

Patterns of Male Breast Cancer over Three Decades: A Single Institutional Findings

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ABSTRACT

Introduction: Male breast cancer (MBC) accounts for around 1% of all breast cancers. However, the incidence & patterns of MBC varies in different parts of the world. Due to the rarity of its occurrence, very few literature are available regarding its peculiarities.

Material & Methods: A total of 119 patients of MBC were included in this retrospective analysis, who were registered in a single regional cancer center in India over 30 years period from 1991 to 2020. Data from all patients were collected to evaluate the spectrum and patterns of MBC concerning presentation, distribution, and clinico-pathological characteristics.

Results: Total of 119-patients of MBC were registered in this time. The median age of presentation was 59 years. The right to left ratio was 1.25:1, which indicated that both sides breast was equally affected. Most of the patients (68.1%) presented late in the disease course with locally advanced or metastatic lesions. The majority of breast lesion was central or retro-areolar in location and infiltrating ductal carcinoma histology was found in more than 90% of patients. Estrogen and progesterone receptor positivity was seen in 42.9% and 29.4% of patients, respectively. The most common metastatic site was bone.

Conclusion: Our data regarding MBC patients matched closely with existing literature. However, it is seen MBC patients presented to oncologists in a locally advanced stages; either because of shyness or unaddressed health education. Emphasis should be given to prospective studies to gather more knowledge about the demography and pattern of this rare yet sprouting malignancy.

Keywords: Demography, India, Male breast cancer, Retrospective analysis

INTRODUCTION:

Carcinoma of the male breast is comparatively a rare event that accounts for ~1% of all breast cancer globally with a relatively high incidence rate in some countries of Southern Africa [1]. The risk of being diagnosed with breast cancer over a lifetime is 125 times less in males than in females [2]. This uncommonness of male breast cancer (MBC) makes more complications in the population, regarding its awareness and timely intervention. MBC is a malignancy of elderly men that mostly occurred after their 50s, incidence increases with age [3, 4]. The incidence rate differs to a great extent in various geographical and ethnic groups [1, 4]. It varies also with the presence of risk factors in an individual or population; mostly on family history, dark ethnicity, feminization (hereditary or ecological), exogenous estrogen intake, testicular disorders (mumps orchitis, orchietomy, cryptorchidism) or testicular injury, previous exposure of thoracic radiation, liver disease and so on [3]. Klinefelter syndrome (XXY, hyper-estrogenic state) and some germline hereditary changes like BRCA 2 &1, PALB2, CHEK2 have proved etiological impact on the occurrence of MBC [2, 3]. The impact of positive family history, in terms of breast or related cancer (ovary, stomach) in first-degree relatives, is clearly described in different articles; with a 2.5-fold relative risk of MBC in familial cases [5]. There is a high risk of MBC in overweight (body mass index >25 kg/m²) and taller males [4, 5]. In an interesting study, Demers et al depicted that MBC cases are more in occupation with electromagnetic field exposure like electric power workers, telephone linemen, and electricians [6]. However, in most of the studies, the sample size is too small to demonstrate an association of MBC with the risk factors. Furthermore, the majority of the analysis was conducted over a relatively short period. Over time, incidence, pattern, diagnostic, and management approaches have changed for breast cancer both in females and males. The popularity of hormone receptor (HR) identification and treatment orientation shifting according to HR status has brought a dramatic shift in

breast cancer management. Approximately, 80% of patients with MBC are HR-positive, and adding hormonal therapy provides benefits to them [7]. The present study aims to analyse the demographic and clinicopathological characteristics of MBC patients in the only cancer institute of an Indian state and to comment on established risk factors of this rare disease.

Materials and Methods:

This is a retrospective study for 30 years from 1st January 1991 to 31st December 2020 in a regional cancer center cum teaching institute of Northern India. A total of 119 patients of MBC, malignancy confirmed by either fine needle aspiration cytology (FNAC) or biopsy (mainly tru-cut and wedge biopsy), were included in this study. Before reviewing the records, we excluded patients with sarcoma, melanoma, or lymphoma in the male breast from this analysis. These 119 patients had epithelial carcinoma and their records were analysed for demographic profiles including age, background, co-morbidities & family history, addiction status, and clinicopathological characters encompassing tumor size, pathological stage, histology, receptor status & metastatic depiction. An immunohistochemistry (IHC) assay was performed to identify hormone and human epidermal growth factor receptor 2 (HER-2) status. Metastatic work-up was done with at least chest radiography and abdominal ultrasonography; computed tomography (CT) scan, magnetic resonance imaging (MRI), bone scintigraphy, and positron emission tomography (PET) scan were also done when indicated. All the patients were staged on basis of clinical examination and imaging available according to female breast cancer tumor, nodes, metastases (TNM) staging of American Joint Committee on Cancer (AJCC) classification [8]. All the records were collected and analysed using Microsoft Excel version 2019 and Statistical Package for Social Sciences (SPSS) version 26.

Results:

Throughout 3-decades, a total of 119 patients of MBC were registered in our department; which accounted for approximately 1.3% of all breast cancer cases. The medi-

an age at the time of diagnosis was 59 years (range 30-86 years). Nearly 69% of the MBC patients were from rural backgrounds. Body mass index (BMI) was available for only 43 patients, mean BMI was 25.7 (range 18.1-32.6). The viral markers, comprising of Hepatitis-B (HBV), Hepatitis-C (HCV), and human immune-deficiency virus (HIV), were non-reactive in 36 patients and unknown in the rest of them. A significant family history of other cancers was found in 7 (5.9%) patients (table 1). Fifty-one patients (42.9%) were having associated co-morbidities like gynecomastia, hypertension, diabetes, and benign prostatic hypertrophy (BPH) (figure 1). The rest of the patients did not give any history of co-existing diseases.

The bulk of the patients (70.6%) were found to be chronic smokers, mostly in form of bidi or hookah. About 41.2% were also alcoholics. The breast lump was invariably the chief complaint in all MBC patients; associated symptoms like nipple discharge, weight loss, anorexia, and bony pain were present in some of them. The average time for symptoms was 25.4 months with a broad

range of 1 month to 20 years. As far as the laterality was concerned, more than half (54.6%) of the MBC cases were right-sided, only 2 patients were having bilateral disease and the rest have left-sided carcinoma. Central or retro-areolar involvement by breast lump was seen in the majority of the patients (72.3%); involvement of other quadrants was scattered. The mean tumor size of all MBC patients was found to be 5.7 cm (range 2-10 cm); obviously, the most common T staging was T3 (52.9%). Among all the patients, 60.5% presented with axillary lymphadenopathy and 20.2% had metastatic lesions at initial presentation. The most common metastatic site was bone (figure 2). Particulars of tumor characteristics including TNM and prognostic staging and metastatic profiles are illustrated in table 2.

On microscopic histopathological examination, invasive ductal carcinoma (IDC) was identified in 91.6% of patients; followed by undifferentiated and papillary carcinoma in 6 and 4 patients, respectively. Details of other histopathological findings of tumor-encompassing ductal carcinoma in situ (DCIS) presence, histological

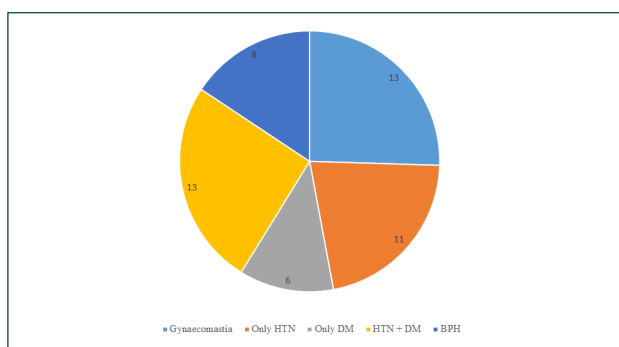


Figure 1. Comorbidities among male breast cancer patients

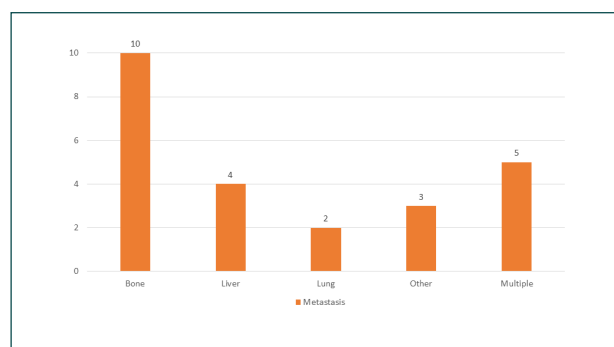


Figure 2. Different metastatic sites in patients of male breast cancer

Table 1. Family history of male breast carcinoma patients

Relation	Cancer
Mother (1st degree)	Breast cancer (2 cases) Ovarian cancer (1 case)
Sister (1st degree)	Endometrial cancer
Father (1st degree)	Breast cancer
Grandmother (2nd degree)	Breast cancer
Father (1st degree)	Prostate cancer

Table 2. Tumor characteristics of the male breast cancer patients

Characteristic		No. of patients (%)
Tumor size - Mean (range)		5.7 (2-10) cm
Site	Retro-areolar/ central	86 (72.3%)
	Upper outer quadrants	13 (10.9%)
	Lower outer quadrants	10 (8.4%)
	Inner quadrants	07 (5.9%)
	Scar recurrence	03 (2.5%)
Nipple involvement		77 (64.7.5%)
Tumor size (T)	T1	03 (2.5%)
	T2	31 (26.1%)
	T3	63 (52.9%)
	T4a	12 (10.1%)
	T4b	10 (8.4%)
Nodal involvement (N)	N1	05 (4.2%)
	N2	45 (37.8%)
	N3	22 (18.5%)
	N0 (Not involved)	47 (39.5%)
Stage	II	38 (31.9%)
	IIa	26 (21.8%)
	IIb	12 (10.1%)
	III	57 (47.9%)
	IIIa	36 (30.2%)
	IIIb	07 (5.9%)
	IIIc	14 (11.8%)
	IV	24 (20.2%)
Early disease		38 (31.9%)
Locally advanced disease		57 (47.9%)
Metastatic disease		24 (20.2%)

grading, lympho-vascular invasion, HR, and HER-2 status were depicted in tabular format (table 3). Molecular subtyping was done according to these pathological findings in a limited number of patients and mentioned.

Discussion:

Our hospital, a regional cancer center, is the only tertiary cancer center cum teaching institute and serves all the cancer patients of this state, especially those of rural backgrounds. A few major cancer centres in India have published retrospective studies on MBC depicting demographic and clinicopathological profiles of their in-

stitution-treated patients (table 4) [4, 9-23]. As incidence, demography, risk factors, and tumor properties vary over geographical and cultural differences, it is worthy to report the same in our hospital-addressed MBC patients. In the present study, the incidence of MBC (1.3%) is slightly higher than the global average of 1% but matched closely with other Indian studies i.e., A study by Pawar et al (2021) done in MBC patients of Patna, Bihar [23]. However, Shah et al (2009) and Khandelwal et al (2021) reported a higher incidence rate of MBC in Kashmir (4.1%) and Punjab (1.9%), respectively [6,12]. This might be due to geographical variations. The hallmark of the present

Table 3. Histopathological characteristics of male breast cancer patients

Characteristic	Parameter	Number (%)
Histology	IDC	109 (91.6%)
	Undifferentiated	06 (5.04%)
	Papillary	04 (3.36%)
Ductal carcinoma in-situ (DCIS)	Present	38 (31.9%)
	Absent	29 (24.4%)
	Unknown	52 (43.7%)
Bloom Richardson Grading	I	0
	II	34 (28.6%)
	III	22 (18.5%)
	Unknown	63 (52.9%)
Lympho-vascular invasion (LVI)	Present	41 (34.5%)
	Absent	26 (21.8%)
	Unknown	52 (43.7%)
Hormone receptor (HR)	Only ER	23 (19.3%)
	Only PR	7 (5.9%)
	ER+PR	28 (23.5%)
Her-2-neu	Positive	12 (10.1%)
	Negative	46 (38.7%)
	Unknown	61 (51.3%)
TNBC		27 (22.7%)
Molecular subtype	Luminal A	23 (19.3%)
	Luminal B	26 (21.8%)
	Basal like / TNBC	27 (22.7%)
	Her-2 enriched	12 (10.1%)
	Unknown	31 (26.1%)

IDC: infiltrating ductal carcinoma, ER: estrogen receptor, PR: progesterone receptor, TNBC: triple negative breast cancer,

article is that it demonstrates the MBC data of thirty years' time period, which, to the best of our knowledge, is the first study on MBC in India spanning over 3-decades. The median age in this analysis was 59 years, which consolidated the conclusion of previous studies that MBC patients present in the older population in comparison to females [24]. However, in comparison to the Western literature, where the median age of MBC patients is 67 years, the MBC patients in the present study presented in the younger age [25]. This variation demarcates the need of such study around different parts of world. The family history of the present analysis (5.9%) was very much less than the reported 20% data [26]. Among different Indian studies, Gogia et al (2015) and Pothamsetty et al (2017)

documented family history of MBC patients being 10% and 15.4%, respectively [17, 20]. A Nigerian study by Ahmed et al (2012) revealed 2.5% family history, which is surprisingly quite low [27]. The topographical variation might be one of the reasons for such diverse values. Genetic testing of all MBC patients, recommended globally, was not possible in our institution due to logistic issues. Hence percentage of patients having BRCA and other contributory mutations could not be identified. A high level of BMI is one of the established predisposing factors of MBC [4]. In the current analysis, the mean BMI was 25.7; 26 patients were overweight, while 9 patients were obese. In our study, most of the MBC patients presented late with a mean duration of symptoms of 25.4

Table 4. Studies on male breast cancer patients in India

Author	Year	Period	Institute (Place)	Number of patients	% of breast cases	Median age	Locally advanced disease	ER/PR +ve
Shukla et al [9]	1996	-	-	41	-	54.2	41%	43%
Rai et al [10]	2005	1996 – 2000	PGIMER	30	0.5%	56	43.3%	-
Mitra et al [11]	2007	-	-	79	-	67	90%	83%
Shah et al [12]	2009	1983-2007	SKIMS	32	4.1%	55	56.2%	62.5%
Chikaraddi et al [13]	2012	2010 – 2001	KIDWAI	26	0.4%	57	50%	81%
Shah et al [14]	2012	-	-	42	-	56	43%	27% / 62%
Mukherjee et al [15]	2014	2003-2009	KOLKATA	33	-	60	57.6%	54.5%
Sundriyal et al [16]	2015	2005-2014	DHARMSHILA	18	1.03%	60	28%	89%
Gogia et al [17]	2015	1996-2012	AIIMS, DELHI	27	0.8%	62.6	-	78%
Patel et al [18]	2016	-	GCRI, GUJARAT	25	-	-	-	-
Ram et al [19]	2017	2010-2016	RGCI, Delhi	27	-	62.6	15%	78%
Pothamsetty et al [20]	2017	-	-	33	-	56	87%	56.5%
Yadav et al [21]	2018	-	PGIMER, Chandigarh	81	-	57	42%	42% / 26.5%
Chhabra et al [22]	2019	2010-2017	DBOG	106	-	-	-	-
Khandelwal et al [4]	2021	2015-2019	TMC, Punjab	34	1.9%	62.5	39.1%	76.5%
Pawar et al [23]	2021	2016-2021	IGIMS, Patna	16	1.1%	58	81.25%	75%

ER: estrogen receptor, PR: progesterone receptor, DBOG: Delhi breast oncology group

months. This might be due to unawareness of health conditions and the irrational use of ayurvedic medicines around our state.

In the present study, approximately three fourth of the total patients had central quadrant or retro-areolar MBC, and around 64.7% had nipple involvement. These findings are very much consistent with the existing literature [28]. More than 90% of the MBC patients of our institu-

tion revealed IDC histology, which is similar to female breast cancer and also consistent with Tata Medical Centre (2021) study on MBC [4]. DCIS positivity and comparatively higher histological grade of breast tumours were reported in the present study, which is also in line with the global values [29]. Existing studies demonstrated a high percentage of hormone receptor positivity (estrogen receptor, ER= 90%; progesterone receptor, PR=

81%) in MBC than in females counterparts. A few Indian studies also revealed ER/PR positivity in the range of 77-89% [11,13,16-17,19]. However, our analysis showed relatively less ER/PR values. This may be due to the lack of hormone receptor testing facilities in the early 90s. The incidence of triple-negative MBC patients (22.7%) in our study is similar to the 22% incidence of female breast cancer [17].

The limitation of the present study includes the retrospective nature of the analysis and hormonal profile unavailability in more than half of the patients. Another important fact not to miss, this analysis was conducted on patients of MBC for 3-decades. Over this huge period, demography & culture changed a lot; simultaneously patients' profiles, diagnostic approach (indication of hormone & HER-2 testing, imaging modalities), staging, and therapeutic strategy also changed. These affect the overall outcome of our analysis.

Conclusion:

Male breast cancer patients represent 1.3% of all breast cancer cases in our institute. Our study patients had a predominant locally advanced stage at the time of first presentation, invasive ductal carcinoma histopathology, central quadrant presentation, similar triple-negativity rate as female breast cancer, younger age at presentation in comparison to the Western literature but older age presentation in comparison to females. For future knowledge, more multicentric prospective trials should be conducted to the prognostic and predictive factors which might help to enhance the treatment outcome in male breast cancer patients

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