Section: General Surgery

Original Research Article

5-YEAR SURVIVAL ANALYSIS IN BREAST CARCINOMA AMONG YOUNG WOMEN (≤ 40 YEARS) WITH RESPECT TO ESTROGEN AND PROGESTERONE RECEPTOR STATUS: A SINGLE CENTRE EXPERIENCE

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Abstract

Background: Breast cancer (BC) in young women is uncommon and accounts for 4-5% of breast cancer in the West. There are unexplored issues for BC in this particular group in India. **Aim:** To study the 5-year survival pattern in young women (≤ 40years) with early and locally advanced breast cancer who were operated in a tertiary care centre in Kerala, India and to compare the differences in survival with respect to estrogen[ER] and progesterone receptor [PR] status in these patients. **Materials and Methods:**A longitudinal study was conducted in 42 female breast cancer patients aged ≤ 40 years with histologically proven invasive ductal carcinoma who had undergone modified radical mastectomy between 1st July 2008 and 31st July 2009. Overall survival was calculated in months, either from the date of diagnosis or from the date of surgery up till 31 December, 2013. The Kaplan-Meier method was used to estimate the overall survival and survival with respect to ER and PR status. **Results:** Overall survival rate at the end of 5 years was 66.7%. A majority of the patients were ER-positive (59.5%) and PR -positive (64.3%). **Conclusion:** Women under 40 years of age diagnosed with breast cancer have a poor prognosis, and this association is strongest among young women with estrogen and progesterone receptor- negative breast cancer.

INTRODUCTION

The burden of breast cancer (BC) is increasing, and it stands as the most common malignancy among women in India.[1] BC in young women is uncommon, accounting for 4%-5% of BC cases in the West.[2] Detecting BC in young women is vital because tumour behaviour is typically more aggressive, and associated with higher mortality compared to their older counterparts.[3,4] There are unexplored issues regarding BC in this specific group in India. The objectives of this study were to evaluate the 5-year survival pattern in young women (≤40 years) with early and locally advanced BC who underwent surgery at a tertiary care centre in Kerala, India, and to compare survival differences with respect to estrogen receptor (ER) and progesterone receptor (PR) status in these patients.

MATERIALS AND METHODS

A retrospective study was conducted among 42 female BC patients aged ≤40 years with histologically proven invasive ductal carcinoma who had undergone modified radical mastectomy (MRM) between July 1, 2008, and July 31, 2009 in the Department of General Surgery. During the study, 189 patients were undergone MRM for invasive ductal carcinoma. The study was approved by the institutional ethics committee. Patients with a secondary tumour of the breast and patients with metastatic presentation were excluded. All data including age, menopausal status, and pathological characteristics (grade [modified Bloom Richardson grade], stage of the disease [American Joint Committee on Cancer], tumour size, and axillary nodal status) were recorded. All patients underwent standard treatment modalities including neoadjuvant and/or adjuvant chemotherapy, radiotherapy, chemoradiation, hormone therapy, and MRM, depending on the stage of presentation and hormone receptor status. ER and PR status were assessed by

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immunohistochemistry [Figure 1] and specimens in which more than 10% of the tumour nuclei stained positive were reported hormonereceptor-positive. ER status was determined using the Bio Genex monoclonal mouse IgG (Clone 1D5) (Bio Genex, USA), and PR status was determined using BioGenex monoclonal mouse IgG (Clone 1A6) (BioGenex, USA). Antigen retrieval was done using the BioGenex EZ Retriever system (BioGenex, USA). Overall survival (OS) was calculated in months, either from the date of diagnosis or from the date of surgery up till December 31, 2013. Statistical analysis was performed with SPSS (IBM SPSS Statistics for Windows, version 21.0. IBM Corporation, Armonk, NY, USA, 2012). Pathologic variables were compared using the Chi square test. Logistic regression analysis was carried out to assess the independent association between different variables and survival. The Kaplan-Meier method was used to estimate the OS and survival with respect to ER and PR status. $P < 0.05$ was considered statistically significant. Outcome-based on hormone receptor status was compared between patients with age ≤40 and those with age >40 years.

RESULTS

ut of the 189 patients who underwent MRM, only 42 (22%) were ≤40 years. The mean age of the study population was 35 (SD-3.49) years. General characteristics of the study population are presented in Table 1. Fifty-four per cent had tumour sizes between 2-5 cm, and only 7% had tumour sizes 3 lymph nodes. Twenty-six (61.9%) patients had grade 2 disease. TNM stage 2 (59.5%) was the most common, followed by stage 3 (33.3%). Fourteen patients (33.3%) received neoadjuvant chemotherapy, and 38 patients (90.5%) received postoperative radiotherapy. Twenty-eight patients (66.7%) received hormonal therapy. A majority of the patients were ER-positive (59.5%) and PR-positive (64.3%). The mean follow-up time was 44.9 (SD 15.31) months. The overall survival (OS) rate at the end of 5 years was 66.7% [Figure 2]. The patterns of ER and PR expression and their relation to outcomes are shown in Figures 3 and 4, respectively. Among ER-negative patients, only 7 survived (41.2%), and in PR-negative patients, only 4 survived (28.6%). The survival rate in the >40 years group was 72.8% at 5 years. Kaplan-Meier survival curves for ER and PR status are depicted in Figures 5 and 6. While age, nodal status, ER, and PR status showed associations with survival, only ER ($p = 0.024$) and PR ($p = 0.41$) status were found to have an independent association with breast cancer (BC) survival [Tables 2 and 3]. The distribution of outcomes based on age group and hormone receptor status is presented in Table 4.

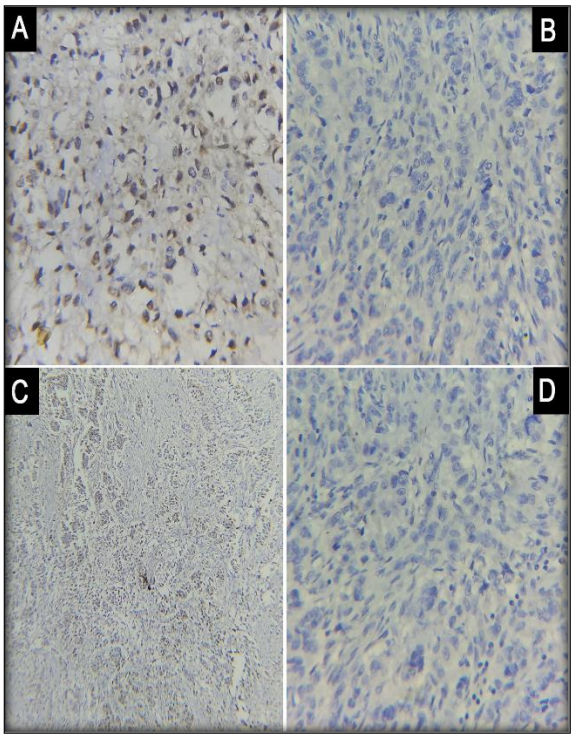

Figure 1: Immune Histochemistry Images for Estrogen and progesterone receptors

[A-Estrogen Receptor positive, B-Estrogen Receptor Negative, C- Progesterone Receptor positive, D-Progesterone Receptor negative]

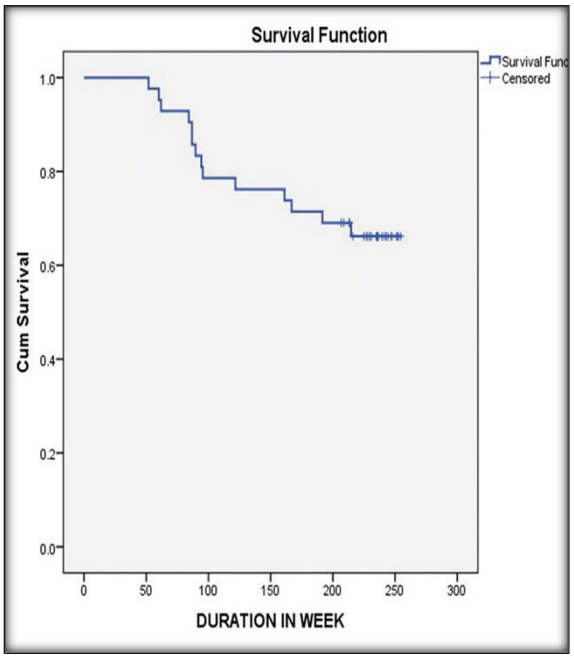

Figure 2: Kaplan-Meier Curve for overall survival

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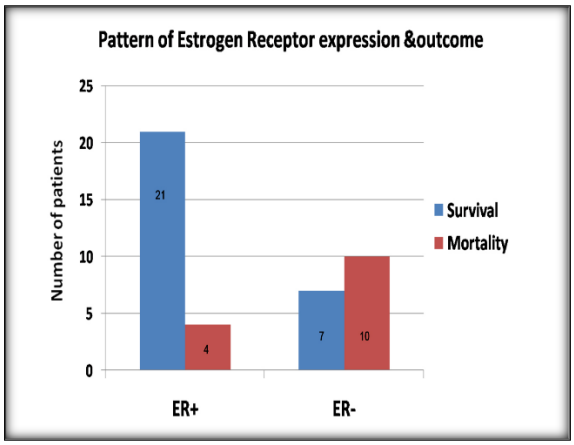

Figure 3: Pattern of estrogen receptor (ER) expression and outcome

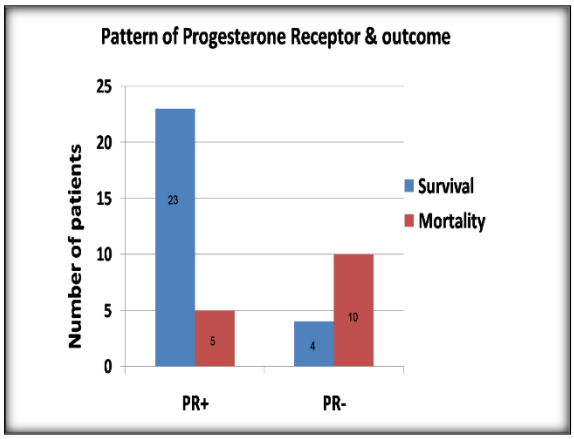

Figure 4: Pattern of progesterone receptor (PR) expression and outcome

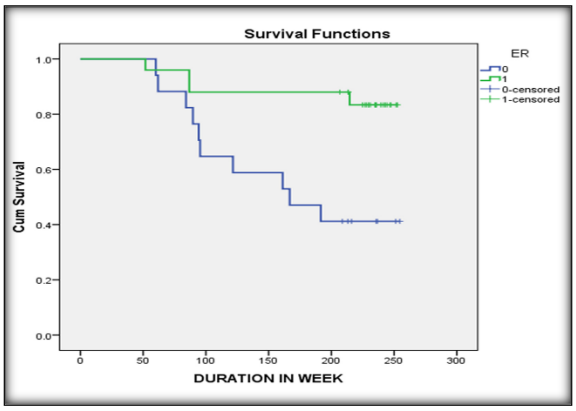

Figure 5: Kaplan-Meier survival curve with respect to estrogen receptor status

[p =0.004 - Log Rank test] [ER- estrogen receptor, 0-Negative, 1-Positive]]

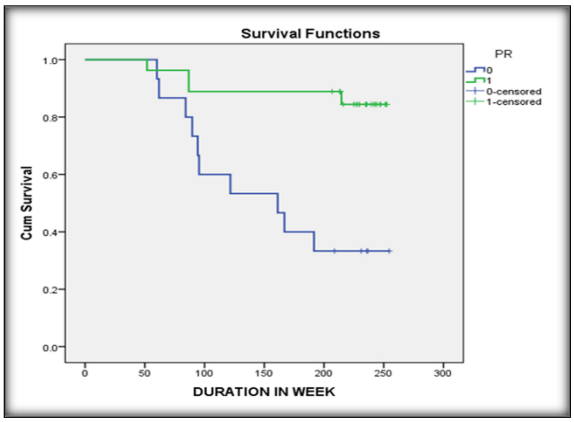

Figure 6: Kaplan-Meier Curve for survival with respect to progesterone receptor status

[p =0.0001 Log Rank test [PR- progesterone receptor, 0-Negative, 1-Positive]

Table 1: General characteristics of the study population

Variable	N	%
Grade		
1	2	4.8
2	26	61.9
3	14	33.3
Tumor size		
<2cm	3	7.1
2-5cm	23	54.8
>5cm	16	38.1
Nodal status		
LN Negative	13	31
1-3 LNs	11	26.2
>3LNs	18	42.9
Stage		
1	3	7.1
2	25	59.5
3	14	33.3
ER status		
ER+	25	59.5
ER-	17	40.5
PR status		
PR+	27	64.3
PR-	15	35.7
Neoadjuvant chemotherapy		
Yes	14	33.3
No	28	66.7

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Radiotherapy		
Yes	38	90.5
No	4	9.5
Tamoxifen		
Yes	28	66.7
No	14	33.3
Outcome		
Survival	28	66.7
Mortality	14	33.3

[LN-Lymph node, ER- Estrogen receptor, PR- Progesterone receptor]

Table 2. Association of different variables to survival of breast cancer among study population (Univariate analysis)

Pathological Variables and other factors	p- value
Age	0.04
Tumor size	0.143
Tumor grade	0.439
Stage	0.072
Nodal status	0.027
Estrogen receptor status	0.004
Progesterone receptor status	0.001
Neoadjuvant chemotherapy	0.541

Table 3: Multinomial Logistic Regression analysis

		Adjusted RR	95% CI for adjusted RR	
Variable			Lower	Upper
Axillary nodal status	0.96	0.41	0.055	2.571
ER status	0.024	5.367	1.12	14.949
PR status	0.041	2.859	1.16	3.03

[RR - risk ratio, CI-Confidence interval ER- Estrogen receptor, PR- Progesterone receptor, Cox-Snell R2-36]

Table 4: Distribution of outcome based on age group and hormone receptor status

Age group	≤40 (N=42)		>40 (N=147)	
	Survival (N=28; 66.7%)	Mortality (N=14; 33.3%)	Survival (N=107; 72.8%)	Mortality (N=40; 27.2%)
ER- positive	21	4	67	15
ER- negative	7	10	40	25
PR- positive	23	5	70	16
PR- negative	4	10	37	24

[ER Estrogen receptor, PR Progesterone receptor, N-Number]

Table 5: Prognostic factors affecting OS in various studies of young female BC

Study	Year	Age	Factors affecting OS	
Present study		≤ 40	ER and PR status	Kerala
Gogia A et al.,2014,[10]	2000-2011	≤ 35	TNBC, Stage	India
Barso S et al., 2010,[12]	2000-2008	≤ 35	Size, grade, LVI,LN involvement	South Africa
Hartley M C et al.,2006,[14]	1998-2002	≤ 40	ER negativity and Stage	US
Mathew A et al.,2004,[6]	1990-93	≤ 40	LN involvement, Tumor size	Kerala
Gonzalez-Angulo A M et al.,2005,[15]	1990-2002	≤ 35	Grade, Family history of ovarian tumor, HR negativity, Grade	US
Abahssain H et al.,2010,[13]	2003-2007	≤ 35	Triple negative status	Morocco

[ER- Estrogen receptor, PR- Progesterone receptor, TNBC-Triple negative breast cancer, HR-Hormone receptor, LVI- Lympho vascular invasion]

DISCUSSION

BC in young women is known to be more aggressive, exhibiting potentially complex biological features.[4] This study aimed to evaluate the 5-year survival patterns in young women (≤40 years) with early and locally advanced BC who underwent surgery at a tertiary care centre in Kerala, India. Additionally, the study aimed to compare survival differences with respect to ER and PR status among these patients. Twenty-two per cent of the study population was 40 years or younger, aligning with findings from other studies in the Indian subcontinent.[5,6] In the United States, around ten thousand women aged < 40 years are diagnosed with invasive BC annually, constituting 5% of all women diagnosed with BC.[2] The Asian Breast Cancer Society reports a rate of 13%.[7] The higher rate of young BC in India may be partially attributed to inadequate access to healthcare for older patients in rural areas of the country.

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The 5-year overall survival (OS) rate at the end of 5 years was 66.7%, which surpasses the rate reported in a previous study in Kerala two decades ago and is comparable to the data from the US.[6,8] However, the 5- year survival rate of the current study was lower compared to that of all BC patients (71%) reported during the study period. [9] Among the study population, 59.5% were ER-positive, and 64.3% were PR-positive patients. Within the ER-positive group, the mortality rate was 16%, whereas in the ER-negative group, it was 58.8%. For PR-positive patients, the mortality rate was 17.9%, while in PR-negative patients; it was 71.4% [Figures 3 and 4].

A similar finding has been reported in several studies, associating hormone negativity with a shorter OS.[9,10] In a large genomic analysis of young breast cancer (BC) patients, Anders et al., reported 367 differentially expressed genes in tumours of young women compared to older patients.[11] Among various pathological variables in young BC patients, only age, nodal status, ER, and PR status emerged as significant prognostic factors for OS in univariate analysis. Notably, only ER and PR status showed a statistically significant independent association with OS [Tables 2 and 3]. Table 5 illustrates a comparison of prognostic factors affecting OS in various studies of young female BC. [6, 10, 12-15] Several extensive studies have reported that young age at diagnosis is an independent prognostic factor for survival and is associated with a high risk of recurrence.[11, 16]

CONCLUSION

Differences in risk factors and gene expression suggest that breast cancer in young women may represent a distinct entity. Women under 40 years of age diagnosed with BC have a poor prognosis, and this association is strongest among young women with ER and PR negative BC. Our data suggest that breast carcinoma in young patients may exhibit a worse prognosis, emphasizing the need for prospective studies in this population.

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