Original Research Article

Study to evaluate the clinicopathological characteristics and prognostic factors in patients of breast carcinoma below 35 years of age (a study of 200 cases)

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Abstract

Introduction: Breast cancer is one of the most common malignancies among women in most developed and developing regions of the world. In India, breast cancer is the second most common cancer (after cervical cancer). Breast cancer at young age has been reported to have a more aggressive behavior and unfavorable prognosis compared to the older patients. **Aims and Objectives:** To evaluate prognosis through pathological tumour size, histological grade, mitotic index, lymph node status, distant metastasis and oestrogen & progesterone receptor positivity in young patients ≤ 35 years. **Material and Methods:** This prospective study was carried out for a period of three years from June 2015 to May 2018. Total of 200 cases of breast carcinoma were studied, out of them patients with ≤35 years were considered as case group and above 35 years of age as control group. **Results:** Total of 200 cases of breast carcinoma was reported in various age groups in histopathology. Total cases in age group ≤35 years were 28 out of total 200 cases. In age group ≤35 years out of 28 cases, 09 cases showed positive family history, 22 cases showed lymph node metastasis, most common stage of breast carcinoma was stage III, most common histological grade was Grade III and 15 cases were negative for markers ER/PR. **Conclusion:** Breast cancer is uncommon in young women but it co-relates with a less favorable prognosis. Tumors in younger patients had higher co-morbidity and better screening procedures should be used even in females younger than 35 years of age.

Keywords: Breast carcinoma, Bloom Richardson grading, Er/Pr, young female

Introduction

Breast cancer is one of the most common malignancies among women in most developed and developing regions of the world. In India, breast cancer is the second most common cancer (after cervical cancer) in female. Breast cancer accounts for 22.2% of all new cancer diagnosis and 17.2% of all cancer deaths among women in India [1]. Breast cancer at young age has been reported to have a more aggressive behavior and unfavorable prognosis compared to the older patients. In breast cancer, young refers to women below 35 years of age [2, 3]. The value of cytological and histological grading of breast carcinoma is well established [4, 5]. The objective of this study is to evaluate the association of clinico-pathological characteristics of breast carcinoma in females below 35 years and to determine the prognostic factors for breast cancer.

Aims and Objectives

The objective of this study is to evaluate the association of clinico-pathological characteristics of breast carcinoma in females below 35 years and to determine the prognostic factors for breast cancer.

Material and Methods

Type of study: Prospective study was carried out for a period of three years from June 2015 to May 2018.

No of cases studied: Total of 200 cases of breast carcinoma were studied, out of them patients with ≤35 years were considered as case group and above 35 years of age as control group.

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Sample collection: All surgical modified radical mastectomy specimens labeled as Carcinoma/malignant were considered as samples.

Exclusion criteria included

a) The patients who were diagnosed as in situ cases.

b) Patients who were diagnosed as breast carcinoma on fine needle aspiration cytology, but were lost to follow up.

c) Male breast cancer.

Statistical Method: Sensitivity and specificity was used to determine the prognosis in breast carcinoma.

Scoring System: Histopathology sections were studied for typing of breast carcinoma and were graded according to Modified Bloom Richardson grading system and staged according to the TNM staging [6].

Elston and Ellis modified Bloom-Richardson grading system [6].

Feature	Score 1	Score 2	Score 3
1) Tubule Formation	>75%	10-75%	<10%
2) Nuclear Pleomorphism	Small nuclei with regular outline, uniform chromatin, minimal variation in nuclear size.	Nuclei larger than normal open vesicular chromatin, moderate variation in size and shape.	Large pleomorphic hyper chromaticnuclei, prominent or multiple nucleoli, coarse clumped chromatin
3) Mitoses per10 hpf	0 – 5	6 – 10	>/=11

Histological grade:

Grade I – Score 3-5well differentiated;

Grade II – Score 6-7moderately differentiated;

Grade III – Score 8-9poorly differentiated.

Result

A prospective study of cases diagnosed as carcinoma of breast on histopathology was carried out at Department of pathology, in our tertiary care center. This study was carried out during period of June 2015 to May 2018. During this period 200 cases of breast carcinoma were reported in various age groups in histopathology.

Peak incidence of breast carcinoma cases was seen in 46-55 years age group, 57 cases out of total 200. Mean age of presentation was 51.2 years. Minimum age recorded was 25 years and maximum was 92 years.Total cases noted in age group ≤35 years were 28(14%) out of total 200 cases (100%).

In age group ≤35 years, 09 (32.14%) cases showed positive family history out of 28 cases (100%). In age group > 35 years 15 (8.7%) out of 172(100%) had positive family history.

In age group ≤35 years the most common tumor size observed was 2 to 5 cm in 17 (60.98%) cases followed by <2 cm in 6 (21.95%) cases out of total 28 (100%) cases while in age group >35 years most common tumor size observed was 5 to 10 cm in 72 (41.86%) cases followed by 2 to 5 cm in 67 (38.76%) out of total 172 (100%) cases seen in this age group.

In age group ≤35 years, 22(78.57%) cases out of 28 casesinvolved lymph nodes and in age group >35 years cases 102(59.30 %) out of 172 cases involved lymph nodes.

Overall most common histological subtype observed was Invasive ductal carcinoma (NOS) in 165(82.35%) out of 200(100%). In age group ≤35 years 24(85.36%) out of 28(100%) were IDC (NOS) type. And in >35 years age group Invasive ductal carcinoma was most common in 141(81.97%) of cases.

Overall TNM stage II was found to be the most common stage 96(48%) out of 200(100%) followed by stage III in 70(35%) cases. In age group ≤35 years stage III was found common 16(56.10%) out of 28 cases followed by stage II in 08(29.27%) cases. TNM stage III was more common in age group ≤35 years and comparatively stage II was more common in age group >35 years.

Table-I: **Comparison table showing TNM stages in patients ≤35 years and >35 years (n=200).**

TNM staging	I	II	III	IV	Total
Age ≤35 years	03 (9.75%)	08 (29.27%)	16 (56.10%)	01 (4.88%)	28 (100%)
Age>35 years	25 (14.7%)	88 (51.16%)	54 (31.01%)	5 (3.10%)	172 (100%)
Total	28 (16%)	96 (48%)	70 (35%)	06 (3%)	200 (100%)

In age group ≤35 years the most common histological grade (using Elston and Ellis proposed modified version of Bloom and Richardson's method) observed was grade III in 16 (58.54%) cases followed by grade II in 10(34.15%) casesout of total 28(100%) cases while in age group >35 years most common histological grade observed was grade IIin 87(50.39%) cases followed by grade III in 58(34.11%) out of total 172 (100%) cases seen in this age group. Higher histological grades were common in age group ≤35 years.

Table-II: Comparison table showing histological grading in cases ≤35 years and > 35 years (n =200).

Histological grade	No. of cases (≤35 years)	No. of cases (>35 years)	Total
Grade I	02(07.32%)	27(15.50%)	29
Grade II	10(34.15%)	87(50.39%)	97
Grade III	16(58.54%)	58(34.11%)	74
Total	28(100%)	172(100%)	200

The study of IHC markers (ER & PR) showed that in age group ≤35 years a larger proportion of cases 15(53.65%) were negative for both markers & 11(39.02%) cases were positive for both markers whereas in age group >35 years 41(24.03%) were negative and 118(68.22%) were positive for ER/PR positive. A higher ER/PR negativity was recorded in age group ≤35years

Table-III: **Comparison Of Immunohistochemical Markers Estrogen (ER) and progesterone (PgR) receptor positivity in cases≤35 years and > 35 years.**

IHC marker	No. of cases (≤35 years)	No. of cases (>35 years)
ER+ve/PgR+ve	11(39.02%)	118(68.22%)
ER+ve/PgR-ve	01(04.88%)	09(05.42%)
ER-ve/PgR+ve	01(02.44%)	04(02.33%)
ER-ve/PgR-ve	15(53.65%)	41(24.03%)
Total	28(100%)	172(100%)

Discussion

Breast cancer arising in young women is correlated with inferior survival and higher incidence of negative clinico-pathological features. The biology driving this aggressive disease has yet to be defined [7].

In the present study we investigated the clinic-pathological characteristics and prognostic factors in young patients with breast cancer in comparison to older patients.

Various studies have been carried out in this respect in the past to study the prognostic factors and their role in young age group. Present study is a prospective study which was carried out for a period of three years from June 2015 to May 2018. The observations of the present study and their comparison with other studies are discussed in following paragraphs:

In present study, 14% cases of breast carcinoma out of 200 total cases were present in the age group ≤35 years. This is comparable to Colleoni et al[9], Han et al[13] and Wei et al[17] who studied the same age group but is not comparable to other studies [8, 10-12, 14 -16] where the percentage of cases in young patients (≤35 years) were less.

This discrepancy was present because most of the studied were carried out in early part of 1990's and the awareness was less among the population regarding breast carcinoma presentation in early age group. Also large control groups were considered as compared to present study.

In present study, 32.14% of patients in age group ≤35 years had positive family history of breast carcinoma which is comparable to Guerra et al[12] who studied age group <35 years but less when compared with other studies [11,13,14,17]. Positive family history is a significant risk factor in age group ≤40 years which carries worse prognosis.

In present study, in the age group ≤35 years maximum cases (60.98%) had tumors size of 2 to 5 cm followed by 21.95% having tumors size less than 2 cm. Therefore, larger percentage of the breast carcinoma observed in this age group had comparatively smaller size of tumors that is 5 cms or less which was similar to all other studies [8, 9, 16, 17].

In present study, 78.57% cases in age group ≤35 years had a positive lymph node status which was comparable to studies done by Colleoni et al [9] and Wei et al[17] but more than other Studies [8,13,16].

In present study, the most common histological subtype observed was Invasive ductal carcinoma (Nothing otherwise specified) seen in 85.36% of the cases in age group ≤35 years comparable with others [11, 13, 16] but more than study of Collias et al [8]

In present study, TNM stage III was the most common stage observed in age group ≤35 years, seen in 56.10% of the cases in this age group followed by stage II seen in 29.27% cases.

These results were comparable to study results of and Wei et al [17] and Bal et al (2008) [14] but Han et al (2004) [13] observed stage II as the most common in their studies.

Inspite of smaller tumour size, higher proportion of patients have been reported with a higher TNM STAGE (stage III) as TNM staging takes into account lymph node status and metastasis.

Table-IV: Comparison table showing TNM staging of cases of breast carcinoma in various studies

STUDY	Age group	Total no. of cases	TNM staging			
			I	II	III	IV
Han et al (2004)[13]	<35 years	256	99 (38.7%)	128 (50.4%)	28(10.9%)	
Bal et al (2008)[14]	<35 years	-	19.7%	36.9%	37.7%	5.7%
Wei et al (2014)[17]	≤35 years	283	23 (10.4%)	84 (38%)	114 (51.6%)	-
Present study	**≤35 years**	**28**	**03 (9.75%)**	**08 (29.27%)**	**16 (56.10%)**	**01 (4.88%)**

In present study, grade III (calculated using Elston and Ellis [6] proposed modified version of Bloom and Richardson's method) was found to be the most common grade in age group ≤35 years seen in 58.54% cases of that age group followed by grade II seen in 34.15% cases.

This result was comparable to other studies [8, 9, 11] in which similar results were obtained but Han et al (2004)[13], Wei et al[16] and Wei et al[17] observed that grade II was most common in their studies. Major proportion of cases ≤35 years had a higher tumor grade which is associated with aggressive course and poor prognosis

Table-V: Comparison table showing histological grades observed in cases of breast carcinoma in various studies

Study	Age group	Total no. of cases	I	II	III
Kollias et al (1996)[8]	<35 years	111	7 (6%)	20 (18%)	84 (76%)
Colleoni et al (2001)[9]	<35 years	134	8.2%	29.9%	61.9%
Jimori et al (2002)[11]	<35 years	107	2 (3%)	22 (20%)	83 (77%)
Han et al (2004)[13]	<35 years	256	78 (58.6%)		55 (41.4%)
Wei et al (2013)[16]	<35 years	118	6 (5.1%)	77 (65.3%)	16 (13.6%)
Wei et al (2014) [17]	≤35 years	283	8 (6.2%)	73 (56.6%)	48 (37.2%)
Present study	**≤35 years**	**28**	**02(07.32%)**	**10(34.15%)**	**16(58.54%)**

In present study, 57.1% cases in age group ≤35 years were ER negative which was comparable to results obtained by Han et al[13] & Wei et al[16] but others [11,17] observed more positivity as comparedto present study. In present study, 57.14% cases in age group ≤35 years were PR negative which was comparable to results obtained by Han et al[13] & Wei et al[16] More percentage of younger patients of breast carcinoma had ER/PR –vetumours which are a bad prognostic factor.

Table-VI (A): Comparison table showing ER status in cases of breast carcinoma in various studies.

Study	Age Group	Total no. of cases	ER+ve	ER-ve
Jimori et al (2002)[11]	<35 years	113	20%	80%
Han et al (2004)[13]	<35 years	256	97 (47.1%)	109 (52.9%)
Wei et al (2013) [16]	<35 years	118	47 (39.8%)	71 (60.2%)
Wei et al(2014)[17]	≤35 years	283	135 (57.2%)	101 (42.8)
Present study	**≤35 years**	**28**	**12 (42.8%)**	**16 (57.1%)**

Table-VI (B): Comparison table showing PR status in cases of breast carcinoma in various studies.

STUDY	Age group	Total no. of cases	PR+ve	PR-ve
Han et al (2004)[13]	<35 years	256	73 (36.7%)	126 (63.3%)
Wei et al (2013)[16]	<35 years	118	46 (39%)	72 (61%)
Present study	**≤35 years**	**28**	**12 (42.85%)**	**16 (57.14%)**

Conclusion

The Present study concludes the following points:

- Breast cancer is uncommon in young women but it co-relates with a less favourable prognosis.
- Breast cancer in females less than 35 years of age have smaller tumor size but they have a higher tumor grade with more incidence of metastasis to lymph node. Those tumors are also ER/PR negative tumors. Hence breast carcinoma in younger age group has poorer prognosis.
- Metastasis along with Er/Pr status are good prognostic markers for assessing breast carcinoma
- A better prognostic stratification of patients is important so that patients can receive treatment at an earlier stage of the diagnosis and to avoid unnecessary risk to those patients who do not need additional treatment.
- However there is more morbidity in young patients which can partly be explained by young women often being diagnosed at advanced stages and unfavourable tumor characteristics more often being present.
- Study recommends that women at high risk because of her family history, early age of menarche, multiparity, environmental exposure etc shall start regular screening mammograms even before age of 35 years

What this study adds to our knowledge? The mass in breast at younger age group should be thoroughly examined and proper follow up of such cases should be carried out as incidence of breast carcinoma in younger age group seems to be on the rise. It was found to be 14% in present study. All breast masses should be considered malignant unless proved otherwise.

Findings: Nil; **Conflict of Interest**: None initiated
Permission from IRB: Yes

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