

Male Breast Cancer: An Experience from a Regional Cancer Centre, Tamil Nadu, India

SAKTHI USHA DEVI JEEVARAJAN¹, KUZHALMOZHI MANOHARAN², MUTHULAKSHMI VANNIAPPAN³, AJAY KUMAR ARUNACHALAM⁴, DORIAN HANNIEL TERRENCE SELVARAJ⁵

CC) BY-NC-ND

ABSTRACT

Introduction: Male breast cancer is rare and accounts for less than 1% of all breast cancers. The incidence continues to rise, and most of the existing literature on male breast cancer consists of retrospective studies. Multicentric and randomised studies are scarce, making it difficult to study the biology of the disease and effective therapeutic options.

Aim: To investigate the clinicopathologic characteristics and survival outcomes of male breast cancer.

Materials and Methods: This was a cohort study involving the retrospective collection of data from 39 male breast cancer patients, who were included for analysis from a total of 1,871 carcinoma breast cases between January 2018 and October 2022 (data obtained from the Hospital Based Cancer Registry of Government Arignar Anna Memorial Cancer Hospital and Research Institute, Karapettai, Kanchipuram, Tamil Nadu, India). Patient variables related to age, family history, pathological details (including tumour grade, Immunohistochemistry (IHC) and stage of the disease), treatment details and follow-up information were collected for the study. Statistical analysis for survival was performed using Statistical Package for the Social Sciences (SPSS) software version 26.0.

Results: The majority of patients (20 cases) belonged to the 41-60 years age group, with 10% of patients having a family history of cancer. Stage III was the most common stage of presentation, accounting for 15 (38.5%) cases. Luminal A (46.2%) was the most common molecular subtype, followed by Basal type (23.1%). The median Overall Survival (OS) was 46 months (95% CI: 31-40.5-51.5), and the median Disease-Free Survival (DFS) was 44 months (95% CI: 25.21-62.78). Patients with Luminal A subtype had the highest median OS.

Conclusion: Present study concluded that these patients experience an early onset of the disease, with most being hormone receptor positive and commonly presenting in a locally advanced stage. Patients in the Luminal A group have a good prognosis, and survival also depends on the stage of the disease. These groups of patients are unique and heterogeneous among various populations. Although there are many studies comparing male and female breast cancer, the biology of male breast cancer still needs to be studied in detail. There should be a comparison with female breast cancer in prospective randomised multicentric trials to yield therapeutic implications.

INTRODUCTION

The incidence of male breast cancer varies on a worldwide basis, but most studies report an incidence rate of less than 1% of all breast cancer cases [1]. Worldwide, the female-to-male incidence ratio is 122:1. The incidence of male breast cancer continues to rise, as shown by various previous literature [2]. The incidence of male breast cancer continues to rise, as shown by various previous literature [2]. The incidence of male breast cancer continues to rise, as shown by various previous literature [2]. The incidence of male breast cancer has increased by 40%, which exceeds that of women by 25%, according to Surveillance, Epidemiology, and End Results (SEER) data from 1975 to 2015 [3]. In Tamil Nadu, male breast cancer constitutes about 0.5% of all male cancers [4]. The lifetime cumulative risk (0-74 years; CR%) for male breast cancer in Tamil Nadu is 0.047 [4]. Increasing age is one of the important risk factors for male breast cancer. The age-specific rate in Tamil Nadu is highest in the 65-74 years age group (ASpR-2.4) [4].

Breast cancer in men is poorly understood and studied due to its low incidence, as many trials on breast cancer exclude men, and only a few prospective trials have been conducted to date. Treatment protocols for male breast cancer are extrapolated from studies conducted on female breast cancer, since no randomised trials of local therapy have been conducted. Most breast cancers in men are Estrogen and Progesterone Receptor (ER, PR) positive, and endocrine therapy is an important component of treatment [5]. The biology of the disease, the response to treatment, and the prognosis differ between men and women. The risk of death in men was 43% greater than that in women during the follow-up period [6]. In recent years, male breast cancer patients have had worse

Keywords: Chemotherapy, Oestrogen, Progesterone

survival outcomes compared to those of female patients [6]. Over the years, survival rates for both men and women have improved, but men have lagged behind women in terms of breast cancer outcomes [7].

The main objectives of this study were to determine the various demographic and clinicopathologic characteristics of male breast cancer and to analyse survival outcomes, as well as to contribute present study findings to the existing literature. The significant number of male breast cancer cases analysed in this study can aid in the formulation of treatment guidelines.

MATERIALS AND METHODS

This was a cohort study that analysed the data of patients diagnosed with male breast cancer from a Regional Cancer Centre in Tamil Nadu, India from January 2018 to October 2022 retrospectively (data taken from our cancer registry). Around 1,871 breast carcinoma cases were registered for treatment in our institute.

Inclusion criteria: Only males--39 patients irrespective of age, stage and treatment were included in the study.

Exclusion criteria: Those who had not undergone continuous treatment or follow-up were excluded from the study.

Male breast cancers that had been treated elsewhere previously and that were brought in for further management were also included in the study. Patient variables related to age, family history, pathological details, treatment details, and follow-up details were collected for analysis. IHC for ER, PR, Human Epidermal growth factor Receptor 2 (HER2) expression, and Ki-67% expression was performed according to standard ASCO (American Society of Clinical Oncology)/CAP (College of American Pathologists) guidelines [8,9].

Procedure for IHC: Initially, de-paraffinisation was performed on the wax block. Then, antigen retrieval was conducted using the appropriate retrieval buffer. Peroxidase blocking was incubated for 5 to 10 minutes. Next, primary and secondary antibodies were incubated along with the chromogen substrate. Haematoxylin staining was performed, and the block was dehydrated.

The ER and PR positivity were assessed based on the ALLRED scoring system [Table/Fig-1.2], which consists of two scores: Proportion of Nuclear Staining Score (0-5) and Intensity of Staining Score (0-3). The total score is obtained by summing both scores [8,9]. Any patient who scored three or more was considered positive [Table/Fig-3,4]. HER2 positivity is detected based on the percentage of membrane staining for HER2 in cancer cells [Table/ Fig-5,6]. All patients were discussed in a multidisciplinary team board, and all clinical characteristics-including grade, stage and

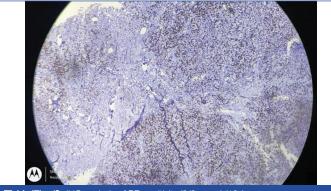
% of ER positive cells	Proportion score	Intensity of staining	Intensity score		
0	0	None	0		
<1	1	Weak	1		
1 to 10	2	Intermediate	2		
11 to 33	3	Strong	3		
34 to 66	4				
>/=67	5				
[Table/Fig-1]: Allred score.					

Allred score – proportion + intensity score	Final result
0/8	Negative
1/8 to 2/8	Negative
3/8 to 4/8	Weak positive
5/8 to 6/8	Moderate positive
7/8 to 8/8	Strong positive
Table / Fig. 01. Allword approximate representation	

[Table/Fig-2]: Allred score interpr



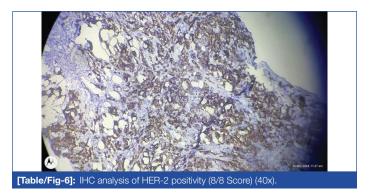
[Table/Fig-3]: IHC analysis of ER



[Table/Fig-4]: IHC analysis of PR positivity (8/8 score) (10x)

Staining pattern	Score	HER2 expression
No staining is observed / membrane staining is observed in <10% of tumour cells	0 +	Negative
A faintly perceptible membrane staining is detected in >10 % of tumour cells. The cells are only stained in part of their membrane.	1 +	Negative
A weak to moderate complete membrane staining is observed in >10% of cells	2 +	Weakly positive/ equivocal
A strong complete membrane staining is observed in > 30 % of tumour cells	3 +	Strongly positive

[Table/Fig-5]: HER-2 scoring system



IHC markers, along with the patient's performance status-were analysed to formulate treatment policies based on standard practice guidelines.

STATISTICAL ANALYSIS

The primary endpoints are median OS and DFS. The median follow-up period was 33 months. Subset survival analysis was also conducted for each stage and different molecular subtypes. Median OS and median DFS were calculated using the Kaplan-Meier method, and statistical analysis was performed using SPSS software version 26.0.

RESULTS

Socio-demographic characteristics: From 2018 to 2022, 39 male breast cancer patients were registered in our institute's cancer registry and included for analysis. The basic demographic details of all patients are listed in [Table/Fig-7]. The most commonly affected age group was between 41 and 60 years (n=20, 51.3%), followed by 61 to 80 years (n=14, 35.9%). Only three patients were less than 40 years old. Since many of our patients come from a rural population, most of them are unskilled labourers 26 (66.7%). Skilled labourers and professional workers account for 9 (23.1%) and 3 (7.7%), respectively. Left-side breast cancers 22 (56.4%) are more common than right-side breast cancers 17 (43.6%), which is purely incidental and insignificant. The laterality in breast cancer can affect the quality of functional work after surgery, especially if it affects the

Variable		
21-40	3 (7.7)	
41-60	20 (51.3)	
61-80	14 (35.9)	
>80	2 (5.1)	
Skilled labourer	9 (23.1)	
Unskilled labourer	26 (66.7)	
Professional	3 (7.7)	
Others	1 (2.6)	
Right	17 (43.6)	
Left	22 (56.4)	
Yes	4 (10.3)	
No	35 (89.7)	
	41-60 61-80 >80 Skilled labourer Unskilled labourer Professional Others Right Left Yes	

Table/Fig-71:

dominant hand. No patients had bilateral cancers. Only 4 (10.3%) patients had a family history of malignancies. Among the four patients, two had a family history of breast cancer, while two had a family history of stomach cancer. None of them underwent Genetic Mutation Analysis (NGS) to rule out germline mutations involving BRCA and other genes.

Clinicopathological Characteristics

The clinicopathological characteristics of the patients are illustrated in [Table/Fig-8]. The most common AJCC stage group among non metastatic breast cancer patients was stage IIIB 8 (20.5%), followed by stage IIA 7 (17.9%) and stage IIB 6 (15.4%). Overall, stage III is the most common stage of presentation 15 (38.5%). Upfront metastatic cases account for 10 (25.6%), among which T3N1M1 was the most common AJCC prognostic group. Ductal Carcinoma-No Special Type (NOS) was the most common histological type identified, comprising 35 (89.7%) of cases, followed by medullary carcinoma (three patients) and papillary carcinoma (one patient). No patients had lobular carcinoma. Eighteen patients (46.2%) had Grade 2 tumours, followed by Grade 3 (nine patients, 23.1%) and Grade 1 (six patients, 15.4%).

Variables	n (%)			
	Stage IA	T1N0M0	1 (2.6)	
	Stage IIA	T2N0M0	7 (17.9)	
	Stage IIB	T2N1M0	6 (15.4)	
	01 1114	T2N2M0	1 (2.6)	
	Stage IIIA	T3N1M0	3 (7.8)	
		T4bN0M0	2 (5.1)	
	Stage IIIB	T4bN1M0	3 (7.8)	
Clinical staging		T4bN2aM0	3 (7.7)	
	Stage IIIC	T4bN3cM0	3 (7.7)	
		T2N1M1	1 (2.6)	
		T3N1M1	4 (10.3)	
	Stage IV	T4bN1M1	2 (5.1)	
		T4bN2aM1	1 (2.6)	
		T4bN3cM1	2 (5.1)	
	Ductal carcinoma –	NOS type	35 (89.7)	
Histological type	Medullary carcinom	3 (7.7)		
	Papillary carcinoma	L	1 (2.6)	
	Grade 1		6 (15.4)	
Grade of tumour –	Grade 2	18 (46.2)		
Pathological	Grade 3		9 (23.1)	
	Not available/missir	6 (15.4)		
	ER positive		27 (69.2)	
	PR positive	22 (56.4)		
IHC	HER2 Positive	6 (15.4)		
	Ki 67	≤20%	17 (45.9)	
	N 07	>20%	20 (54)	
	Luminal A		18 (46.2)	
	Luminal B	8 (20.5)		
Molecular subtype	HER 2 enriched	2 (5.1)		
	Basal	9 (23.1)		
	Not available/missir	2 (5.1)		
[Table/Fig-8]: Clinico-pathologic characteristics of all patients.				

As previously mentioned, IHC was performed according to standard ASCO/CAP guidelines. Most of the patients were ER positive 27 (69.2%) and PR positive 22 (56.4%). Only 15.4% of patients had HER2 positivity. Molecular subtypes are defined as follows: Luminal A (ER-positive and/or PR-positive and HER2-negative), Luminal B (ER-positive and/or PR-positive and HER2-positive), HER2 type (ER-

negative and PR-negative and HER2-positive), and Basal type (ERnegative, PR-negative, and HER2-negative, also known as Triple Negative Breast Cancer). IHC was not available or was missing for two patients. Luminal A (18 patients, 46.2%) was the most common molecular subtype, followed by Basal type (nine patients, 23.2%). The Ki-67 proliferative marker was also included. Fifty-four percent of patients have high Ki-67 levels, with values greater than 20%. Ki-67 does not influence staging.

Surgery

A total of 26 patients underwent surgery. All patients underwent total mastectomy with axillary lymph node dissection. The clinical and pathological staging of all patients is compared in [Table/Fig-9]. It was found that among the patients with a pathological stage of pT1N0, 50% had a clinical stage of IA and IIA. Among those with a pathological stage of pT2N0, 62.5% had a clinical stage of IIA. Among those with pT2N1a, 50% had a clinical stage of IIB. Patients with pT2N2a had a clinical stage of IIIA and IIIC, respectively. The distribution of clinical and pathological stages was dissimilar, with a p-value of <0.05, indicating that clinical staging does not correlate with pathological staging.

Additionally, [Table/Fig-9] shows the pathological prognostic staging, which applies to patients with breast cancer who were treated with surgery as the initial treatment. Pathological prognostic stage does not apply to patients treated with systemic therapy or radiation prior to surgical resection (neoadjuvant therapy). After excluding patients who received neoadjuvant chemotherapy for pathological prognostic staging, authors found that 13 patients (68.4%) were down-staged when comparing clinical stage with pathological prognostic staging. Five patients (26.3%) had similar clinical and pathological prognostic stages, and only one patient (5.2%) was upstaged in the pathological prognostic stage [Table/Fig-9].

In present study, only seven patients received neo-adjuvant chemotherapy before surgery. Eight cycles of neo-adjuvant chemotherapy (four cycles of Adriamycin and cyclophosphamide followed by four cycles of paclitaxel±Trastuzumab) for all seven patients were administered. None of the patients achieved a complete pathological response. Other pathologic characteristics and details of adjuvant treatment are shown in [Table/Fig-10]. The average number of lymph nodes removed during axillary lymph node dissection was 13.77 ± 6.37 , and the average number of positive lymph nodes was 2.31 ± 3.49 . The mean lymph node density for histopathologically positive cases was 0.16. Lymphovascular invasion was present in 34.6% of patients. All patients who did not receive neo-adjuvant chemotherapy completed their adjuvant chemotherapy (73.1%, n=19). Post-mastectomy radiation was planned for 13 patients, but only nine patients completed the treatment.

Survival Analysis

Overall (OS) and Disease-Free Survival (DFS): The minimum follow-up period to calculate OS was six months. [Table/Fig-11] illustrates Kaplan-Meier curves showing OS and DFS for the entire cohort. The median OS was 46 months (95% CI 40.5-51.5), and the median DFS was 44 months (95% CI 25.21-62.78). OS and DFS were also calculated for non metastatic cases that underwent surgery. [Table/Fig-12] shows Kaplan-Meier curves for OS and DFS of patients who underwent surgery. The OS for those who underwent surgery was 46 months (95% CI 26.4-65.5), while the DFS for those who underwent surgery was 26 months (95% CI 0-54.7).

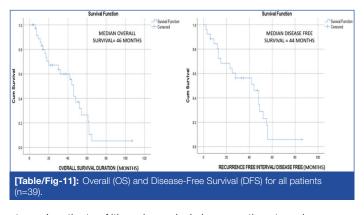
Stage-wise Overall Survival (OS): [Table/Fig-13] shows the survival curve for all stages. We had only one stage 1 case, who survived for 46 months. He is alive and on regular follow-up. The median OS for stage 2 was 48 months (95% CI 25.26-70.73), and the median OS for stage 3 was 42 months (95% CI 21.4-62.35). The mean survival for stage 4 patients was 30 months, as authors were unable to compute median survival due to the low number of

Sakthi Usha Devi Jeevarajan et al., Male Breast Cancer - Experience from a Regional Cancer Centre of Tamil Nadu, India

www.jcdr.net

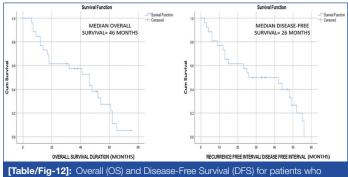
Clinical-TNM Staging	Clinical prognostic group	Neo-adjuvant therapy status	Pathological staging	Grade	ER Status	PR Status	HER2 Status	Pathological prognostic stage
T2N0M0	IIA	No	pT2N1a	Grade2	Positive	Negative	Positive	lb
T2N0M0	IIA	No	pT1N0	Grade 2	Negative	Negative	Negative	lla
T4bN2aM0	IIIB	Yes	pT3N1a	Grade 2	Negative	Negative	Negative	Not applicable
T4bN0M0	IIIB	No	pT2N0	Grade 2	Positive	Positive	Negative	la
T4bN3cM0	IIIC	Yes	pT2N2a	Grade 3	Negative	Negative	Negative	Not applicable
T2N1M0	IIB	No	pT2N1a	Grade 1	Positive	Positive	Negative	la
T4bN3cM0	IIIC	Yes	pT2N3a	Grade 2	Positive	Positive	Negative	Not applicable
T4bN1M0	IIIB	Yes	pT2N1a	Grade 2	Positive	Positive	Negative	Not applicable
T1N0M0	IA	No	pT1N0	Grade 1	Positive	Positive	Positive	la
T3N1M0	IIIA	No	pT3N1a	Grade 2	Positive	Positive	Negative	lb
T2N1M0	IIB	No	pT2N1a	Grade 2	Positive	Positive	Negative	lb
T4bN1M0	IIIB	Yes	pT4bN1a	Grade 3	Positive	Positive	Negative	Not applicable
T4bN3cM0	IIIC	Yes	pT3N3a	Grade 3	Positive	Positive	Negative	Not applicable
T2N1M0	IIB	No	pT2N1a	Grade 2	Positive	Positive	Positive	lb
T2N0M0	IIA	No	pT2N0	Grade 2	Negative	Negative	Negative	lla
T2N1M0	IIB	No	pT3N1a	Grade 2	Positive	Positive	Negative	lb
T2N1M0	IIB	No	pT4N1a	Grade 2	Negative	Negative	Negative	IIIc
T2N1M0	IIB	No	pT2N0	Grade 2	Negative	Negative	Negative	lla
T3N1M0	IIIA	Yes	pT2N1a	Grade 2	Positive	Positive	Negative	Not applicable
T2N0M0	IIA	No	pT2N0	Grade 3	Negative	Negative	Negative	lla
T3N1M0	IIIA	No	pT2N0	Grade 1	Negative	Negative	Positive	lla
T2N0M0	IIA	No	pT2N0	Grade 2	Positive	Negative	Negative	lia
T2N1M0	IIB	No	pT2N0	Grade 2	Negative	Negative	Negative	lla
T2N0M0	IIA	No	pT2N0	Grade 1	Positive	Positive	Negative	la
T2N2M0	IIIA	No	pT2N2a	Grade 3	Positive	Positive	Negative	llb
T4bN1M0	IIIB	No	pT4bN1a	Grade 2	Positive	Positive	Negative	Illa

Variable		n (%)/ M±SD	
Average no. of lymph nodes retrieved		13.77±6.37	
Average no. of lymph nodes positive		2.31±3.49	
LVSI Status	Positive	9 (34.6)	
	Negative	16 (61.5)	
	Not available	1 (3.8)	
Neo-adjuvant chemotherapy		7 (26.9)	
Adjuvant chemotherapy		19 (73.1)	
Adjuvant radiotherapy		9 (34.6)	
Adjuvant endocrine therapy		17 (65.3)	
[Table/Fig-10]: Other pathologic characteristics, neo-adjuvant and adjuvant treatment details.			



stage 4 patients. Although survival drops as the stage increases, the sample size was not powered enough to show a statistically significant survival difference among individual stages.

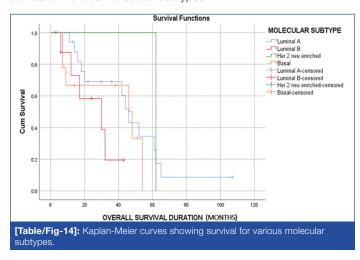
Molecular subtype and survival: The median OS for Luminal-A type was 46 months (95% CI 39.7-52.2), while the median OS



underwent surgery (n=26) Survival Functions stage 1.0 stage 1 Stage 2 stage 3 stage 4 0.8 stage 1-censored Stage 2-censored stage 3-censored stage 4-censored ÷ **Cum Survival** 0.6 0.4 0.2 0.0 120 20 60 OVERALL SURVIVAL DURATION (MONTHS) [Table/Fig-13]: KAPLAN-MEIER curves showing survival for various stages of

for Luminal-B type was 30 months (95% Cl 3.6-56.3%). Median survival could not be calculated for the HER-2 enriched subtype

because only two patients in present study had the HER-2 enriched molecular subtype. One patient had a survival of three months, and the other had a survival of 62 months. The median OS for the basal type was 21.8 months (95% CI 3.2-88.7). Present study results clearly indicate that Luminal A patients have a better prognosis and survival compared to Luminal B and basal subtype patients. However, present study sample size was underpowered to show a significant difference. [Table/Fig-14] shows Kaplan-Meier survival curves for various molecular subtypes.



Metastasis: Around 25.7% (10 patients) had upfront metastasis at presentation, and another 10 patients (25.7%) developed metastasis later during follow-up. Nine patients had multiple metastasis involving various organs, including bones, lungs, liver, brain, and non regional nodes, with bone being the most common site. Five patients had isolated bony metastasis, three patients had isolated lung metastasis, one patient had isolated brain metastasis. In our study, two patients developed local recurrence following surgery, but both of them also had synchronous systemic metastasis.

DISCUSSION

The incidence of breast cancer in men, as reported by other Indian studies, ranges from 0.4 to 2.8% [10-14]. In present study, the incidence was 2.1% among all breast cancers. When comparing this to Western literature [5,6], many Indian studies, including present, report an incidence of more than 1%. In Western populations, the median age for male breast cancer is greater than 65 years [5]. In contrast, many Indian studies show the median age of presentation to be less than 60 years [11,12]. This finding was consistent with present study, as 51% of patients were between 40 and 60 years of age. The family history of malignancy among these patients varies widely in many Indian studies, ranging from 7 to 20% [15-17]. In present study, it is around 10%.

BRCA testing and other mutation analyses were not conducted on present study patients, as these facilities are lacking in our centre. Infiltrating ductal carcinoma was the most common subtype in present study (89.7%) and is also predominant in other Indian studies (over 90%), as there is a scarcity of lobular tissue in male breast cancer [10-14]. Other types encountered include medullary carcinoma and papillary carcinoma. The majority of Indian studies report stage III as the most common presentation [10-13]. However, two Indian studies by Khandelwal S et al., and Chhabra MK et al., identified stage IV and stage II as the most common presentations, respectively [Table/Fig-15] [15,18]. In present study, 38.5% of patients were at stage III, and 33.3% were at stage II. This variation in presentation among Indian studies is likely due to differences in awareness rates of male breast cancer in different parts of our country and varying access to healthcare.

It is internationally recognised that the majority of male breast cancer patients are ER, PR positive and HER-2 negative [5,19]. In present

study, the rates of ER and PR positivity were comparable to those obtained in other studies [15]. Luminal A was the most common subtype, which aligns with findings by Khandelwal S et al., [15].

For all patients who underwent surgery (n=26, 100%), mastectomy with axillary lymph node dissection was the procedure performed. This is due to the paucity of breast tissue in male breast cancer, which makes reconstruction less feasible [20]. Additionally, many of the patients presented with advanced tumours. Although breast-conserving surgery is feasible in male breast cancer, the majority of Indian studies report 100% mastectomy rates [10-13,16]. Present study also found that clinical staging does not correlate with pathological staging, and none of the patients had a complete pathological response. The reasons for this are unknown, suggesting that the biology of male breast cancer differs from that of female breast cancer and warrants further research.

Authors compared clinical stage with pathological prognostic stage and found that approximately two-thirds of patients were down-staged in pathological prognostic staging. However, ONCOTYPE Dx facility was not available to evaluate genomic profiling based on pathological prognostic staging. The rates of adjuvant chemotherapy (73%) are higher in present study compared to the study by Giordano SH et al., (24%) [21]. This indirectly implies that we had a higher proportion of patients with advanced stages.

Survival studies for male breast cancer across the globe are limited due to its low incidence. Most studies conducted to date are retrospective studies and case series [2,5,12,13,15,16,18], and only a few have included survival analysis. The 5-year survival rates for stage I, stage II, stage III, and stage IV, as reported by Giordano SH, are 87%, 74%, 57%, and 16%, respectively [5]. A study by Ram D et al., showed the actuarial 5-year survival to be 92.30%, with a DFS of 76.30% [16]. This improved survival is likely due to a higher number of stage II patients in that study.

In present study analysis, the median OS and DFS for the entire cohort were 46 months and 42 months, respectively. The DFS in present study is roughly equal to the OS, which may be attributed to deaths from co-morbid illnesses and other causes. Similar findings were observed in 1,986 male breast cancer patients in the SEER database, diagnosed between 1988 and 2001, where the DFS was greater than the OS, likely due to the older average age of that population and deaths from other co-morbid conditions [22]. The median OS could not be calculated for stage I, as there was only one patient in the stage I group. Stage II patients (48 months) had better survival than stage III (42 months) and stage IV (30 months) patients; however, these findings should be confirmed in a large-volume, multicentric prospective study.

Authors also investigated whether survival differs based on molecular subtype and found that the Luminal A group has increased survival compared to Luminal B patients, while the Luminal B group has greater survival than the Basal group.

These findings are similar to those related to female breast cancer. The major limitations in calculating the statistical significance of this finding are the low number of cases, and the HER-2 enriched group had only two cases, which makes them unfit for comparison with other groups. Hormone receptor negativity was associated with poorer survival but was not an independent prognostic factor in multivariate analysis [23]. Additionally, whether HER-2 overexpression in male breast cancer is a marker of poor survival remains uncertain.

The follow-up for male breast cancer is the same as that for women. The usefulness of follow-up mammograms in men has not been established. Authors conducted regular clinical examinations every three months for the first two years and every six months for the next three years. Authors did not perform regular mammograms for these patients. Imaging is conducted only when there are symptoms suggestive of recurrence or second primary tumors.

Limitation(s)

The short follow-up period of six months was a drawback. Longer follow-up is necessary. BRCA and other mutation analyses were not conducted.

CONCLUSION(S)

Male breast cancer, especially in India, is on the rise, as shown by the increasing incidence compared to Western literature. Present study concluded that these patients have an early age of disease onset, most of whom are hormone receptor positive and commonly present in locally advanced stages. Luminal-A group patients have a good prognosis, and survival also depends upon the stage of the disease. This group of patients is unique and heterogeneous among various populations. Even though there are many studies comparing male and female breast cancer, the biology of male breast cancer still needs to be studied in detail and should be compared with female breast cancer in prospective randomised multicentric trials in order to yield therapeutic implications. Additionally, awareness among the general public that breast cancer can also occur in males should be fostered, utilising proper tools that involve all stakeholders and draw on Indian data.

REFERENCES

- [1] Jemalf A, Tiwari RC, Murray T, Ghafoor A, Samuels A, Ward E, et al. Cancer statistics, 2004. CA Cancer J Clin. 2004;54(1):8-29. Doi: 10.3322/ caniclin.54.1.8.
- [2] Speirs V, Shaaban AM. The rising incidence of male breast cancer. Breast Cancer Res Treat. 2009;115(2):429-30. Doi: 10.1007/s10549-008-0053-y. [PubMed] [CrossRef] [Google Scholar].
- Noone AM, Howlader N, Krapcho M. SEER web site. National Cancer Institute; [3] Bethesda, MD: April 2018. SEER cancer statistics review; pp. 1975-2015. Available from: https://seercancergov/csr/1975_2015/ Based on November 2017 SEER data submission. [Google Scholar].
- Cancer incidence and mortality (year 2017), incidence trend (2012-17) & [4] estimates (2018-2021) for Tamilnadu state, Tamilnadu cancer registry project (TNCRP).

- Giordano SH. Breast cancer in men. N Engl J Med. 2018;378(24):2311-20. [5] [6] Liu N, Johnson KJ, Ma CX. Male breast cancer: An updated surveillance, epidemiology, and end results data analysis. Clin Breast Cancer. 2018;18(5):e997e1002. doi.org/10.1016/j.clbc.2018.06.013.
- Anderson WF, Jatoi I, Tse J, Rosenberg PS. Male breast cancer: A population [7] based comparison with female breast cancer. J Clin Oncol. 2010;28:232-39.
- [8] Hammond ME, Hayes DF, Dowsett M, Allred DC, Hagerty KL, Badve S, et al. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. J Clin Oncol. 2010;28:2784-95
- Estrogen and Progesterone Receptor Testing in Breast Cancer: ASCO/CAP [9] Guideline Update. JCO 38, 1346-1366(2020).DOI:10.1200/JCO.19.02309.
- [10] Shah P, Robbani I, Shah O. Clinicopathological study of male breast carcinoma: 24 years of experience. Ann Saudi Med 2009;29(4):288-93. Available from: https://doi.org/10.4103/0256-4947.55314.
- [11] Ghoshal S, Rai B, Sharma SC. Breast cancer in males: A PGIMER experience. J Cancer Res Ther. 2005;1:31-33. Available from: https://doi.org/10.4103/0973-1482,16087
- [12] Chikaraddi S, Krishnappa R, Deshmane V. Male breast cancer in Indian patients: Is it the same? Indian J Cancer. 2012;49:272. Available from: https://doi. org/10.4103/0019-509X.104484.
- Sundriyal D, Kotwal S, Dawar R, Parthasarathy KM. Male breast cancer in India: [13] Series from a cancer research centre. Indian J Surg Oncol. 2015;6:384-86. Available from: https://doi.org/10.1007/s13193-015-0473.
- [14] Miao H, Verkooijen HM, Chia KS, Bouchardy C, Pukkala E, Larønningen S, et al. Incidence and outcome of male breast cancer: An international population-based study. J Clin Oncol. 2011;29:4381-86. Available from: https://doi.org/10.1200/ JCO.2011.36.8902.
- [15] Khandelwal S, Goel P, Sharma R, Sancheti S, Chaudhary D, Goel A, et al. Presentation and spectrum of male breast cancer in a rural cancer center in a subunit of tata memorial center, India. Indian J Surg Oncol. 2021;12(2):330-34. Doi: 10.1007/s13193-021-01306-8.
- Ram D, Rajappa SK, Selvakumar VP, Shukla H, Goel A, Kumar R, et al. Male [16] breast cancer: A retrospective review of clinical profile froma tertiary care center of India. South Asian I Cancer. 2017;6(4):141-43. Available from: https://doi. org/10.4103/sajc.sajc 2 17
- [17] Gogia A, Raina V, Deo S, Shukla NK, Mohanti BK. Male breast cancer: A single institute experience. Indian J Cancer. 2015;52:526-29. Available from: https:// doi.org/10.4103/0019-509X.178399.
- [18] Chhabra MK, Chintamani, Kadyaprath, G, Srivastva A, Selvakumar V, Ranjan P. Male breast cancer- An Indian multicenter series of 106 cases. Indian J Surg. 2021;83(Suppl 2):333-40. Available from: https://doi.org/10.1007/s12262-019-01953-w.
- [19] Chavez-Macgregor M, Clarke CA, Lichtensztajn D, Hortobagyi GN, Giordano SH. Male breast cancer according to tumour subtype and race: A populationbased study. Cancer. 2013;119:1611-17.
- [20] Cloyd JM, Hernandez-Boussard T, Wapnir IL. Poor compliance with breast cancer treatment guidelines in men undergoing breast-Conserving surgery. Breast Cancer Res Treat. 2013;139(1):177-82. Available from: https://doi. org/10.1007/s10549-013-2517-y.
- [21] Giordano SH, Perkins GH, Broglio K, Garcia SG, Middleton LP, Buzdar AU, et al. Adjuvant systemic therapy for male breast carcinoma. Cancer. 2005;104:2359-64. Available from: https://doi.org/10.1002/cncr.21526.
- [22] Giordano SH. A review of the diagnosis and management of male breast cancer. Oncologist. 2005;10:471-79.
- Giordano SH, Cohen DS, Buzdar AU, Perkins G, Hortobagyi GN. Breast [23] carcinoma in men: A population-based study. Cancer. 2004;101:51-57.

PARTICULARS OF CONTRIBUTORS:

- Associate Professor, Department of Surgical Oncology, Kalaignar Centenary Super Speciality Hospital, Guindy, Chennai, Tamil Nadu, India.
- Associate Professor, Department of Pathology, Government Arignar Anna Memorial Cancer Hospital, Chengalpattu Medical College, Chengalpattu, Tamil Nadu, India. 2 Assistant Professor, Department of Pathology, Government Arignar Anna Memorial Cancer Hospital, Chengalpattu Medical College, Chengalpattu, Tamil Nadu, India.
- З.
- Assistant Professor, Department of Surgical Oncology, Saveetha Medical College, Thandalam, Chennai, Tamil Nadu, India
- Postgraduate Student, Department of Surgical Oncology, Government Arignar Anna Memorial Cancer Hospital, Chengalpattu Medical College, Chengalpattu, 5. Tamil Nadu. India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Sakthi Usha Devi Jeevarajan,

51, Neeraraghavan Street, New Washermanpet, Tondiarpet, Chennai-600081, Tamil Nadu, India.

E-mail: sakthiushadevi@gmail.com

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? No
- Was informed consent obtained from the subjects involved in the study? No
- · For any images presented appropriate consent has been obtained from the subjects. NA

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Aug 17, 2024
- Manual Googling: Dec 30, 2024
- iThenticate Software: Feb 11, 2025 (11%)

Date of Submission: Aug 16, 2024 Date of Peer Review: Oct 26, 2024 Date of Acceptance: Feb 13, 2025 Date of Publishing: Mar 01, 2025

ETYMOLOGY: Author Origin

EMENDATIONS: 8