



## HISTOPATHOLOGICAL SPECTRUM OF MALE BREAST LESIONS - A RETROSPECTIVE STUDY DONE IN A TERTIARY CANCER CARE HOSPITAL

### Oncopathology

**Dr. Hitesha Bhandari\*** DNB Pathology Resident, Bhagwan Mahaveer Cancer Hospital and Research Centre, Jaipur, Rajasthan. \*Corresponding Author

**Dr. Anjali Sharma** HOD Pathology, Bhagwan Mahaveer Cancer Hospital and Research Centre, Jaipur, Rajasthan.

**Dr. Rishikesh Dipak Nilapwar** DrNB Surgical Oncology Resident, Bhagwan Mahaveer Cancer Hospital and Research Centre, Jaipur, Rajasthan.

### ABSTRACT

The male breast cancer (MBC) is rare and represents less than 1% of all malignancies in men. We illustrate the experience of our team about the histopathological spectrum of 100 male breast cancer cases among total 3750 breast cancer cases in a retrospective study of 15 years done at our centre. The average age was 58.59 years. Right laterality was more common than left, Modified Radical Mastectomy remained treatment of choice in 94.59% cases. Invasive ductal carcinoma 58/74(78.38%) and Gynaecomastia 19/26(73.07%) were the most common malignant and benign male breast cancers found. Male breast cancer has many similarities to female breast cancer but distinct functions need to be appreciated. More research needs to be done for understanding of the disease aggressive nature and rarity.

### KEYWORDS

Male Breast Cancer, Invasive ductal carcinoma, Gynaecomastia, Mastectomy

### INTRODUCTION

Breast lesions are the leading cause of morbidity and mortality among women worldwide, comprising of broad histological spectrum of lesions with different characteristics.[1] Breast cancer in males is relatively uncommon, SEER cancer database 2023 states worldwide occurrence of 300,590 (15%) cases of breast cancer, with estimated occurrence of 2800 male breast cancer with mortality rate of 530 (18.92%).[2] Lung cancer(10.6%) is the most common cancer in adult male in India and estimated incidence rate of 5649 cases of male breast cancer is made.[3] Breast lesions are diverse, extending from inflammatory non-neoplastic to life threatening invasive carcinomas with diverse characteristic features.[4]

Major risk factors are represented by hormonal imbalance (caused by the metabolic syndrome even in young patients,[5] hyperthyroidism, testicular disorders of development, traumatic or infectious origin or antiandrogenic medication, environmental conditions such as exposure to radiation and patients with a positive first degree family history have a 2.0 times greater risk, which increases to more than 5.0 times with the number of affected relatives and relatives of the first onset. Clinically, in most cases it manifests as a painless mass, usually unilateral, with a marked tendency of infiltration in the adjacent structures. When extended to the nipple or skin, nipple retraction or ulceration is observed. Mammographic investigation is done in all advanced stages, it seems that mammography provides the most accurate size measurement[6]; for BIRADS system of scoring, the protocol is identical to females.[7]

Most common genetic mutations for breast cancer risk are BRCA1 and BRCA2.[8] The moderate risk BRCA1/2 mutation affects the pathways in DNA repair, having contribution of <5% risk for BC.[9] In cases MBC, BRCA2 mutations are more common than BRCA1, responsible for 60–76% of MBC in high-risk families while the frequency of BRCA1 mutations varies from 10% to 16%.[10,11] Among benign male breast lesions, gynaecomastia represents the most prevalent condition. Invasive ductal carcinoma (IDC) is the most common malignant cancer in males.[12] Modified triple assessment are useful diagnostic modality for evaluation of breast lesions with accuracy of 98%.[13] The triple assessment comprises of clinical breast examination, diagnostic mammography and fine needle aspiration cytology.[14] Treatment for breast lesion depends on the root cause which may vary from simple pain medication to breast conservation surgery, Radical mastectomy with axillary lymph node dissection. For the diagnosis and categorization of breast lesions histopathology still plays an important role.[10] However awareness and routine screening is less appreciable among males due to its rarity.

Our study is done to assess and identify the histopathological spectrum and prevalence of benign and malignant male breast lesions at tertiary

cancer hospital.

### MATERIAL AND METHODS

A retrospective analysis based on data retrieved from the Pathology Department at Bhagwan Mahaveer Cancer Hospital and Research Centre across a study period of 15 years was conducted. The histopathology reports of breast cancer patients were undertaken from January 2007 to March 2021.

The following inclusion criteria of patients for this analysis were as follows: (a) patients with invasive breast carcinoma, (b) patients with available histological grade and lymph node status (c) available formalin-fixed, paraffin embedded samples with good quality (d) All mastectomy specimens and wide local excision specimens which were received for histopathological examination suspected for neoplastic and non-neoplastic lesions of the breast during the study period were included in the study. We excluded from the study patients who had no follow-up after initial diagnosis done pre-operatively.

The study was approved by Ethical Committee and informed consent was obtained. Total cases comprised almost 3750 where female cases were excluded for this study so 100 male breast cancer cases were finally approved. Relevant history, examination findings, age and clinical diagnosis were recorded from hospital registration form. Gross examination findings of specimens were recorded. All grossed, processed, stained sections of haematoxylin and eosin were reviewed and observed under microscope. All the cases were reported as per CAP protocol Breast.

### RESULTS

Three thousand and seven hundred fifty cases of breast carcinoma were reported at our centre, 100 cases were reported involving the male breast during the study period. All the cases were considered primary to the breast. The patients ranged in age from 30 to 83 years, mean age 58.59 years and median age 61 years was found as illustrated in Table 4. Of all the cases, 91(91%) cases were inhouse cases, operated at our centre whereas 9(9%) cases were outside cases for review, as shown in Table 2. Out of 100 male breast lesions, 74(74%) cases were found to be malignant and 26(26%) cases were found benign breast cases depicted in Table 1.

Among 74(74%) malignant cases, most common tumor laterality found was Right 37(50%) cases on whom Right Modified Radical Mastectomy (MRM) followed by 34(44.59%) cases of left side laterality who had undergone Left MRM whereas mastectomy was done in 3(5.40%) cases so laterality could not be determined as depicted in Table 3. The various histologic subtypes and their proportional distribution are outlined in Table 5. Pure invasive ductal carcinoma not otherwise specified was the most common histologic subtype, representing 58(78.38%) of all cases. Other well-represented

histologic subtypes were found, 4(5.40%) cases of infiltrating duct carcinoma with minimal invasion, 2(2.70%) cases each of mucinous carcinoma and metaplastic carcinoma, 3(4.05%) cases of poorly differentiated carcinoma. Other variants constituted 1(1.35%) cases of invasive papillary carcinoma, Invasive Lobular carcinoma, Phylloides tumor, Squamous cell carcinoma and Undifferentiated Pleomorphic sarcoma respectively. The benign breast lesion distribution is as follows: most common histological type found gynecomastia was seen in 19(73.07%) cases. Fibrocystic disease was seen in 7(26.92%) cases shown in Table 6.

**Table 1: Morphological Spectrum Of Male Breast Lesions**

Lesions	Percentage
Malignant cases	74 (74%)
Benign cases	26 (26%)
Total	100 (100%)

**Table 2: Distribution Of In House And Review Cases Retrieved**

Lesions	Percentage
Inhouse cases	91(91%)
Review cases	9(9%)
Total	100(100%)

**Table 3: Distribution Of Malignant Cases Based On Laterality**

Laterality of Malignant lesions	Percentage
Right	37(50%)
Left	34(44.59%)
Not identified	3(5.40%)
Total	74(100%)

**Table 4: Mean And Median Age Among Male Patients With Breast Lesion**

	Age (In years)
Mean age	58.59 year
Median age	61 year

**DISCUSSION**

Male breast cancer has many resemblance to female breast cancer but distinct functions are there that need to be appreciated. In recent years, there has been an increase in the incidence of this disease. In the NCDB dataset, a little over seven percent (7.2%) of the cases were diagnosed in 2004 which has reached 10.3% by 2014, this value of incidence has increased steadily.[15] The average age at diagnosis for men with breast cancer is 67years, which is about 5–10 years the average age at diagnosis for females.[16] The average age found in our patients was 58.59 years which was lower than found in other series.

Similar to female breast cancers, MBC is result of the concurrent effects of different risk factors, that includes disorders related to hormonal imbalances between excess of estrogen and a deficiency of testosterone, it may occur endogenously due to testicular abnormalities such as undescended testes, congenital inguinal hernia, orchitis,

**Table 5: Histopathological Spectrum Of Malignant Male Breast Cancers Identified During The Study Period**

Lesions	Percentage
Invasive Ductal Carcinoma	58(78.38%)
IDC with minimal invasion	4(5.40%)
Mucinous Carcinoma	2(2.70%)
Invasive Papillary Carcinoma	1(1.35%)
Poorly differentiated Carcinoma	3(4.05%)
Invasive Lobular Carcinoma	1(1.35%)
Others-	
Phylloides Tumor	1(1.35%)
Squamous Cell Carcinoma	1(1.35%)
Metaplastic Carcinoma	2(2.70%)
Undifferentiated Pleomorphic Sarcoma	1(1.35%)
Total	74(100%)

**Table 6: Histopathological Spectrum Of Benign Male Breast Cancers Identified During The Study Period**

Lesions	Percentage
Gynecomastia	19(73.07%)
Fibrocystic disease	7(26.92%)
Total	26(100%)

orchidectomy and testicular injury. few occupational and

environmental exposures, and genetic risk factors such as BRCA 1 and 2 gene mutations.[17]

The frequency, distribution, and histopathological spectrum of the various subtypes of MBC as compared with female counterpart may provide a valuable insight into the pathogenesis of both. Hittmair et al.[18] showed that in the male breast, papillary ductal carcinoma insitu(DCIS) occurred with a much higher frequency (46% ) than micropapillary, cribriform patterns (22% ). 5/114 showed comedo-type DCIS. It was concluded that predominance of papillary patterns among intraepithelial male breast lesions depicts relative abundance of ducts and the poorly developed terminal-ductal lobular units in male breast, true comedo DCIS is rare in male breast so authors speculated that the fully developed lobular environment and the female type hormonal influence might be required for its development.

In this study, we investigated in detail the frequencies and distribution of the various histologic subtypes in a large data set of invasive carcinomas seen at a tertiary cancer care center over 15 year period. Among 74 malignant cases, most common IDC occurred in 58(78.38%) cases, Fiala L et al. [19] and Ojara EA et al.[20] found similar results in their studies. Giordano et al.[8] reported that 2.6% of invasive malignancies in males were papillary carcinomas, as compared with 0.6% in females (p<0.0001), our cases depicted 1.35% occurrence rate

This study also confirms the occurrence of lobular carcinoma in the male breast, 1(1.35%) cases were found which was confirmed on Immunohistochemical findings with ER,PR positive 90%, 3+ each and E-cadherin negative. Joshi et al.[21] found one (4%) lobular carcinoma out of 27 cases, while Goss et al.[22] found 4 (1.9%) cases out of a total of 229. In the series of Giordano et al.[8], lobular carcinomas constituted 1.5% for their MBC.

MBC is usually unilateral, and rarely involves both breasts.[23] Similarly our findings show unilateral distribution of male breast cancers with Right 37(50%) and left 34(44.59%) however 3(5.40%) cases lacked laterality. Modified mastectomy was the most common surgical approach, and adjuvant hormone therapy is recommended in hormone receptor positive patients.[24] In our case, MRM was performed in 71(94.59%) cases whereas simple Mastectomy was done in 3(5.40%) cases. Gynecomastia was the most common benign breast lesion found in our study with 19(73.07%) cases, similar finding was found in study done by Narula HS et al.[25] who found gynecomastia is seen in 50% of all men and Johnson RE et al.[26] found it as the most common benign breast pathology, found in up to 55% of male breasts in 1 autopsy specimen series.

Sundriyal D et al. [27] found incidence of MBC 1.03 % . Other studies of MBC from India have variably reported the incidence. Chikaraddi SB et al.[28] have reported an incidence rate of 0.4 % of all breast cancer. A study done by Rai B et al.[29] from north India, revealed the incidence 0.5 % while Shah P et al.[30] have reported a relatively high incidence of 4.1 % from Kashmir. In our study incidence rate was found 2.66%.The majority of male breast lesions are benign; malignancy of the male breast is rare.[31] But in our case study, malignant cases 74(74%) cases were found more as compared to benign 26(26%) as our institution is a tertiary cancer care centre.

**CONCLUSION**

Invasive carcinoma of the male breast have variable histomorphological spectrum and distribution, which is comparable to invasive carcinoma of the female breast. Invasive Lobular carcinoma is exceedingly rare but was seen in this series. Breast cancer in Indian males is seen at a relatively early age and the disease has more aggressive nature. A comprehensive multi-institutional study is required to exactly delineate the behaviour of the disease and to better understand the clinical spectrum.

**REFERENCES**

- Nikumh D, Kanthikar S, Suryawanshi K, Jagtap S, Dravid N, Gondane S. Histopathological Spectrum of Unusual Breast Lesions: A Seven Year Retrospective Review. *Indian J Pathol Oncol* 2016;3(3):456.
- Common cancer sites - cancer stat facts [Internet].SEER. <https://seer.cancer.gov/statfacts/html/common.html>
- Mthur P, Sathishkumar K, Chaturvedi M, Das P, Stephen S. Cancer incidence estimates for 2022 & projection for 2025: Result from National Cancer Registry Programme, India. *Indian J Med Res*. 2023;0(0):0. [http://dx.doi.org/10.4103/ijmr.ijmr\\_1821\\_22](http://dx.doi.org/10.4103/ijmr.ijmr_1821_22).
- Moolamalla RM, Raghu K. Histopathological spectrum of neoplastic and non-neoplastic breast lesions-a two year study. *Int J Sci Stud* 2017;4(11):158-62.
- Obata A, Okauchi S, et al. Advanced breast cancer in a relatively young man with severe

- obesity and type 2 diabetes mellitus. *J Diabetes Investig* 2017;3:395-396.
6. Schanz S, Schreiber G, Zitzmann M, et al. S1 guidelines: Gynecomastia in adults. *JDDG* 2017;4:465-472.
  7. Khalkhali I, Cho J. Male breast cancer imaging. *The Breast Journal* 2015;3:217-218.
  8. S.H. Giordano, D.S. Cohen, A.U. Buzdar, et al., Breast carcinoma in men: a population-based study. *Cancer* 101 (2004) 51–57.
  9. S.H. Giordano, A review of the diagnosis and management of male breast cancer. *Oncologist* 10 (2005) 471–479.
  10. K.C. Johnson, S. Pan, Y. Mao, Risk factors for male breast cancer in Canada, 1994–1998. *Eur. J Cancer Prev.* 11 (2002) 253–263.
  11. H.T. Sorensen, M.L. Olsen, L. Mellemkjaer, et al., The intrauterine origin of male breast cancer: a birth order study in Denmark. *Eur. J. Cancer Prev.* 14(2005) 185–186.
  12. Yen PPW, Sinha N, Barnes PJ, Butt R, Iles S. Benign and malignant male breast diseases: Radiologic and pathologic correlation. *Can Assoc Radiol J.* 2015;66(3):198-207. doi.org/10.1016/j.carj.2015.01.002.
  13. Solanki PV, Juneja IA, Chaudhari ND. Modified triple assessment in the diagnosis of breast lump in Saurashtra region of Gujarat. *Int Surg J.* 2020;7(10):3289. http://dx.doi.org/10.18203/2349-2902.isj202004124.
  14. Tan SM, Behranwala KA, Trott PA, Nasiri NA, Moskvic E Brown G et al. A retrospective study comparing the individual modalities of triple assessment in the preoperative diagnosis of invasive lobular breast carcinoma. *Eur J Surg Oncol* 2002; 28: 203-8.
  15. Konduri S, Singh M, Bobustuc G, Rovin R, Kassam A. Epidemiology of male breast cancer. *Breast.* 2020 Dec;54:8-14. doi: 10.1016/j.breast.2020.08.010.
  16. Cutuli B, Le-Nir CC, Serin D, Kirova Y, Gaci Z, Lemanski C, et al. Male breast cancer. Evolution of treatment and prognostic factors. Analysis of 489 cases. *Crit Rev Oncol Hematol.* 2010 Mar;73(3):246-54. doi: 10.1016/j.critrevonc.2009.04.002.
  17. Thomas DB, Jimenez LM, McTiernan A, Rosenblatt K, Stalsberg H, Stenmagen A, et al. Breast cancer in men: risk factors with hormonal implications. *Am J Epidemiol.* 1992 Apr 1;135(7):734-48. doi: 10.1093/oxfordjournals.aje.a116360.
  18. Hittmair AP, Lininger RA, Tavassoli FA (1998) Ductal carcinoma in situ (DCIS) in the male breast: a morphologic study of 84 cases of pure DCIS and 30 cases of DCIS associated with invasive carcinoma—a preliminary report. *Cancer.* 15(83):2139–2149.
  19. Fiala L, Coufal O, Fait V, Foretová L. Male breast cancer—our experience. *Rozhl Chir.* 2010 Oct;89(10):612-8.
  20. Ojara EA. Carcinoma of the male breast in Mulago Hospital, Kampala. *East Afr Med J.* 1978 Oct;55(10):489-91.
  21. Joshi MG, Lee AKC, Loda M, Camus MG, Peterson C, Heatley GJ, Hughes KS (1996) Male breast carcinoma: an evaluation of prognostic factors contributing to a poor outcome. *Cancer.* 77:490–498.
  22. Goss PE, Reid C, Pintilie M, Lim R, Miller N (1999) Male breast carcinoma: a review of 229 patients who presented to the Princess Margaret Hospital during 40 years: 1955–1996. *Cancer.* 85:629–639.
  23. Lakhani SR, Ellis IO, Schnitt SJ, Tan PH, van de Vijver MJ. WHO Classification of Tumours of the Breast. 4th edition. Lyon: *IARC*; 2012.
  24. Korde LA, Zujewski JA, Kamin L, Giordano S, Domchek S, Anderson WF, Bartlett JM, et al. Multidisciplinary meeting on male breast cancer: summary and research recommendations. *J Clin Oncol* 2010; 28: 2114-22.
  25. Narula HS, Carlson HE. et al. Gynecomastia-pathophysiology, diagnosis and treatment. *Nat Rev Endocrinol.* 2014;10:684-698. doi: 10.1038/nrendo.2014.139
  26. Johnson RE, Murad MH. et al. Gynecomastia: pathophysiology, evaluation, and management. *Mayo Clin Pro.* 2009;84:1010e5.
  27. Sundriyal D, Kotwal S, Dawar R, Parthasarathy KM et al. Male Breast Cancer in India: Series from a Cancer Research Centre. *Indian J Surg Oncol.* 2015 Dec;6(4):384-6. doi: 10.1007/s13193-015-0473-1.
  28. Chikaraddi SB, Krishnappa R, Deshmane V (2012) Male breast cancer in Indian patients: is it the same? *Indian J Cancer* 49(3):272–276.
  29. Rai B, Ghoshal S, Sharma SC. Breast Cancer in males: a pgimer experience. *J Cancer Res Ther* 2005;1(1):31–33.
  30. Shah P, Robbani I, Shah O (2009) Clinicopathological study of male breast carcinoma: 24 years of experience. *Ann Saudi med* 29(4):288–293.
  31. Ng AM, Dissanayake D, Metcalf C, Wylie E. Clinical and imaging features of male breast disease, with pathological correlation: a pictorial essay. *J Med Imag Radiat On.* 2014;58(2): 189–198.