

Study of Carcinoma Breast in Women under 40 Year of age at A Tertiary Care Hospital in Central India

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A B S T R A C T

Introduction: Breast cancer among young women is a relatively uncommon. Many of the times the diagnosis is delayed in these patients owing to the reluctance of surgeons to subject young females to mammography because of the involved radiation. Current study was conducted to study various aspects of carcinoma breast occurring in patients younger than 40 years of age.

Material and Methods: This was a prospective study conducted in the surgery department in which 57 patients less than 40 years of age and diagnosed to be having carcinoma breast were included on the basis of a predefined inclusion and exclusion criteria. The risk factors, clinical presentation, staging and outcome were studied in these cases. Statistical analysis was done using SPSS16.0 version software. P-value less than 0.05 was taken as statistically significant.

Results: The most common affected age group was found to be between 35-40 years (56.14%). Common symptoms included lump in breast (100%), pain (19.29%) and discharge (17.54%). Majority of the patients had their first child birth at age less than 20 years. Upper outer quadrant was the most commonly affected site (56.14%) and nipple retraction (19.29%) was the most common sign in the studied cases. Most common tumor and clinical staging were found to be T3 (33.33%) and T III B (28.07%) respectively. Surgery and hormonal therapy were the most common treatment modalities given to these patients (85%). Most common histopathological type was found to be infiltrating ductal carcinoma.

Conclusion: Our study concludes that age less than 40 yrs is associated with diagnosis of breast cancer at an advanced stage and young patients presenting with breast lumps should not in any way be considered different from relatively older patients and all standard screening and diagnostic investigations must be carried out for early diagnosis and proper interventions.

Key words: Carcinoma Breast, Young Females, Histopathology, Staging

INTRODUCTION

Carcinoma breast is one of the most common cancer related morbidity and mortality seen in postmenopausal women. Over the past several decades there has been a steady and large increase in the incidence of the disease¹. 1 in 8 women has a lifetime risk of developing breast cancer. Changes in dietary patterns, increased prevalence of obesity, use of contraceptive hormones and hormone replacement therapy in perimenopausal women are the important factors responsible for increased incidence of breast carcinoma throughout the world². One of the other important cause is increase utilization of screening mammography which may be responsible for detection of asymptomatic patients having carcinoma breast. In India breast cancer is the second most common cause cancer related deaths. The natural history

of breast cancer is characterized by heterogeneity amongst patients and long duration of disease³.

Breast carcinoma in young women (before the age of 40 years) is reported to be uncommon comprising only of 5-7% of all the cases diagnosed with carcinoma breast. Certain regions and ethnicities are found to have increased risk of developing carcinoma breast at a relatively younger age⁴. A relatively higher proportion of the population in middle east and Africa are found to be having breast carcinoma below the age of 40 years, reaching as high as up to 20%. The exact cause of such a propensity in certain regions and ethnicities are not known but underlying genetic differences and environmental factors are thought to be the important contributing factors⁵.

Age alone has been shown to be an independent risk factor

for breast cancer. 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 recurrence⁶. The diagnosis in young females is usually delayed because of low index of, firm breasts hindering clinical and radiological interpretation also causing missing of small breast lumps. Additionally, primary care gynecologists or surgeons may also be reluctant to advice mammography in young patients because of the involved radiation. Breast carcinoma in young patients are characterized by decreased hormone sensitivity, higher levels of human epidermal growth factor receptor 2 expressions, aggressive growth patterns and poor outcomes as compared to the carcinomas encountered in patients with relatively elderly age group. Relatively late detection and more aggressive nature of breast carcinoma is responsible for poor outcomes in these patients. 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 one⁷. Management of the breast cancer requires multidisciplinary approach comprising of surgeons, radiotherapists, medical oncologists, pathologists and other professionals such as counselors. Surgery with adjuvant radiotherapy has now become a standard procedure for patients with breast cancer⁸. This was a hospital based observational study conducted to study various aspects of carcinoma breast occurring in patients younger than 40 years of age. Our emphasis was in comparing tumor characteristics between very young (≤ 30 years) and young (30- 40 years) patients and to compare tumor characteristics between operable and advanced stage cancers.

MATERIAL AND METHODS

This was a hospital based observational study conducted at department of surgery. Total 57 patients who fulfilled predefined inclusion criteria and were below 40 years of age were included in study. Any patient having any of the exclusion criteria was excluded from the study. The duration of the study was 2 years.

A detailed history including history of carcinoma breast in any of the family members was noted. Demographic details of all the patients were noted. A thorough clinical examination was done in all the cases. Routine investigations such as complete blood count, Bleeding and Clotting Time, routine urine examination, Renal and hepatic function tests, random blood sugar, ECG, chest X-Ray was done in all the cases. All patients included in this study had undergone mammography, sonomammography and FNAC to know histopathology study of specimen.

The patients were treated by various types of mastectomies (simple mastectomy, simple mastectomy with axillary clearance, modified radical mastectomy) and by chemotherapy, radiotherapy and hormonal therapy as indicated.

Cases were followed up till the end of study, the follow up included clinical examination for recurrence of the tumor at the operated site, recurrence in axilla and postoperative complications like lymphedema. Patients who complained of symptoms of metastasis were investigated to find the

metastasis.

Inclusion Criteria

1. All cytologically or histologically proven cases of carcinoma breast.
2. Age of the patients ≤ 40 years.
3. Patients giving informed consent to be the part of study.

Exclusion criterion

1. Patients not giving consent.
2. Patients refusing treatment.
3. Women with pre-existing breast cancer and those who have received any kind of chemo or radiotherapy in the past.

STATISTICAL ANALYSIS

Data was collected and tabulated into a master sheet and statistical tests were applied to test the significance of association. The results were studied using appropriate statistical methods. All the patients were followed up for a period of two months from starting of treatment. The results were studied using appropriate statistical methods. P less than equal to 0.05 was taken as statistically significant. Microsoft word and excel were used for generating charts and graphs

RESULTS

This was a prospective study of carcinoma breast in patients below 40 years of age in which 57 patients were included. The most common affected age group was found to be between

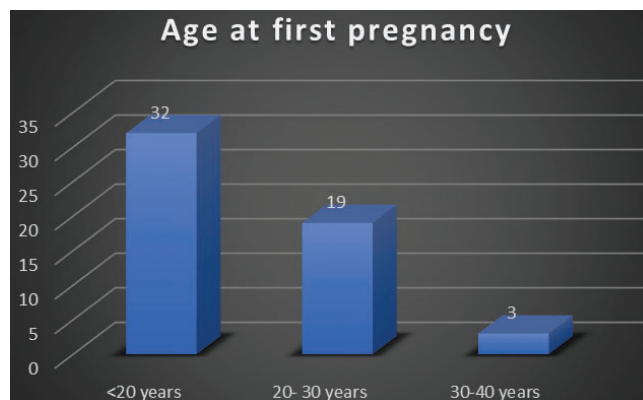


Figure-1: Age at first pregnancy in the studied cases.

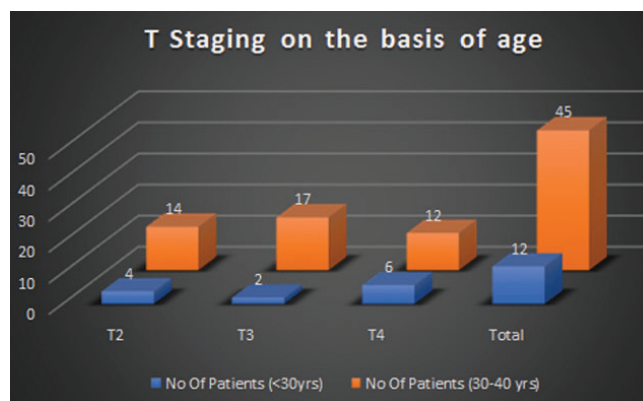


Figure-2: T Stage wise distribution in young and very young.

35-40 years (56.14%) followed by 30-35 years (24.56%) and 25-30 years (15.78%). Youngest patient was 19 yrs old girl and oldest of patient was a 40 yrs old lady. The mean age of the studied cases was found to be 35.24 yrs. Family history was positive only in 2 cases (table-1).

Lump in breast was the most common symptom which brought patient to consultation and was present in all the cases (100%). The other common symptoms included pain (19.29%), nipple discharge (17.54%) and axillary mass (12.28%). Right sided lumps were more common than left sided ones, with 35 (61.40%) patients presenting with Right

breast lumps. Nipple discharge was reported to be blood stained in 2 patients (table-2).

Patients' obstetric history was noted and patients were classified according to parity. Majority of the patients (61.40%) were para 2 or para 1 (19.29%) (figure-1). Nulliparous women made the smallest group of patients (5.26%). Majority of the patients had their first child birth at age less than 20 years. 16

Age group	Number of patients	Percentage
15- 20 yrs	1	1.75%
20- 25 yrs	2	3.50%
25- 30 yrs	9	15.78%
30- 35 yrs	14	24.56%
35- 40 yrs	32	56.14%
Total	57	100%

Table-1: Age wise distribution of the patients

Symptoms	Number	Percentage
Lump	57	100%
Pain	11	19.29%
Discharge	10	17.54%
Axillary mass	7	12.28%
Menstrual irregularity	4	7.01%
Metastatic symptoms	4	7.01%

Table-2: Symptoms in the studied cases.

Clinical stage	Number of patients	Percentage
II A	14	24.56%
II B	12	21.05%
III A	10	17.54%
III B	16	28.07%
IV	3	5.26%
undetermined	2	3.51%
Total	57	24.56%

Table-3: TNM staging of the disease.

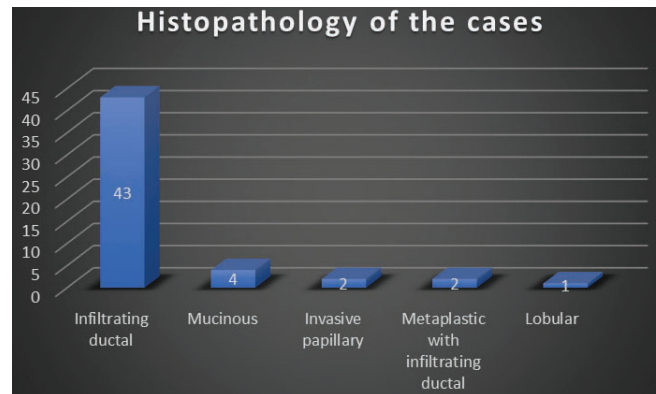


Figure-3: Histopathological subtypes of carcinoma.

Treatment option	Number of patients	Percentage
Surgery	49	85.96%
Neoadjuvant chemotherapy	6	10.52%
Adjuvant chemotherapy	43	75.43%
Hormonal therapy	48	84.21%
Palliative chemotherapy	3	5.26%
Radiotherapy	18	31.57%

Table-4: Treatment modalities offered

Parameter	Number of patients	Percentage
Lymph nodal involvement	13	26.53%
Positive surgical margins	13	26.53%
Grades	Grade I- 4 Grade II- 20 Grade III- 13	8.16% 40.81% 26.53%
ER/ PR status	2 out of 8 patients positive	25%

Table-5: Histopathological attributes of tumor masses

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%)	P value = 0.3015
Higher grade lesions (Gr II+ Gr III)	7 patients (58.33%)	26 patients (57.77%)	P value = 0.9724
ER/ PR status	Done in 3, all negative	Positive in 2 out of 5 patients	P value = 0.9333
Number of patients with positive margins	4 (33.33%)	10 (22.22%)	P value = 0.6551

Table-6: Comparison between young and very young age groups

Tumor character	Operable breast cancers (stage IIA+IIB+ IIIA) n= 36	Advanced breast cancers (stage IIIB+IV) N= 19	P value
Average age	35.19	34.94	0.8645
Mean duration of lump	3.1 month	2.94 month	0.6868
Number of very young (≤ 30 yrs) patients	6	6	0.3514
Number of nulliparous patients	1	2	0.5432
Number of patients not breast fed	3	1	0.7432
Number of patients with early age at 1 st pregnancy (<20 yrs)	20	11	0.8679
Average diameter of lump	4.82 cm	8.10 cm	0.00022
Node positivity (N1 + N2)	16 (44.44%)	9 (47.36%)	0.8359
Higher grade tumors	21 (58.33%)	11(57.89%)	0.9750

Table-7: Comparison between operable and advance staged tumors

patients whose first pregnancy was before 20 years of age had advanced lesions with 5 patients having stage III A lesions and stage III B and stage IV showing 10 and 1 patients respectively. 22 out of 32 patients conceiving at <20 years 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 2B disease, another had stage III B disease, stage could not be labelled in one case because of Tx status.

Family history was inquired in every subject and was positive in two cases from ≤ 30 years age group with both giving history of breast lump in second degree relatives. All the patients were inquired about the duration of lump. Duration of lump ranged from 1 month to 6 months duration with an average of 3.08 months. Increase in Duration of lump was associated with adverse presentation, 10 patients presented after 5/ >5 months and 7 out of 10 (70%) presented with advanced T stage. 5 patients were having T4 lesions and 2 patients had T3 lesions.

Patients in very young age group (≤ 30 years) had mean lump size of 5.6x6.2 cm which was slightly larger than young age group (30- 40 years) which had mean lump size of 5.2x5.4 cm. No patient had small <2cm breast lump. Maximum patients fell under >5cm category highlighting the advanced presentation of young breast cancer. Mean lump size was 5.08x5.32 cms. Two of the patients presented after prior lumpectomies hence lump size could not be made out. 22 patients i.e. 38.59% had left sided lesions. Majority of patients had right sided lumps with 35 patients (61.4%). There were no patients with bilateral lumps. Most of the tumor masses originated in upper outer quadrant with a toll of 32 patients amounting to 56.14% of total bulk. Next to follow were central region tumors which were found in 13 patients or 22.80% of patients.

The analysis of clinical signs showed that the most common clinical sign in the studied cases was nipple retraction (19.29%) followed by peau'de orange appearance (17.54%) and nipple deviation (15.78%). Satellite nodules and ulcers were seen in 8.77% patients each. There was no case with T0 or T1 lesion. Majority of the patients had either T3 (33.33%), T2 (33.33%) or T4 (31.57%) lesions which was seen in 37 patients i.e. 64.8% of patients (figure-2).

When very young (≤ 30 years) patients were compared with young age group (30- 40 years) very young population had

66.66% (8 out of 12) patients showing advanced tumor masses (T3, T4), same was found in 29 out of 45 patients of young age group (64.44%).

Thus, almost half of the patients presented with non-palpable axillary lymph nodes. Node positivity was more or less similar in <30 yrs age group and >30 years age group of patients. Three of the patients had metastatic symptoms of pleural effusion, liver metastasis and bony metastasis (low back pain). One of the patients with metastasis had non-palpable lymph node while other two had N1 and N2 lymph nodes. Majority of the patients were having locally advanced III B stage. When very young patients (≤ 30 years) from the study were compared with young patients (30- 40 years), very young had advanced malignancies in 50% i.e. 6 out of 12 patients in young age group were having stage III B or Stage IV disease (table-3). While in 30- 40 age group this was found in 28.88% patients with 12 patients having stage III B and single patient showing stage IV disease. Since two of the patients presented after lumpectomy were labelled as Tx hence staging could not be done. There were no patients who presented with stage I disease.

Diagnosed patient were treated with multimodality approach consisting of neoadjuvant chemotherapy, surgery, adjuvant chemotherapy, radiotherapy and hormonal therapy. Surgery was offered to 49 patients, surgeries which were offered were modified radical mastectomy in 42 patients i.e. 85.71% of the total surgeries, next in the shelf was simple mastectomy which was offered to 7 out of 49 patients or 14.28% of the total surgeries. Completion radiotherapy was given to 18 patients with positive margins or nodal involvement (table-4).

Minor complications like cuticular necrosis were top on the list of post-surgical complications of young breast cancer which was seen in 15 patients (26.31%). Next to follow was seroma formation which was observed in 9 patients (15.78%), severe complications like flap necrosis were rare however 3 patients had flap necrosis. 3.51% patients were found to have surgical site infection.

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 (figure-3).

Lymph nodal positivity was found in 13 patients i.e. 22.8% of patients. Surgical margins were found to be involved in 13

patients. 33 out of 49 patients exhibited higher grade tumors which was around 77.3% of the total surgical specimens. Highlighting greater prevalence of higher grade tumors in early onset breast cancers. Very young group had 7 out of 12 patients showing advanced grades (grade II + grade III) i.e. 58.33% same was found in 26 pts of younger group i.e. 57.77%, when margins were compared very young age group showed margin positivity in 33.33% patients as compared to 22.22% of younger age group (table-5).

While analyzing 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), clinicodemographic data was analyzed between these two groups. P value for total number of patients in group was significant which means incidence of young breast carcinomas was higher than very young. Rest of the comparison was statistically insignificant (table-6).

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. The only factor which was statistically significant was average diameter of the lump (table-7).

2 patients expired during the study period. In both the patients there was metastatic spread of the carcinoma. First patient was pregnant and was found to have 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 history of lumpectomy done and presented with ulceroproliferative growth, patient had multiple liver metastasis at the time of presentation, she was started on hormonal and palliation chemotherapy and succumbed after 6 weeks of treatment.

DISCUSSION

This was an observational study which was designed to find out the unique features of breast carcinomas in young female. Breast carcinoma as it was defined was the disease of post-menopausal women and same when presented in premenopausal young females was said to be associated with adverse clinicopathological features an attempt was made to find the same.

Carcinoma breast although a disease of postmenopausal women premenopausal or young breast carcinomas contributed 1-2% of the total breast cancer load. The incidence of carcinoma breast in the patients younger than 40 years was found to be 21% of overall cases of carcinoma breast. Similar incidence was reported by Sunita saxena et al⁹ who found the incidence of carcinoma breast in patients younger than 40 years to be 22%. Low parity and nulliparity are important risk factors for development of carcinoma breast at relatively younger age. In our study we had 3 nulliparous females out of which two presented with advanced tumor masses (T4). Nulliparity has long been thought a risk factor for developing breast cancer Velentgas and Daling¹⁰ stated that breast cancer risk increases with late age at 1st confinement and females with low parity.

In our 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 our study with majority having given birth at earlier age suggesting role of other factors in causation. Some of the authors like Razif SM et al¹¹ and B MacMohan et al¹² found that the risk of developing breast cancer increases with increased age at first pregnancy.

We noted positive family history in two of very young ≤ 30 patients (3.5%) both had one second degree relative with breast lumps Anderson and Badzioch et al¹³ found that the patients with a positive family history was more likely to develop breast carcinoma at a younger age while the other authors like Ashutosh et al found that incidence of family history (13%, 2 patients) was similar in both young breast cancer group and general population¹⁴.

In our cases most common presenting complaint was breast lump which was present in all the patients (100%). Breast lump was the commonest presentation of breast cancers in studies done by H J G Bloom¹⁵, R Dirk Noyes et al¹⁶, and Paul P Rosen et al¹⁷. In our study when very young and young women with breast cancers were compared with respect to clinical stage histopathological grades ER/ PR status and post-operative margin status there was no statistically significant between the two groups. Thus, very young breast carcinomas do not differ from young breast carcinomas and the management depends upon the staging and grading of tumor¹⁸. 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. Similar conclusions were reported by Legorreta et al¹⁹ and Jeruss JS et al.²⁰

CONCLUSION

our study has shown a major proportion of young females (those less than 40 years) with breast cancer presented with advanced stage signifying the importance of need of awareness of the fact that carcinoma breast should be suspected in any patient presenting with lump in breast unless proved otherwise. Proper awareness and screening programs can help in avoiding the delay in the diagnosis with its potential hazards.

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