International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

Clinicopathological Profile of Male Breast Cancer Patients Managed at a Tertiary Care Center in India.

Dr Rahul Agarwal[1], Dr Brijesh Kumar Shukla[2], Dr Ashish Agarwal[3], Dr Syed Alim[4]

[1]Associate Professor, Department of General Surgery, ASMC and M.B Hospitals Bahraich, Uttar Pradesh, India
[2]Assistant Professor, Department of General Surgery, ASMC and M.B Hospitals Bahraich, Uttar Pradesh, India
[3]Professor, Department of Anaesthesia, ASMC and M.B Hospitals Bahraich, Uttar Pradesh, India
[4]Senior Resident, Department of General Surgery, ASMC and M.B Hospitals Bahraich, U.P, India*

Corresponding Author:

Dr Syed Alim
Senior Resident, Department of General Surgery, ASMC and M.B Hospitals Bahraich, U.P, India
Email id:
Rahul.rahulagarwal0807@gmail.com

Received: 17-01-2026
Accepted: 25-02-2026
Available online: 28-02-2026

ABSTRACT

Background: Breast cancer in male subjects is a rare disease which contributes to nearly 1% all the cancers seen in male subjects. Male usually present with the disease in the advanced stages. However, it is less studied in the male subjects in India.
Aim: The present study was aimed to assess the clinicopathological profile as histological subtypes, tumor characteristics, and treatment modalities in male subjects with breast cancer in Indian context.
Methods: The study assessed 60 male subjects that presented with the breast cancer to the Institute within the defined study period. In all the subjects clinicopathological profile as histological subtypes, tumor characteristics, and treatment modalities were assessed. The data gathered were analyzed statistically.
Results: The most common location and presentation was retro areolar area and presentation was a painless lump in the breast of the subjects. Mean tumor size was 3.3cm. Most common presentation stage was II and most common histological subtype was invasive ductal carcinoma. Luminal A, luminal B, and triple-negative breast cancer was seen in 76%, 20%, and 4% subjects. Upfront surgery was done in 83% subjects with breast conservation surgery (BCS) and modified radical mastectomy (MRM) in 8% and 83% subjects respectively. In 17% (n=8) subjects, Neoadjuvant chemotherapy (NACT) was done. Disease was relapsed in 34% subjects. Mean relapse time was 32 months and 23% mortality rate was seen. Overall mean survival rate was 40 months.
Conclusion: The present study concludes that majority of the male breast cancer present with early-stage cancer, hormone receptor-positive, and invasive ductal carcinoma. The stage of the disease and status of the hormone receptor contribute to the main prognostic factor in male breast carcinoma.

Keywords*:* Breast conservation surgery**,** Hormone receptor (HR), Invasive ductal carcinoma, male breast cancer, modified radical mastectomy.

INTRODUCTION

Breast cancer in male subject's accounts for nearly 1% of all the cancers seen in the male subjects and less than 1% of all the cases of breast cancer seen clinically. There are various genetic factors that have been linked to breast cancer in males including mutation in BRCA2 which is considered to contribute to majority of inherited breast cancer in men, positive family history, and Klinefelter syndrome. Also, there are suspected factors that lead to breast cancer including CHEK2 mutations, Cowden syndrome, CYP17 polymorphism, and androgen receptor (AR) gene mutations.[1]

Owing to the exiguity in male breast cancer cases, the existing literature has limited studies that assessed the breast cancer in male subjects. Majority of the data concerning the management of breast cancer in male subjects has not been in randomized design as done in male subjects. The risk associated with the breast cancer in these subjects include various

hormone related disorders as exposure to the radiation, testicular disorders (cryptorchidism, mumps orchitis, and orchidectomy), and obesity.[2]

Other suspected epidemiological risk factors for male breast cancer include dietary factors (meat intake and alcohol intake), high temperatures), polycyclic aromatic hydrocarbons, electromagnetic fields, occupational exposures, gynecomastia, and prostrate cancer. Presentation of male breast cancer is usually a painless lump which is usually presented late and in stage III and IV in >40% of the subjects. Nearly 50% subjects have minimum one lymph node involved at the time of diagnosis. Surgery performed is usually mastectomy with sentinel node biopsy or axillary clearance. Majority of these tumors are positive for hormone receptor. Chemotherapy and radiotherapy are usually done for indications similar to the breast cancer in females.[3]

In cases of metastasis, primarily the treatment is done with the hormonal therapy, however, chemotherapy can also lead to palliation. Assessment of 1-year and 5-year survival rate in the male subjects with breast cancer can help in guiding the healthcare-related decisions concerning the early detection of the breast cancer and in establishment of programs that can support the male that are breast cancer survivors and males that are at high risk of the breast cancer.[4] The present study was aimed to assess the clinicopathological profile as histological subtypes, tumor characteristics, and treatment modalities in male subjects with breast cancer in Indian context.

MATERIAL AND METHODS

The present clinical assessment study was aimed to assess the clinicopathological profile as histological subtypes, tumor characteristics, and treatment modalities in male subjects with breast cancer in Indian context. The study was done at Department of General Surgery, ASMC And M.B Hospitals Bahraich, Uttar Pradesh. The study subjects were from Department of General Surgery of the Institute. Verbal and written informed consent were taken from all the subjects before study participation.

The study assessed 60 male subjects that presented with the breast cancer to the Institute within the defined study period. In all the subjects clinicopathological profile as histological subtypes, tumor characteristics, and treatment modalities were assessed. The data gathered were analyzed statistically.

In all the subjects, data were gathered concerning clinicopathological characteristics that was retrieved from the medical and patient records of the Institute. After data collection, the male breast cancer was classified into four molecular subtypes as basal subtypes according to ER, PR, and HER2/neu status—Luminal A, luminal B, HER2/neu-enriched.

A cytogenetic study was done to diagnose various syndromes as Klinefelter syndrome which was not following the retrospective manner as the electronic medical records were not sufficient. The data gathered were analyzed statistically with chi-square test, Fisher's exact test, Mann Whitney U test, and SPSS (Statistical Package for the Social Sciences) software version 24.0 (IBM Corp., Armonk. NY, USA) using ANOVA, chi-square test, and student's t-test. The significance level was considered at a p-value of <0.05.

RESULT

The present clinical assessment study was aimed to assess the clinicopathological profile as histological subtypes, tumor characteristics, and treatment modalities in male subjects with breast cancer in Indian context. Among 60 subjects assessed, no risk factor was seen in any subject and mean age of diagnosis was 57 years. The most common location was retro areolar seen in 70% subjects followed by subareolar area in 10% and remaining 3% each in other quadrants. Tumor laterality was equal. Most common presentation was lump and ulcer seen in 80% and 20% subjects respectively. Mean tumor size was 3.3 cm. most common presentation stage was II followed by I and III as seen in 47%, 23%, and 20% subjects respectively (Table 1).

S. No	T	n	%	N	n	%	Stage	n	%
1.	**T_{18}**	2	3	**N0**	22	36	**Stage 0**	4	6.7
2.	**T1**	8	13	**N1**	30	50	**Stage 1**	12	20
3.	**T2**	26	43	**N2**	8	13	**Stage 2**	28	47
4.	**T3**	8	26	**N3**	0		**Stage 3**	12	20
5.	**T4**	16	27				**Stage 4**	4	6.7

Table 1: Clinical staging and grading of cancer in study subjects

It was seen that invasive ductal carcinoma with no special type was most commonly seen histological subtype in 77% subjects where Grade 2 and Grade 3 tumors were seen in 61% and 39% subjects respectively. Papillary carcinoma was seen in 10% (n=6) subjects and ductal carcinoma in situ in 6% (n=4) subjects where two had previously undergone a lumpectomy and other 2 had vague lump. In 3% (n=2) subjects, mucinous carcinoma was seen and other 3% had medullary carcinoma. Most common molecular subtype was luminal A followed by luminal B and TNBC in 76%, 20%, and 4%

subjects respectively. Among 60 subjects, 6.7% (n=4) subjects, de novo metastatic breast cancer (MBC) was seen where no further therapy was given. In 93.3% non-metastatic subjects, definitive treatment was planned where 10 subjects did not visit for further recalls.

In 46 subjects, 83% (n=38) subjects were planned as upfront surgery where 74% (n=34) subjects underwent MRM (modified radical mastectomy) and 4 subjects underwent breast conservation surgery with tumor size of 1-1.5cm. A separate incision was used for the axillary clearance. Neoadjuvant chemotherapy was done in 17% (n=8) study subjects. NACT was completed in 6 subjects followed by MRM and NACT was being continued in 2 subjects. In 44 subjects, adjuvant treatment was planned where 26 showed a complete compliance and 18 subjects were irregular. Adjuvant hormonal therapy, radiotherapy, and chemotherapy was done in 20, 12, and 22 subjects respectively (Table 2 and 3).

S. No	Histological subtypes	n=30	%	Molecular subtypes	n=30	%
1.	**Medullary**	2	3	HER2/neu-enriched	0	0
2.	**Mucinous**	2	3	Triple negative	2	4
3.	**Papillary**	6	10	Luminal B	8	20
4.	**Invasive ductal carcinoma (NST)**	36	77	Luminal A	50	76
5.	**Ductal carcinoma in situ**	4	6.7			

Table 2: Pathological characteristics of male breast cancer in study subjects

S. No	Parameter	n	%
1.	**Surgery**		
a)	BCS	4	8
b)	Modified radical mastectomy	34	74
c)	Operated somewhere else	8	17
d)	Upfront surgery	38	83
2.	**Neoadjuvant chemotherapy**	8	17
3.	**Adjuvant chemotherapy**	22	50
4.	**Adjuvant radiation therapy**	12	27
5.	**Hormonal therapy**	20	45

Table 3: Treatment modalities adopted in study subjects

In 18 subjects that were irregular for adjuvant treatment, 12 subjects showed recurrent disease where 10 subjects had distant metastasis and 2 subjects had locoregional recurrence in chest wall with skeletal metastasis. In 26 subjects that were compliant with the treatment, 4 subjects showed distant metastasis 2 each in bone and lung being on hormonal therapy. In 14 subjects, mortality was reported 4 with metastatic cancer at initial presentation, 6 patients who defaulted during adjuvant treatment, and 4 patients who had recurrence after completion of treatment. Subjects had mean relapse of 30 months. In 23% subjects, mortality was seen in subjects that were non-compliant with treatment. Three-year overall survival rate was 40 months (Table 4).

S. No		n=16
1.	**>1 site (brain, adrenal gland, mediastinal lymph nodes)**	4
2.	**Skeletal**	6
3.	**Liver**	2
4.	**Lung**	2
5.	**Skeletal metastasis with loco regional recurrence**	2

Table 4: Recurrence in the study subjects

DISCUSSION

In 60 subjects assessed, no risk factor was seen in any subject and mean age of diagnosis was 57 years. The most common location was retro areolar seen in 70% subjects followed by subareolar area in 10% and remaining 3% each in other quadrants. Tumor laterality was equal. Most common presentation was lump and ulcer seen in 80% and 20% subjects respectively. Mean tumor size was 3.3 cm. most common presentation stage was II followed by I and III as seen in 47%, 23%, and 20% subjects respectively. These characteristics were comparable with the work of Wang F et al[5] in 2019 and Comersi S et al[6] in 2021 where authors assessed male subjects wit comparable characteristics in their studies as in the present study.

The study results showed that invasive ductal carcinoma with no special type was most commonly seen histological subtype in 77% subjects where Grade 2 and Grade 3 tumors were seen in 61% and 39% subjects respectively. Papillary carcinoma was seen in 10% (n=6) subjects and ductal carcinoma in situ in 6% (n=4) subjects where two had previously undergone a lumpectomy and other 2 had vague lump. In 3% (n=2) subjects, mucinous carcinoma was seen and other 3% had medullary carcinoma. Most common molecular subtype was luminal A followed by luminal B and TNBC in 76%, 20%, and 4% subjects respectively. Among 60 subjects, 6.7% (n=4) subjects, de novo metastatic breast cancer (MBC) was seen where no further therapy was given. In 93.3% non-metastatic subjects, definitive treatment was planned where 10 subjects did not visit for further recalls. These results were consistent with the findings of Pemmaraju N et al[7] in 2012 and Xu S et al[8] in 2012 where subtypes in similar proportion were also reported by the authors in their studies.

It was seen that in 46 subjects, 83% (n=38) subjects were planned as upfront surgery where 74% (n=34) subjects underwent MRM (modified radical mastectomy) and 4 subjects underwent breast conservation surgery with tumor size of 1-1.5cm. A separate incision was used for the axillary clearance. Neoadjuvant chemotherapy was done in 17% (n=8) study subjects. NACT was completed in 6 subjects followed by MRM and NACT was being continued in 2 subjects. In 44 subjects, adjuvant treatment was planned where 26 showed a complete compliance and 18 subjects were irregular. Adjuvant hormonal therapy, radiotherapy, and chemotherapy was done in 20, 12, and 22 subjects respectively. These findings were in agreement with the results of Eggemann H et al[9] in 2013 and Yadav S et al[10] in 2020 where surgical data comparable to the present study was also reported by the authors.

Among 18 subjects that were irregular for adjuvant treatment, 12 subjects showed recurrent disease where 10 subjects had distant metastasis and 2 subjects had locoregional recurrence in chest wall with skeletal metastasis. In 26 subjects that were compliant with the treatment, 4 subjects showed distant metastasis 2 each in bone and lung being on hormonal therapy. In 14 subjects, mortality was reported 4 with metastatic cancer at initial presentation, 6 patients who defaulted during adjuvant treatment, and 4 patients who had recurrence after completion of treatment. Subjects had mean relapse of 30 months. In 23% subjects, mortality was seen in subjects that were non-compliant with treatment. Three-year overall survival rate was 40 months. These results correlated with the findings of Leone JP et al[11] in 2016 and Chhabra MK et al[12] in 2021 where adjuvant treatment data similar to the present study was also reported by the authors in their studies.

CONCLUSION

Within its limitations, the present study concludes that majority of the male breast cancer present with early-stage cancer, hormone receptor-positive, and invasive ductal carcinoma. The stage of the disease and status of the hormone receptor contribute to the main prognostic factor in male breast carcinoma.

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