

# Male breast cancer: A 10-year experience of a tertiary care center in North India

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## ABSTRACT

**Background:** Male breast cancer (MBC) is a rare disease and accounts for ~1% of all cancers in men. Poor level of awareness often results in late presentation and delayed diagnosis. An increased incidence is seen in recent years. However, Indian literature is scant and we hereby present our data analyzed from a tertiary care center in North India. **Aim:** This study was done to analyze the demographic data, tumor characteristics, and management of MBC in Indian subset of patients and compare it with the literature available. **Study and Design:** This was a retrospective study from a tertiary care center. **Materials and Methods:** Data were collected from review of records of all male patients of carcinoma breast over a period of 10 years, i.e., from January 2005 to December 2015, who followed at our Institute. **Results:** During the study period, 53 cases of MBC were encountered; with ages of patients ranged from 35 to 80 years and a mean age of 60 years. As risk factor; 17 (32%) patients had sedentary life, six (11.3%) patients were obese, and four (7.5%) patients had positive family history. Breast lump was most common presenting symptoms seen in 39 (73.6%) patients. Within each breast, tumor was localized most commonly in central region (43.3%), followed by upper outer quadrant (32%). Stage I, II, III, and IV disease were encountered in 7.5%, 28.2%, 52.7%, and 11.3% of patients, respectively. Follow-up ranged from 1 to 144 months, with a median of 24 months. **Conclusion:** Male breast carcinoma is a disease of elderly people. Most of the patients presented late and in advanced stage of disease. Bone is the most common site of metastases.

**Key words:** Breast carcinoma, India, males

## INTRODUCTION

Male breast cancer (MBC) is a rare disease and accounts for ~1% of all cancers in men.<sup>[1]</sup> However, in the past 25 years, an increased incidence is seen.<sup>[2]</sup> It represents 0.5 and 1% of all breast cancers diagnosed every year in the United States and the United Kingdom.<sup>[3]</sup> However, in Tanzania and some areas of Central Africa, breast cancer accounts for up to 6% of all cancers in males.<sup>[4]</sup> The high incidence of MBC seen in Central and Eastern Africa is explained by hyperestrogenism due to higher rates of endemic hepatic infectious diseases.<sup>[5]</sup> Incidence of breast cancer rises with

age in both men and women, but at the time of diagnosis, men are 5–10 years older than women.<sup>[6-9]</sup> A number of factors have been considered to be related to increased risk for breast carcinoma in men. These include age, genetic and family history, Klinefelter syndrome, exogenous estrogen or testosterone use, obesity, primary testicular conditions (orchitis/epididymitis, undescended testes, and testicular injury), lack of exercise, and previous radiation exposure to the chest wall.<sup>[10,11]</sup> A positive family history of breast cancer is seen in 15–20% of men with breast cancer compared with only 7% of the general male population. Two breast/ovarian cancer genes, BRCA1 and BRCA2, account for 80% of multiple-case breast cancer families, similarly as seen in women. However, the risk appears to be higher with inherited BRCA2 rather than BRCA1 mutations.<sup>[12]</sup> As

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in women, clinical evidence supports that tumor size and axillary lymph node involvement are important prognostic factors.<sup>[13]</sup> Histologic subtypes for invasive carcinomas are similar in men and women, but the relative distributions differ. Approximately 90% of MBC are invasive ductal carcinomas; in women, the frequency of ductal histology is 70%–75%. Lobular cancers account for 1.5% of cases in men in contrast to 15% of cases in women. Lobular histologic subtype is rare in men due to lack of acini and lobules in the normal male breast. Ductal carcinoma *in situ* (DCIS) accounts for a significantly higher proportion of breast cancers in women compared with men (approximately 20% vs. 10%, respectively). Papillary and cribriform are the most common, growth patterns, and the majority of these tumors are low grade. Paget disease and inflammatory breast cancer are rare in men. Data from more than 2000 male patients in the Surveillance, Epidemiology, and End Results Cancer Registry show that 93.7% of MBCs are ductal or unclassified carcinomas, 2.6% are papillary, 1.8% are mucinous, and only 1.5% are lobular. Approximately 90% of MBCs express the estrogen receptor (ER), and 81% express the progesterone receptor (PR). As in female breast cancer, the rates of hormone-receptor positivity increased with increasing patient age. Studies have shown lower rate of human epidermal growth factor receptor 2 (her2)-neu overexpression in men (2%–15%) in contrast to women (18%–20%).<sup>[14,15]</sup> Triple-negative tumors are very rare in men, and prognostic significance of grading and ki-67 labeling index is yet to be established in men unlike women, where they are established prognostic factors. Most information on MBC has been collected from retrospective studies done over several years, and results of trials in female patients were extrapolated for treatment recommendations in men. MBC and female breast cancer share many similarities, but they differ in age at diagnosis, frequency of the histological types, and frequency of expression of hormone receptors.

Data on MBC in Indian patients have been a rarity. We present here our series of MBC patients over a 10-year period. This study was done to analyze the demographic data, tumor characteristics, and management of MBCs in Indian subset of patients and compare it with that of literature.

## MATERIALS AND METHODS

We analyzed all male patients diagnosed as carcinoma breast over a period of 10 years, i.e., from January 2005 to December 2015, within our institutes or elsewhere and were referred to our institute for further management. Patient records, surgical reports, pathology reports, follow-up examination, and study notes present in patient files were examined and patients were evaluated

in terms of age, presenting signs and symptoms, risk factors, primary tumor pathology, surgery performed, histopathological details of operated specimen, including resection margin status, tumor size, lymph nodes involved, grade, lymphovascular invasion, ER/PR, her2-neu status, adjuvant/palliative treatment strategy (chemotherapy, hormonal therapy, and radiation), details of recurrence, follow-up, and survival, were obtained. Staging was done according to the American Joint Committee on Cancer Criteria (tenth edition). All patients underwent routine laboratory investigations; complete blood count, kidney function test, liver function test, alkaline phosphatase, chest radiography, and abdominal ultrasound. Mammogram, diagnostic contrast-enhanced computed tomography chest, abdominal ± pelvis, bone scan, or magnetic resonance imaging/computed tomography brain were done when indicated by clinical suspicion. Patients were followed up to the end of December 2015.

### Statistical analysis

Data were analyzed using SPSS statistical package version 20 (IBM Corporation). Quantitative data were presented as median and range. Qualitative data were expressed as frequency and percentage.

## RESULTS

From January 2005 to December 2015, 53 male patients with diagnosis of breast carcinoma presented to our institute. Their age and history of risk factors are shown in Table 1. The median age of diagnosis was 60 years, ranging between 35 and 80 years. Patients were divided into four groups by age: <49 years, 50–59 years, 60–69 years, and >70 years. Only six patients (11.3%) were younger than 49 years which means that it is mainly a disease of elderly. A positive family history of carcinoma breast was reported in 7.5% of patients, history of testicular trauma was present in 5.6%, 11.3% were obese, and 32% of patients had sedentary lifestyle. There was no patient with clinical Klinefelter syndrome or previous history of chest wall irradiation. Tumor characteristics are summarized in Table 2. Most

**Table 1: Patient characteristics (n=53)**

Feature	n (%)
Age	
0-49	6 (11.3)
50-59	13 (24.5)
60-69	20 (37.7)
≥70	14 (26.4)
Risk factors	
Sedentary lifestyle	17 (32.0)
Obesity	6 (11.3)
Family history	4 (7.5)
Testicular trauma	3 (5.6)
None	23 (43.3)

**Table 2: Tumor characteristics (n=53)**

Characteristic	n (%)
Symptom	
Breast lump	39 (73.6)
Skin ulceration	7 (13.2)
Nipple discharge	4 (7.5)
Bony pain	3 (5.6)
Side	
Right	25 (47.1)
Left	28 (52.8)
Site	
Upper outer	17 (32.0)
Upper inner	5 (9.4)
Central	23 (43.3)
Lower outer	4 (7.5)
Lower inner	4 (7.5)
Stage	
I	4 (7.5)
IIA	7 (13.2)
IIB	8 (15.0)
IIIA	6 (11.3)
IIIB	10 (18.8)
IIIC	12 (22.6)
IV	6 (11.3)
Histology	
IDC	53 (100.0)
Lymphovascular invasion	
Absent	16 (30.2)
Present	27 (50.9)
Not available	10 (18.9)
Grade	
I	3 (5.7)
II	29 (54.7)
III	16 (30.2)
Not available	5 (9.4)
Estrogen receptors	
Absent	5 (9.4)
Present	26 (49.1)
Not available	22 (41.5)
Progesterone receptors	
Absent	7 (13.2)
Present	24 (45.3)
Not available	22 (41.5)
her2/neu	
Absent	23 (43.3)
Present	2 (3.7)
Not available	28 (52.8)

IDC: Infiltrating ductal carcinoma, HER2: Human epidermal growth factor receptor 2

common mode of presentation was a breast lump (73.6%), followed by skin ulceration (13.2%), nipple discharge in 7.5%, and bony pain in 5.6%. Left-sided involvement (52.8%) was slightly higher than right (47.1%). Within each breast, tumor occurred most frequently in the central region (43.3%). The second most common site was upper outer quadrant (32.0%). Most of the tumors belonged to stage III (52.7%). Management was individualized according to different tumor and patient characteristics. Various treatment modalities received by patients are shown in Table 3. The majority of patients underwent modified radical mastectomy (MRM), i.e., 75.4%, followed by lumpectomy with axillary sampling (AS) in 13.2%. However, six patients (11.3%) presented with metastatic disease and they underwent biopsy only for histological diagnosis;

among them, the first one had metastases in brain, lung, and liver; second had metastases in bone, lung, and liver; third had in lung; and remaining three had metastases in bones only. Following surgery, patients were assessed for adjuvant treatment (chemotherapy, hormonal therapy, and radiotherapy). In our series, 46 patients (86.7%) received chemotherapy, in 37 patients as adjuvant and as palliative in nine patients. Radiotherapy (to tumor bed ± drainage areas) was received by a total of 42 patients; it included all patients who underwent lumpectomy with AS (seven patients) and 35 patients from MRM group (with indications of tumor size more than 5 cm, positive nodal dissection, or positive resection margin). ER/PR receptor status was available for only 31/53 patients (58.4%) as it was not done in our institute before 2007 (13 patients) and was not also available in another nine patients diagnosed after 2007. Among these 31 patients, hormonal therapy was indicated in 27 patients as three patients were triple-negative and one patient was ER/PR-negative and nonavailable her2-neu. Twenty-one patients received tamoxifen (39.6%) and two patients received letrozole (3.7%). Only 25 patients were analyzed for all the three receptors, i.e., ER/PR along with her2-neu, and we encounter only two patients (8%) with positiver2-neu, but none received targeted therapy.

During the median follow-up period of 24 months (range; 1–144 months), three patients developed locoregional failure, with chest wall recurrence in one patient and other two being relapse in supraclavicular area. Different sites of recurrence/metastases either alone or in combination are shown in Table 4a. Six patients (11.3%) were metastatic at presentation and other 12 patients metastasized later. Overall frequency of various metastatic sites is shown in Table 4b. At the time of closure of study, 23 patients were dead and thirty were alive and they continued with follow-up.

## DISCUSSION

In our study, median age of diagnosis was 60 years while a median age of approximately 68 years was reported by other studies. A lower mean age can be possibly due to the low life-expectancy of our society. The greatest incidence occurs 5–10 years later in males than in females.<sup>[16,17]</sup> Histopathological differences between men and women are due to the lack of classic lobular structure in men. Infiltrated ductal carcinoma (IDC) is the most frequently seen MBC and it accounts for 85%–90% of all MBCs.<sup>[18]</sup> In our study, all cases (100%) were IDC. We had no patients with DCIS possibly because in our environment patient are usually referred late to a health center till they do not have main complaints. In addition, breast cancer is considered a cancer specific to females, so clinical suspicion remains very low in initial stages. Factors associated with the

**Table 3: Management (n=53)**

Treatment modality	n (%)
Surgery	
Biopsy only	6 (11.3)
Lumpectomy + AS	7 (13.2)
MRM	40 (75.4)
Chemotherapy	
Adjuvant	37 (69.8)
Palliative	9 (16.9)
No chemotherapy	7 (13.2)
Endocrine therapy	
Tamoxifen	21 (39.6)
Letrozole	2 (3.7)
None	30 (56.6)
Local radiotherapy*	
Node involvement	31 (58.4)
Tumor size	27 (50.9)
Lumpectomy + AS	7 (13.2)
Positive resection margin after MRM	2 (3.7)
None	11 (20.7)

\*Many patients had more than one indication for local radiotherapy. MRM: Modified radical mastectomy, AS: Axillary sampling

**Table 4a: Site of metastases (n=53)**

	n (%)
Bone	7 (13.2)
Bone + liver	1 (1.9)
Bone + liver + lung	1 (1.9)
Bone + lung	3 (5.7)
Brain	2 (3.8)
Brain + liver + lung	1 (1.9)
Pulmonary	3 (5.7)
Locoregional	3 (5.6)
None	32 (60)

**Table 4b: Overall frequency of metastatic sites\* (n=53)**

	n (%)
Bone	12 (22.6)
Lung	8 (15.0)
Liver	3 (5.6)
Brain	3 (5.6)
Locoregional	3 (5.6)
None	32 (60.3)

\*Many patients had metastases at more than one sites

development of MBC include genetics and family history, alterations of the estrogen to androgen ratio, and some primary testicular conditions (such as cryptorchidism, testicular trauma, orchitis, and epididymitis). In males, most cases of breast cancer are sporadic, but a familial form exists where an increased risk of developing breast cancer is seen in both men and women.<sup>[19]</sup> In our study, four cases (7.5%) had positive family history of breast cancer in first-degree relative. We could not comment upon genetic mutations because none of our patients were assessed for BRCA-1/BRCA-2 mutations. Risk factors such as use of estrogen or testosterone, hepatic dysfunction, obesity, marijuana use, thyroid disease, or an inherited condition, such as Klinefelter syndrome, are considered to be due to altered estrogen to androgen ratio associated

with these conditions. Klinefelter syndrome is a rare condition resulting from the inheritance of an additional X chromosome.<sup>[20]</sup> In our series, 17 patients had sedentary lifestyle, six patients were obese (grade I to grade II obesity), and history of testicular trauma was present in three patients. However, there were no patients with clinical Klinefelter syndrome or previous chest wall radiation in our study. A possible explanation to increased risk of MBC in patients with primary testicular conditions is due to lower androgen production, resulting in a higher than normal estrogen to androgen ratio. Mostly, patients of MBC present with a unilateral firm slightly irregular, painless, or minimally tender subareolar mass. Nipple involvement is rare and there is a slight left-sided predilection with a left to right ratio of 1.07:1.<sup>[21]</sup> In our study, most cases presented with breast lump (73.6%) with left-sided involvement seen in 52.8% of patients. In 43.4% of cases, tumor was localized in the central retroareolar region, followed by upper outer quadrant in 32%. In males, breast cancer tends to present in advanced stages than in females.<sup>[22]</sup> In the present study, 52.7% of patients were in stage III (IIIA 11.3%, IIIB 18.8%, and IIIC 22.6%) and 11.3% were in stage IV. As is clear, most of our patients were in advanced stage of disease and thus emphasizing the need for greater attention and awareness for risk identification to ensure early detection of cases. There is always a delay in male patients since the first symptom until they seek medical advice, which results in an advanced stage of disease presentation. It may be because breast cancer is considered primarily a disease of females, and its diagnosis in a male is often met with a sense of disbelief.<sup>[23]</sup> MBCs have high rates of hormone-receptor expression. According to various studies, approximately 90% of MBCs express the ER and 81% express the PR. In our study, among the patients analyzed for ER/PR (31 patients), ER was positive in 83.8% (26 patients) and PR in 77.4% (24 patients). While PR frequency was close to that reported in the literature, the ER ratio was slightly lower. Breast cancer in males is significantly more likely to express hormone receptors than in females, even after adjustment for tumor stage, grade, and patient age.<sup>[14,24]</sup> In MBC, the her2-neu proto-oncogene is less likely to be overexpressed than in females. In a recent study, only 5% patients of MBCs overexpressed her2-neu.<sup>[25,26]</sup> In our study, two patients were positive for her2-neu proto-oncogene though it was tested in 25 patients only, accounting for a total of 8% positivity. Initial studies have found equivalent rates of her2-neu overexpression between male and female breast cancers.<sup>[27]</sup> However, those studies were performed before improved standardization of methodology and probably overestimated her2-neu overexpression. We also confirmed that triple-negative cancers are rare among men, with only three cases (12%) in our series. Surgical excision is the mainstay treatment for MBC and MRM with axillary lymph node dissection, or sentinel node biopsy is

treatment of choice. Previously, most patients were treated with radical mastectomy, but retrospective studies showed that the outcome for men is equally good when treated with less invasive surgery.<sup>[28]</sup> Larger studies from female breast cancer patients also support the use of MRM over radical mastectomy.<sup>[29]</sup> In our study, MRM was performed in 75.4% of the patients; lumpectomy with AS in 13.2% and 11.3% underwent biopsy only. None of our patients received neoadjuvant chemotherapy. Recommendations for adjuvant chemotherapy are based on benefits that have been observed in clinical trials performed in women. There is strong evidence of data supporting the use of adjuvant chemotherapy in women;<sup>[30]</sup> however, there is little information on the effectiveness of adjuvant chemotherapy in men. Retrospective studies have supported the use of adjuvant chemotherapy to lower the risk for recurrence in men.<sup>[31]</sup> In our study, chemotherapy was received by 86.7% of patients; 69.8% as adjuvant and 16.9% as palliative. Postoperative radiotherapy is an important part of adjuvant treatment and does achieve local control, but no effect is observed on survival.<sup>[32]</sup> To determine which male patients would derive benefit from adjuvant radiation, Perkins *et al.* studied a series of 142 MBC patients treated at The University of Texas M. D. Anderson Cancer Center.<sup>[33]</sup> Their results showed locoregional failure in 18% of patients, with chest wall and supraclavicular areas being most common sites of relapse. Predictors of local regional failure included margin status, tumor size, and the number of involved axillary lymph nodes. In the present study, adjuvant radiotherapy was used in 42 patients (79.2%) with indication as positive nodes, tumor size more than 5 cm, patients undergone lumpectomy, or those with positive resection margins. However, on follow-up, we observed locoregional recurrence in three patients. Two patients recurred in supraclavicular area and one developed chest wall recurrence, and all the three had received radiation to chest wall with drainage sites. Adjuvant hormonal therapy has a role in patients of MBC with hormone receptor-positive tumors. In retrospective series, a reduced risk of breast cancer recurrence and death has been observed by use of tamoxifen in the adjuvant setting.<sup>[34]</sup> Furthermore, in the metastatic disease, tamoxifen has shown activity against MBC. In the present study, tamoxifen was given to 39.6% of patients and letrozole was received by 3.7%. We had only two patients with positive her2-neu, but none received trastuzumab.

## CONCLUSION

MBC is a rare disease and occurs in elderly people. Most of our patients had advanced stage of disease probably because they reported late to health care center after having initial symptoms. This should be looked with great concern and there is need for educating the people about this rare

disease and increase their awareness regarding the risk factors associated. In many ways, it is similar to female breast carcinoma but with some distinct differences such as much rarer lobular histology, and we did not encounter any patient of lobular carcinoma. Treatment failure is common feature and bone being the most common site of relapse. Hormone receptor positivity is very common.

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## Conflicts of interest

There are no conflicts of interest.

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