (3 patients). When data was compared for patients aging ≤ 30 years with those of age 30- 40 years, incidence of metastatic symptoms was higher in very young age group 2 out of 12 (16.66%) as compared to younger age group which was 1 out of 45 patients (4.44%)

Figure 3: Clinical photographs showing ulcerated mass.

Figure 4: Clinical photograph showing large lump.

Out of 57 patients only one was unmarried and presented at the age of 19 years. 3 patients were nulliparous were less than 30 years old, rest 54 had one or more children. Majority of the patients had their first child birth at age less than 20 years. Patients whose first pregnancy was before 20 years of age numbered 32 and 16 (50%) out of these had advanced lesions with stage III A, III B and IV with 5, 10 and 1 patients respectively. Out of these, 22 patients had advanced histopathological grades (Gr II + Gr III) which compounded to 68% of the group population. Amongst 3 women who conceived at age >30 years, one patient had stage IIB disease, another had stage III B disease, stage could not be labeled in one case because of Tx status.

Family history was positive in two cases from ≤30 years age group with both giving history of breast cancer in second-degree relatives. 35 patients (61.4%) had right sided lump, 22 patients (38.59%) had left sided lesion. There were no patients with bilateral lumps. Tumor involved upper outer quadrant in 32 patients (56.14%), central quadrant in 13 patients (22.80%), upper inner in 5, lower outer in 6 and lower inner in only 1 patient.

Upper outer quadrant lesions had 46.87% node positivity with 10 patients showing N1 involvement and 5 patients exhibiting N2 lesions. Both lower outer and lower inner quadrant taken together 4 out of 7 patients were showing node positivity.

Lump size

Mean lump size was 5.32 cm. No patient had <2cm breast lump. Maximum patients fell under >5cm category highlighting the advanced presentation of young breast cancer. Two of the patients presented after prior lumpectomies (Tx) **(**Table 2).

Table 2: Lump size.

Lump size	Number	Percentage
<2 cm	0	0
2- 5 cm	23	40.35
>5 cm	32	56.14
Total	55	

Table 3: T staging of tumor masses.

T stage	Number of patients			
	Very young <30 years	Young 30-40 years	Total	Total (%)
Tx	1	1	2	3.50
T0/TIS/T1	0	0	0	0.0
T2	4 (33.33%)	14 (31.11%)	18	31.57
T3	2 (14%)	17 (37.78)	19	33.33
T4	6 (50%)	12 (26.67%)	18	31.57
Total	12	45	57	

There was no case with T0 or T1 lesion. Only 32% patients had T1 lesion, whereas 64.8% had T3/T4 tumours (Table 3).

Table 4: Nodal status of the patients.

Nodal status	No. of patients	Percentage
N 0	31	54.38
N 1	17	35.08
N 2	6	14.03
N 3	0	0.0

Thus, almost half of the patients presented with non-palpable axillary lymph nodes. Node positivity was more or less similar in <30 years age group and >30 years age group of patients (Table 4).

M staging

Two patients had metastasis, pleural effusion (1), liver metastasis and bony metastasis (1). One patient with metastasis had non-palpable lymph node while other had N1 and N2 lymph nodes.

Table 5: TNM staging of the disease.

TNM stage	No. of patients	%
II A (T2N0)	14	24.56
II B (T2N1, T3N0)	12 (4+8)	21.05
III A(T3N1+T3N2)	10 (5+5)	17.54
III B (T4N0+T4N1+T4N2)	18 (9+7+2)	28.07
IV	3	5.26
Total	55	

Table 6: Clinical staging.

Clinical stage	No. of patients	Percentage
Early operable	18	31.58
Large operable	18	31.58
Locally advanced	18	31.58
Metastatic	3	5.26

TNM staging

There were no patients with stage I disease. Only 1/3rd of patients had EOBC, 2/3rd had LOBC/LABC (Table 5 and 6).

Table 7: Treatment modalities offered.

Treatment option	No. of patients	%
Surgery	49	85.96
Neoadjuvant chemotherapy	18	31.58
Adjuvant/completion chemotherapy	43	75.43
Hormonal therapy	48	84.21
Palliative chemotherapy	3	5.26
Radiotherapy	20	31.57

Investigations

All the patients were investigated, and tissue diagnosis was obtained in every case, FNAC was done in 56 patients. FNAC confirmed diagnosis in 48 patients. Eight patients required biopsy. So, observed sensitivity of FNAC in our study was 85.71%. Out of 2 Tx patients FNAC was done from residual lump in one patient, other patient had undergone lumpectomy before presentation, so biopsy slides were reviewed. Biopsies were done in 9 patients of which 8 were incisional and 1 was excisional biopsy. Biopsy was conclusive in 100 % cases. Mammography was done in 14 patients and characteristic microcalcifications were seen in 8 patients (sensitivity of 57.14%). ER/ PR status was investigated in 8 patients of which 2 patients were labelled positive (25%), both of these patients were from >30-year age group.

Treatment

Diagnosed patient were treated with multimodality approach consisting of neoadjuvant chemotherapy, surgery, adjuvant chemotherapy, radiotherapy and hormonal therapy. Surgery was offered to 49 patients (modified radical mastectomy in 42 patients (85.71%), simple mastectomy in 7 patients (14.28%), none underwent breast conservation surgery. Radiotherapy was given to 20 patients (18 LABC patients and 2 with positive surgical margins) (Table 7).

Post-surgical complications

Cuticular necrosis, seroma formation, flap necrosis, surgical site infection were seen in 26%, 16%, 5%, 3.5% patients respectively.

Table 8: Histopathological subtypes

Histopathological subtypes	No. of patients	%
Infiltrating ductal	43	75.43
Mucinous	4	7.01
Invasive papillary	2	3.5
Metaplastic with infiltrating ductal	2	3.5
Lobular	1	1.75
Total	52	

Table 9: Histopathological attributes of tumor masses.

Parameter	No. of patients	%
Lymph nodal involvement	13	26.53
Positive surgical margins	13	26.53
Grades	Grade I- 4	8.16
	Grade II- 20	40.81
	Grade III- 13	26.53
ER/ PR status	2 out of 8 patien positive	25

Histopathology

Infiltrating ductal carcinoma was the most common histopathological subtype of all which was found in 43 cases (75.43%), least common was lobular variant which was seen in single patient aged 40 years, there were no cases of lobular carcinoma in under 30-year patients. Maximum (41%) patients had grade II disease) (Table 8 and 9)

Mortality

There were two deaths, both in patients with metastatic disease. One patient was ANC with multiple lung metastasis, in her first trimester of pregnancy and was advised termination of pregnancy. Patient died on the 4th day of admission. Second patient had post-lumpectomy ulceroproliferative growth with multiple liver metastasis, she was started on hormonal and palliation chemotherapy patient succumbed after 6 weeks of treatment.

Comparative analysis of very young and young breast cancer was as follows.

The number of patients in very young group was significantly less than young group. Duration of presentation, node positivity, advanced stage of the disease and positive margin of resected specimen was more in very young group (Table 10).

Table 10: Comparison between young and very young age groups.

Tumor character	Very young (<30 year)	Young (>30-40)	P value
Total number	12	45	<0.0001
Mean duration of lump	2.2 months	4.2 months	-
Mean tumor size	5.6 × 6.2 cm	5.2 × 5.4 cm	-
Node positive patients (N1 + N2)	6 patients (50%)	20 patients (35.08%)	-
Advanced clinical stage (III B + stage IV)	6 patients (50%)	13 patients (28.88%)	0.3015
Higher grade lesions (Gr II+ Gr III)	7 patients (58.33%)	26 patients (57.77%)	0.9724
ER/ PR status	Done in 3, all negative	Positive in 2 out of 5 patients	0.9333
Number of patients with positive margins	4 (33.33%)	10 (22.22%)	0.6551

Table 11: Comparison between operable and advance staged tumors.

Tumor character	Operable breast cancers (stage IIA+IIB+ IIIA) n= 35	Advanced breast cancers (stage IIIB+IV) N= 21	P value
Average age	35.19	34.94	P value = 0.8645 (independent t test) t= 0.1714; dF= 53
Mean duration of lump	3.1 month	2.94 month	P value = 0.6868 (Independent t test) t= 0.4015; dF= 53
Number of very young (≤ 30 year) patients	6	6	P value = 0.3514 (fisher exact test)
Number of nulliparous patients	1	2	P value = 0.5432 (fisher exact test)
Number of patients not breast fed	3	1	P value = 0.7432 (mid p test)
Number of patients with early age at pregnancy (<20 year)	20	11	P value = 0.8679 (chi square test) dF= 1
Average diameter of lump	4.82 cm	8.10 cm	Pvalue=0.00022 Independent t test t= 3.96, dF= 53
Node positivity (N1 + N2)	16 (44.44%)	9 (47.36%)	P value = 0.8359 (chi square test) dF= 1
Higher grade tumors	21 (58.33%)	11(57.89%)	P value = 0.9750 (chi square test) dF= 1

While analysing clinicopathological data we grouped patients in two categories operable breast cancer (stage II A + stage II B + stage III A) and advanced breast cancer (stage III B + stage IV), clinicodemographical data was analyzed between these two groups.

Thus, when etiological factors in early onset breast cancers viz. Nulliparity, breast feeding and protective effect of early age at 1st pregnancy when were independently tested in operable and advanced staged cancer groups no statistically significant association was found.

Average age at presentation (34.94 years) in advanced staged tumors was slightly lesser than operable group, mean duration lump was shorter for advanced group (2.94 months), nodal positivity in advanced stage cancer group (47.36%) was apparently greater than operable group but was not statistically significant. Mean tumor size in advanced stage group was larger than operable

group and this difference was statistically significant, which means advanced stage malignancies had larger lumps. Rest of the parameters like nodal positivity and proportion of higher-grade tumors although differed but the difference was not statistically significant (Table 11).

DISCUSSION

Carcinoma breast is a disease of postmenopausal women, literature from western countries mentions low incidence in premenopausal or young breast carcinomas, 1-2% of the total breast cancer load Noyes RD et al, 4.3% by Horsley et al.[12,13] However we found incidence of 21% comparable to study by Saxena S et al reporting 22%.[14]

National cancer database of American college of surgeons mentioned 0% incidence of breast cancer in women under 20 years of age, Dirk R documented incidence of 2.4%, in the present study we found one case under 20 years (1.75%) of total sample.[11]

Duration of lump i.e. the time for which lump was present before patient presented to clinician was thought to govern prognosis. In our study duration of lump ranged from 1 month to 6 months with average of 3.08 months, increasing duration of lump in our study was associated with advanced lesions. Bloom HJG found duration of lump influences the outlook in low grade tumors unlike high grade tumor in which prognosis is bad whenever they present.[15] Jimor S, Al Sayer H in their study of 113, <35 year women with breast cancer found almost half of the patients presented within 8 weeks duration, 27 presented upto 12 weeks and very few presented after 12 weeks.[16] Ashutosh et al report duration of lump ranging from 2 weeks to 2 years and mention that there was no good evidence that modest diagnostic delay (< 3 months) affects prognosis.[17]

Breast lump was the commonest presentation of breast cancers in present study (100%) comparable to studies done by Bloom HJG, Noyes RD et al, Rosen PP et al whereas Ashutosh et al report that 80% of the women had a clinically distinct mass, 20% presented with focally increased nodularity of the breast, and two out of three of these had a delay of one year or more between their first symptoms and diagnosis.[15,11,18,17]

Nulliparity and late age at first pregnancy is a known risk factor for developing breast cancer- Duffy EMSW, Velentgas and Daling, Razif SM, Sulaiman S, B MacMohan, report that women having their first child when aged under 18 years have only about one-third the breast cancer risk of those whose first birth is delayed until the age of 35 years or more.[19-22] In the present study we had 3 nulliparous females out of which two presented with advanced tumor masses (T4). In the present study majority of the patients 32 (59.25%) had first child birth before 20 years of age and only three patients (5.55%) had first child birth after 30 years. Thus, delayed first pregnancy as a reason for developing breast cancer was not common in the present study with majority having given birth at earlier age suggesting role of other factors in causation. Lactation is thought to decrease the chances of developing breast cancer in premenopausal females Newcomb PA, Storer BE.[23] We found 4 of the patients (7.01%) in the present study did not breast-fed babies, one patient was unmarried. Majority of the females in study had breast fed so this factor was of little significance. Pregnancy was thought to be associated with 1- 3% of breast cancers Noyes RD et al, we had one patient with 1st trimester pregnancy i.e 1.75% who died.[11]

Family history has long been thought to be implicated in causation of breast cancer, Lynch et all, Razif SM, Sulaiman S, Anderson and Badzioch.[24,23,25] Ashutosh et al found incidence of family history (13%, 2 patients) was similar in both young breast cancer group and general population, so that relatives of young carcinoma breast patients do not require intensive screening.[17] We noted positive family history in 2 of very young ≤30 patients (3.5%) both had one second degree relative with breast lumps. Rest of the patients were not having any family history which could possibly be due to increase prevalence of sporadic breast cancer, ruling out genetic abnormalities was not done in present study out of cost constraints.

Ashutosh et al report 7 (58%) T1 lesions, 3 (25%) T2 lesions; and 2 (17%) T3 lesions (classification: TNM, UICC) whereas present study had no patient with T1 lesion and 31% T2, T3 and T4 lesions each indicating advanced disease at presentation.[17] Median tumor size at presentation was 20 mm (range 10-130 mm), compared with 25mm (range 5-80 mm) in all women aged 26-35 seen during the same period (n - 118) (Ashutosh et al), the same was much less than in present study (5.32cm). Patients aged 25 years or less did not have a statistically significant different tumor size than the 26-35 group (P = 0.468) (Ashutosh et al) comparable to our study.[17]

The incidence of nodal positivity was greater in present study which reflects the advanced presentation of early onset breast cancer in our setup. This was in coherence with the findings of S Jimor, Al Sayer H, Rosen PP, Kothari A et al and Anders CK, Hsu DS who found greater incidence of larger tumor masses were associated with greater nodal involvement in young breast cancers.[16-18,26] Croman Net al mentioned commonest site of lump as upper outer quadrant, comparable to present study.[27,4]

Present study showed sensitivity of FNAC to be 85.71% similar to Nquansanquim S 92.5%.[28] Mammography is a screening tool but it is difficult to evaluate young breast mammographically. In present study, 14 patients were evaluated mammographically. It is known to be sensitive in 76% of cases, we report 57.18%. Sonography of breast had sensitivity of 67%.[14] In different studies infiltrating ductal variant is the most common histopathological variety of early onset breast cancer. Rosen et al. reported

that 8% of breast malignancydiagnosed at age 35 years had in situ disease only, Asutosh et al report it to be 13%.[17] Present study did not have any in situ carcinomas highlighting advanced presentation of early onset breast carcinomas in our setup (Table 12).

Table 12: Comparison of studies for histopathological types.

Tumor type	Noyes et al[11] n=125	Paul Rosen[18] n=166	Kollis et al[29] n=111	Present study n=57
Infiltrating ductal	95.2%	76%	67%	75.43%
Medullary	1.6%	11%	12%	-
Infiltrating lobular	-	3%	8%	1.75%
Mucinous	1.6%	1%	-	7.01%
Metaplastic	0.8%	-	-	3.5%

Other Histopathological attributes of the 12early onset breast carcinoma which needs concern, and which decides the management are nodal involvement, margin status grades and ER/PR status. All these factors have been extensively studied by various authors (Table 13).

Table 13: Comparison of different pathological parameters in percentage.

Study parameter	Kollis et al[29] n = 111	Carey K Anders et al[28] n = 46	Present study n = 57
Tumour size			
<2cm	41%	--	0%
2-5 cm	59%	50%	40.35%
>5 cm	0%	--	56.14%
Tumor grade			
I	6%	9%	8.16%
II	18%	29%	40.81%
III	76%	62%	26.53%
ER/PR status	---	74%	25%
Margins involved	---	13%	26.53%

Young patients of breast carcinomas presented with larger lesions having advanced grades in current study as compared to other studies.

Rosen P, Anders C et al, Ashutosh et al all noticed low prevalence of estrogen receptor positivity in early onset breast tumors comparable to present study.[18,26,17] Ashutosh et al had also mentioned relative scarcity of ER/ PR receptors in very young patients and so was observed in this study with no cases below 30 years of age testing positive for ER/PR receptor.[17] Early onset breast carcinomas needs multimodality treatment (Ashutosh et al), surgery has remained the cornerstone in the management of breast cancers since ever in a study by Ashutosh et al, 8 patients (66.6%) underwent MRM and 4 patients (33.3%) underwent breast conservation surgery, however present study had no BCT.[17] Ragaz J et al found radiotherapy combined with chemotherapy after modified radical mastectomy decreases rates of locoregional and systemic relapse and reduces mortality from breast cancer.[30] All the cases in the present study were treated with multimodality treatment.

Minor post-operative complications like cuticular necrosis, seroma formation were common and rate of surgical site infection was slightly greater than the expected 1- 2% range as per Cruse and Foord.[31]

Effects of pregnancy has been considered to have grave prognosis in Ca breast. Harrington, Richards analyzed this association in various time frames but they shared common views about poorer prognosis of this association.[32,33] However the prognosis of pregnant women with breast cancer stage-for-stage is equivalent to that of their non-pregnant counterparts (Zemlickis et al and Reed et al).[34,35]

In the present study we had only one patient with active pregnancy who died out of metastatic disease pointing towards the graveness of association.

Ashutosh et al in their effort to compare breast cancers in women <25 years and those presented between 25-35 years found that these two are not different in terms of presentation and tumor characteristics hence management remains same for both and is decided by clinical stage.

In the present study when very young and young women with breast cancers were compared with respect to clinical stage Duration of presentation, node positivity, advanced stage of the disease and positive margin of resected specimen was more in very young group. There was no statistically significant difference between the two groups. This finding was in concordance with conclusions of Ashuotosh et al.

de La Rochefordiere A et al carried out a multivariate analysis in premenopausal women to find that the worse prognosis of young age was independent of other factors such as clinical tumour size, clinical node status, histological grade, hormone receptor status, locoregional treatment procedure, and adjuvant systemic therapy.[36]

We compared operable patients (stage II A + II B + III A) with advanced tumors (stage III B + IV) and found risk factors like nulliparity and reluctance of breast feeding was not associated with advanced presentation of disease. Early age at 1st pregnancy as was thought to impart protective effect against breast cancer was documented however it does not govern the outlook of disease and has no statistically significant association with clinical stage. Tumors from advanced disease had larger lumps but there was no significant association of clinical stage with higher nodal positivity and higher-grade tumors.

CONCLUSION

Early onset breast cancers incidence and advanced stage at presentation was more in than in western countries. Younger age at first pregnancy imparting protection against breast cancer did not hold true in our study. Nulliparity and reluctance of breast-feeding in causation of breast cancer was documented but they did not seem to influence final clinical outcome. Advanced clinical stages were associated with larger tumor masses at presentation. FNAC was the primary investigation with good sensitivity.

Very young group showed more incidence of node positivity, advanced stage of the disease and positive margin of resected specimen than young age group but had no significant difference with respect to tumour size and histopathological characteristics. Majority of the patients presented with large tumor masses, so breast conservation surgery was not possible. Early onset carcinomas frequently present with advanced stage and early diagnosis and referral to specialty clinic can improve outlook. Results of this study cannot be conferred upon the whole population because of shorter sample size of study.

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