

Corrected and Republished: Breast Cancer in Young Women: Experience from a Tertiary Care Hospital of Coastal India

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ABSTRACT

Background and Aim: Breast cancers are relatively rare among young women amounting up to 6% of all breast carcinoma cases reported in that age group. In younger age groups, breast cancers, though, have a more aggressive behavior and poorer outcome in comparison to patients in the elderly age groups. The aim of the present study was to evaluate the histo-pathological characteristics of breast carcinomas reported in patients lesser than 40 years of age. **Materials and Methods:** Surgical specimens of carcinoma breast received at the Department of Pathology in a tertiary care hospital for a period of 2 years from January 2014 to December 2015 were included in the study. The histo-pathological slides were reviewed and clinical data was collected from the archival records and compared. Statistical analysis was done using IBM SPSS statistics 17 (Chicago, USA). Various tumor characteristics were correlated with the morphological features and the other clinico-pathologic data using Chi-square value (χ^2), paired t-test and Fischer's test. $p < 0.05$ was considered to be statistically significant. **Results:** Infiltrating Ductal Carcinoma-Not otherwise specified (IDC-NOS) was found to be the most common variant of breast carcinoma in both the younger and the elderly age groups followed by the invasive lobular carcinoma and mucinous carcinoma in the younger and invasive lobular carcinoma and mucinous carcinoma and papillary carcinoma in the elderly age groups. Also, stage II followed by stage III were the commonest stages reported in the younger and elderly age groups based on their prevalence as against stage I and IV ($p = 0.006$). **Conclusion:** Breast cancers diagnosed in younger age groups present with an aggressive behavior and poorer outcome in comparison to patients in the elderly age groups. Also, such cancers often tend to present with advanced stages of the disease process and high grades of tumor with lymph nodal involvement and metastasis at the time they are first diagnosed conferring an inferior prognosis illustrating the need for more clinical trials to be conducted on younger patients with breast cancers with an aim to improve the overall outcome in this age group.

Key words: Breast cancers, Tertiary care settings, Younger age groups, TNM staging, Histo-pathology.

INTRODUCTION

The most common cancers diagnosed in women are the breast cancers. These account for the second most common cause of cancer-related deaths in the affected women. Breast cancer is a relatively rare occurrence in the young women amounting to up to 6% of all breast carcinoma cases reported in that age group.¹ In younger age groups, breast cancers, though, have a more aggressive behavior and poorer outcome in comparison to patients in the elderly age groups.²⁻⁵ Recently, a phenomenal change has been noticed in the behavior of breast carcinoma cases wherein more of the young women have been found to be more commonly getting afflicted and being diagnosed with breast carcinomas.⁶⁻⁸ The aim of the present study was to evaluate the histo-pathological characteristics of breast carcinomas reported in patients lesser than 40

years of age and compare them with those reported in the elderly age groups.

MATERIALS AND METHODS

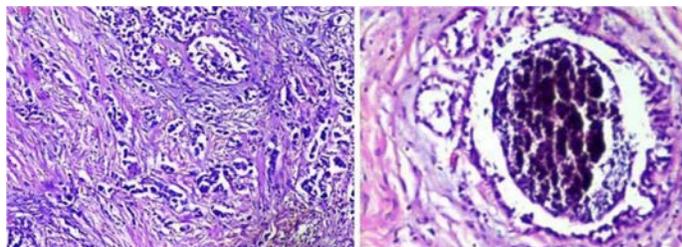
A retrospective study was conducted over a period of 2 years from January 2014 to December 2015 wherein the surgical specimens of carcinoma breast received at the Department of Pathology in a tertiary care hospital were included. The histo-pathological slides were reviewed after mutual discussion by two separate histo-pathologists and clinical data collected from the archival records and compared. All data including the clinical presentation, pathological type and TNM staging of the tumor were compared between the two groups. Carcinoma-*in-situ*, male breast carcinomas and inadequate biopsy samples were excluded from the study. The study was

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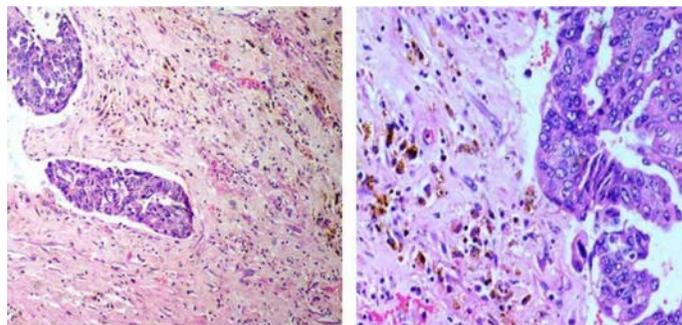
subjected for Ethical Approval from the Institutional Ethical Committee and clearance was obtained before the start of the study. Statistical analysis was done using IBM SPSS statistics 17 (Chicago, USA). Various tumor characteristics were correlated with the morphological features and the other clinico-pathologic data using Chi-square value (χ^2), paired t-test and Fischer’s test. $p < 0.05$ was considered to be statistically significant.

RESULTS

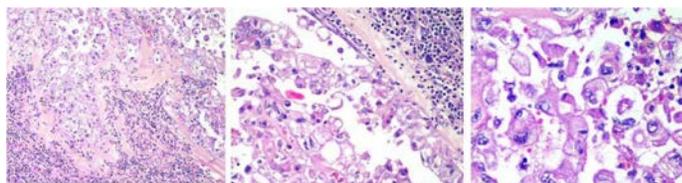
A total of hundred surgical specimens were evaluated out of which 20 cases were reported in patients below 40 years while 80 specimens were from cases above 40 years of age. (Table 1) Infiltrating Ductal Carcinoma-Not otherwise specified (IDC-NOS) (Figures 1a, b and 2a, b) was found to be the most common variant of breast carcinoma in both the younger and the elderly age groups followed by the invasive lobular carcinoma and mucinous carcinoma in the younger and invasive lobular carcinoma and mucinous carcinoma and papillary carcinoma in



Figures 1a, 1b: Tumor cells showing areas of fibrosis and calcification (H&E,100x,200x);



Figures 2a, 2b: Tumor cells showing hemosiderin laden macrophages along with areas of fibrosis (H&E,100x,200x);



Figures 3a- 3b-3c: Lymph nodal tissue showing tumor cells with areas of fibrosis and hyalinization (H&E,100x,200x,400x).

Table 1: Tumor characteristics in breast carcinoma cases reported in the 2 age groups.

Tumor Characteristics	<40 years	>40 years	p-value
n (No. of cases)	20	80	
Histological Type			
Infiltrating Ductal carcinoma	17	69	$p > 0.05$
Lobular carcinoma	2	6	
Papillary carcinoma	0	2	
Mucinous carcinoma	1	2	
Neuro-endocrine carcinoma	0	1	
Tumor size			
T1	2	4	
T2	9	51	$p < 0.017^*$
T3	9	23	
T4	0	2	
Nodal status			
N0	8	41	
N1	7	24	$p < 0.042^*$
N2	3	10	
N3	2	5	
TNM Staging			
Stage 1	2	4	
Stage 2	12	55	$p < 0.006^*$
Stage 3	6	20	
Stage 4	0	1	
Immuno-histochemistry			
ER/PR Positive, Her2 Negative	3	14	
ER/PR Positive, Her2 Positive	4	21	
ER/PR Negative, Her2 Negative	8	15	$p < 0.043^*$
ER/PR Negative, Her2 Positive	2	14	
Not done	3	16	

$p < 0.05^*$ Statistically Significant

the elderly age groups. (Table 1) Also, 9 cases each were reported for tumor size staging T2 and T3 in case of the younger while 51 for tumor size staging T2 and 23 for tumor size staging T3 were reported in the elderly age groups making tumor size staging T2 to be the commonest in the elderly age groups as against tumor size staging T2 and T3 which were reported with equal prevalence in the younger age groups with the results being statistically significant in this regard ($p = 0.017$). (Table 1) Furthermore, younger patients had a greater percentage of lymph nodal involvement being node positive (Figure 3a-c) in the total number of cases reported as compared to the elderly age groups and in this case, too, the results were found to be statistically significant ($p = 0.042$). (Table 1) Also, stage II followed by stage III were the commonest stages reported in the younger and elderly age groups based on their prevalence as against stage I and IV as reported on histo-pathological examination ($p = 0.006$). (Table 1) On immuno-histochemistry of the sampled specimens, the findings revealed ER/PR Positivity while Her2 Negativity in 15% of the cases lesser than 40 years of age and 17.5% of the cases more than 40 years of age. On the contrary, ER/PR Positivity as well as Her2 Positivity was reported in 20% of the cases lesser than 40 years of age and 26.2% of the cases more than 40 years of age. Likewise, ER/PR Negativity with Her2 Negativity was reported in 40% of the cases lesser than 40 years of age and 18.7% of the cases more than 40 years of age as against ER/PR

Negativity and Her2 Positivity reported in 10% of the cases lesser than 40 years of age and 17.5% of the cases more than 40 years of age and the results were found to be statistically significant ($p < 0.043$). (Table 1) Table 2 compares the results obtained in the present study as against the similar studies conducted in the past analyzing the biological behavior and aggressiveness of the breast carcinoma cases reported in those studies.

DISCUSSION

Although breast carcinomas are recognized to occur more commonly in the post-menopausal age, they can occur in the relatively young age, too. In younger age groups, breast cancers, though, have a more aggressive behavior and poorer outcome in comparison to patients in the elderly age groups.⁹⁻¹¹ The incidence of breast cancers is less by 2 to 3% in the west as compared to the Indian population.¹² As per Mohanti *et al.*,⁷ in young Indian women, the incidence of breast cancers was found to be around 5.5% close to the incidence recorded in the study conducted by Das *et al.*⁸ which reported an incidence of 8%. The results of the present study showed a relative incidence of 20% of the cases reported in the younger age groups as per the data retrieved from the archival records of the hospital set-up. Clinically and histo-pathologically, breast cancers

in the young are different from that reported in the elderly age groups.¹³ In the present study, too, the average age at presentation was found to be 64.5 years based on the archival records of the hospital which was similar to the previously reported studies.¹⁴⁻¹⁷ The oldest patient reported was of 78 years of age in the present study as against the youngest patient being just 33 years of age. Lump in the breast was the most common presenting complaint (83%) followed by mastalgia (6%) similar to the common complaints reported in other studies. In addition, 9 cases each were reported for tumor size staging T2 and T3 in case of the younger while 51 for tumor size staging T2 and 23 for tumor size staging T3 were reported in the elderly age groups making tumor size staging T2 to be the commonest in the elderly age groups as against tumor size staging T2 and T3 which were reported with equal prevalence in the younger age groups with the results being statistically significant in this regard ($p = 0.017$). Also, younger patients had advanced stage of the disease with concomitant higher rate of lymph node positivity reported and greater number of lymph nodes involved in the malignant process in the younger age groups as compared to the elderly patients in the present study in close accordance with the similar studies conducted in the past which concluded more aggressive behavior and poorer outcomes in younger age groups in comparison to patients in the elderly age groups ($p = 0.042$).⁹⁻¹¹ On histo-pathological examination, stage II followed by stage III were

Table 2: Clinico-pathologic data correlated with tumor characteristics in breast carcinoma cases reported in the 2 age groups in the previous studies.

Studies	n (No. of cases)		Most common histological type of the tumor		Predominant tumor grade and TNM staging	
	<40 years	>40 years	<40 years	>40 years	<40 years	>40 years
Manilal <i>et al.</i> ⁶	100 (23.8%)	420 (72.2%)	IDC-NOS (87%)	IDC-NOS (81%)	T3 (43.1%) TNM Stage-III (54.8%)	T2 (41%) TNM Stage-II (47%)
Sidoni <i>et al.</i> ¹¹	50	50 (50 Randomly selected matched cases)	IDC-NOS (80%)	IDC-NOS (90%)	TNM Stage-III (58%)	TNM Stage-II (75%)
Zhang <i>et al.</i> ¹⁴	181 (37%)	488 (63%)	IDC-NOS (77.3%)	IDC-NOS (84.4%)	T2 (69.3%) TNM Stage-III (49.2%)	T2 (77.7%) TNM Stage-II (52.2%)
Thapa <i>et al.</i> ¹⁶	263 (27.9%)	681 (72.1%)	IDC-NOS (93.1%)	IDC-NOS (86%)	T3 (55.9%) TNM Stage-III (55.34%)	T2 (54.2%) TNM Stage-II (57.9%)
Thangjam <i>et al.</i> ¹⁸	160 (31%)	347 (68%)	IDC-NOS (85.6%)	IDC-NOS (83.5%)	T3 (58.13%) TNM Stage-III (55.34%)	T2 (69.45%) TNM Stage-II (64%)
Present study	20 (20%)	80 (80%)	IDC-NOS (85%)	IDC-NOS (86.2%)	T2/T3 (45%) TNM Stage-II (60%) Stage-III (30%)	T2 (63.7%) T3 (28.7%) TNM Stage-II (68.7%) Stage-III (25%)

IDC-NOS: Infiltrating Ductal Carcinoma-Not otherwise specified

the commonest stages reported in the younger and elderly age groups as against stage I and IV based on their prevalence ($p=0.006$) in accordance with the findings of the study conducted by Zhang *et al.*¹⁴ which reported stage II to be the predominant stage in both the younger and elderly age groups. Similar studies conducted by Manilal *et al.*,⁶ Sidoni *et al.*,¹¹ Thapa *et al.*,¹⁶ and Thangjam *et al.*,¹⁸ though, found stage III to be the predominant stage reported in the younger women (<40 years) as against stage II which was the most common stage reported in the elderly age groups (> 40 years). As per Colleoni *et al.*,¹⁹ more aggressive behavior of the disease was seen in 48% of the young patients. Again, Infiltrating Ductal Carcinoma-not otherwise specified (IDC-NOS) was found to be the most common variant of breast carcinoma in both the younger and the elderly age groups in the present study followed by the invasive lobular carcinoma and mucinous carcinoma in the younger and invasive lobular carcinoma and mucinous carcinoma and papillary carcinoma in the elderly age groups in agreement with the results of most of the studies conducted previously wherein IDC-NOS has been the most common histological type of breast carcinoma in both the younger and the elderly age groups.^{9-11,13-18} Likewise, the results of the present study revealed a more aggressive and advanced stages of breast carcinomas cases reported in the younger age groups as reported on immuno-histochemistry. Breast cancers with estrogen receptors are referred to as ER-positive (or, ER+) while those with progesterone receptors, PR-positive (or, PR+). Breast cancers which have a significant number of receptors for either estrogen or, progesterone are considered hormone-receptor positive and are much more likely to respond to hormone therapy than cancers which are ER/PR-negative. Likewise, breast cancers which have high levels of a growth-promoting protein called HER2/neu, are called HER2-positive. HER2 positive cancers are more aggressive than HER2 negative cancers. The number of cases with triple negative breast carcinomas was found to be more in the younger age groups in the present study compared to the elderly age groups (40% vs. 18.7%) ($p<0.043$), a finding which was in agreement with most of the previous studies which reported triple negative breast carcinoma cases and high grades of tumor with lymph nodal involvement and poorer prognosis to be commonly seen in association with patients in the younger age groups.²⁰⁻²³ Another important finding of the present study was that almost half of the breast carcinoma cases reported in the younger age groups were found to be ER/PR Negative (8 of the ER/PR Negative as well as Her2 Negative cases and 2 of the ER/PR Negative and Her2 Positive cases) and thus, they were not the potential candidates for hormone therapy as was the case with the elderly age groups wherein most of the cases were found to be ER/PR-positive and thus, more responsive to hormone therapy.

CONCLUSION

To conclude, breast cancers diagnosed in younger age groups present with an aggressive behavior and poorer outcome in comparison to patients in the elderly age groups. Also, such cancers often tend to present with advanced stages of the disease process and high grades of tumor with lymph nodal involvement and metastasis at the time they are first diagnosed conferring an inferior prognosis. This illustrates the need for more clinical trials to be conducted on younger patients with breast cancers with an aim to improve the overall outcome in this age group. Breast cancer awareness and screening programs and easy access to health care delivery systems may, also, help to increase the awareness and detect breast cancers in their early stages. Thus, women in this age group must be educated for regular self examination and early medical attention on discovery of any breast lump that is persistent for more than a certain duration. Also, clinical breast examination at health care delivery systems during routine check-ups should be encouraged to facilitate an early intervention, if at all needed.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

IDC-NOS: Infiltrating Ductal Carcinoma-Not otherwise specified; **TNM staging:** Tumor (T), nodes (N), and metastases (M) staging; **ER Positivity or, ER-positive (ER+)-** Estrogen receptor positive; **PR Positivity or, PR-positive (PR+)-** Progesterone receptor positive; **HER2/neu Positivity-** Growth-promoting protein, HER2/neu-positive; **H&E:** Hematoxylin and Eosin.

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