

## Study on Male Breast Cancer

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### Abstract

**Background :** Male Breast Cancer (MBC) is a rare disease all over the world accounting for less than 1% of all breast cancers. Histopathologically most of the cases are infiltrating ductal carcinoma. Treatment depends on the stage and biological behavior like ER, PR and HER-2 status of the disease, general condition and other comorbidities of the patient. Like female breast cancer, different modalities like surgery, chemotherapy, radiotherapy, hormone therapy, immunotherapy and targeted therapy are the mainstay of treatment. This analytical study was carried out to see the clinical and biological behavior, risk factors and treatment pattern of the disease.

**Materials and methods:** This analytical study was carried out in the Department of Radiotherapy, Chittagong Medical College Hospital and Centre for Specialized Care and Research Hospital, Chattogram from January 2005 to July 2020. Total 28 numbers of patients of postoperative breast cancer were enrolled in the study. Case records including follow up records were collected for all cases. Clinical, histopathological and molecular biomarker data were analyzed.

**Results:** Majority of the patients (20 in number, 71.43%) belonged to age group 51-70 years. 23 patients (82.14%) were smoker. 19 patients (67.8%) had lump in the left breast. Infiltrating duct cell carcinoma was the dominant histopathological type. More than 90% cases were of this type of histopathology. All the cases presented with axillary lymph node metastases. One patient had second malignancy who was previously diagnosed and treated as a case of lung cancer. Two patients had positive family history of breast cancer.

**Conclusion:** As a rare disease, sample size was very small in this study. Comprehensive multi center studies are needed to better understand this disease.

**Key words:** Gynecomastia; Male breast cancer; Smoker; Treatment.

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### Introduction

Male breast cancer is a relatively rare neoplasm accounting for less than 1% of all breast cancers.<sup>1</sup> It accounts for less than 1% of cancers in men.<sup>2</sup> It is a disease of the elderly, with a peak incidence around 60 years of age. Majority of the cases are infiltrating duct carcinomas (70%-95%).<sup>3</sup>

National Cancer Institute data on cancer survival in the US shows increase in the incidence of male breast cancer from 0.86-to 1.08 per 100,000 men.<sup>4</sup> Incidence of male breast cancer with advancing patientage is climbing steadily until a plateau is reached at around age 80.<sup>5,6</sup>

The etiology of male breast cancer is unclear but hormonal levels may play a role in the development of male breast cancer. Benign breast conditions, including history of breast trauma and nipple discharge, have also been reported to increase risk.<sup>7,8</sup> Male breast cancer in patients with BRCA2 mutations tends to present at a younger age and may be associated with a poorer survival.<sup>9</sup> Male breast cancer has high rates of hormone-receptor expression. Approximately 90% of male breast cancers express the estrogen receptor, and 81% express the progesterone receptor.<sup>4</sup> Tumor size and lymph node involvement are two clear prognostic factors for male patients with breast cancer.<sup>3</sup> Men with tumors measuring 2-5 cm. have a 40% higher risk of death than men with tumors <2 cm in maximum diameter.<sup>4</sup>

Male breast cancer is a rare disease, hence data regarding epidemiology, clinical, histopathological and biological behavior of the disease are lacking. Optimal treatment approaches are also not established yet. This hospital based analytical study was done to find out the incidence, clinico-pathological behavior and treatment pattern of the disease among the people living in the southern part of the country.

### Materials and methods

Diagnosed cases of male operable breast cancer patients attended to the Department of Radiotherapy, Chittagong Medical College Hospital and

CSCR for oncological management during the period of 1<sup>st</sup> January 2005 to July 2020 were included in the study. A total number of 28 patients were included in the study. Before commence the study necessary permission was obtained from the proper authorities.

Detail history was taken and thorough physical examination was done. Relevant investigations including complete blood count, liver function test, kidney function test, ECG, ultrasonography of whole abdomen, isotope whole body bone scan were done before surgery to determine the stage of the disease. Three weeks after the surgery base line investigations were done before starting chemotherapy. 20 patients were planned for eight cycles of chemotherapy. Chemotherapy schedule was AC-T (Doxorubicin, Cyclophosphamide, Taxotere) four cycle of AC followed by four cycle of T. 8 patients were planned for sixteen cycles of chemotherapy. Chemotherapy schedule was AC-P (Doxorubicin, Cyclophosphamide, Paclitaxel) four cycle of AC followed by twelve cycle of Paclitaxel weekly. Three weeks after completion of chemotherapy patients were planned for External Beam Radiotherapy in cobalt 60 machine, total dose-50Gy in 25 fractions to chest wall and 50 GY in 25 fractions to supraclavicular nodes.

#### Inclusion criteria

- i) Postoperative histopathologically proven male breast cancer patients of any age.
- ii) Kernofsky performance status  $\geq 60$ .
- iii) No previous history of chemotherapy and radiotherapy.
- iv) Adequate organ function.

#### Results

This analytical study was carried out in the Department of Radiotherapy, Chittagong Medical College Hospital from January 2005 to July 2020. Total 28 numbers of male patients of operable breast cancer were enrolled in the study. In the assigned studied population 23 (82.14%) were smoker.

**Table I :** Distribution of patient by smokers (n=28)

	Population	Percentage (%)
Smoker	23	82.14%
Non Smoker	5	17.86%
Total	28	

**Table II :** Distribution of Patient by status (n=28)

Receptor Status	Population	Percentage (%)
ER +Ve	20	71.43%
PR +Ve	14	50%
Her2 +Ve	3	10.72%
Triple -Ve	3	10.72%

About 75% of the cases hailed from rural area and the rest belonged to urban area.

**Table III :** Distribution of Patient by area (n=28)

	Population	Percentage (%)
Rural Area	21	75%
Urban Area	7	25%
Total	28	

Among the studied population 2(7.14%) were in between age group 30 to 50 years, 20(71.42%) in the age group 51 to 70 years and rest 6(21.4%) were of 71 to 90 years of age. Majority 20 (71.42%) of the patient belonged to age group between 50-70 years.

**Table IV :** Distribution of patient by age group (n=28)

Age	Population	Percentage (%)
(30-50) years	2	7.14%
(51-70) years	20	71.43%
(71-90) years	6	21.43%
Total	28	

Nineteen patients (67.8%) had lump in the left breast and five patients had lump in the right breast.

**Table V :** Distribution of patient by lump position (n=28)

Lump	Population	Percentage (%)
Left Breast	19	67.8%
Right Breast	9	32.2%
Total	28	

Location of the tumor was central or sub-areolar in 14 (50%) patients, followed by upper outer quadrant 7(25%) upper inner quadrant 3(10.72%) lower outer quadrant 2(7.14%) and lower inner quadrant in 2(7.14%).

In 25 patients' histopathology report revealed infiltrating ductal carcinoma. Remaining 3 patients had invasive lobular carcinoma. All the patients were presented with axillary lymph node metastases. Radical mastectomy was done in 80% of patients and simple mastectomy was done in 20% of patients. Second malignancy was observed in one patient who was previously diagnosed and treated for lung cancer. Two patients had positive family history of breast cancer.

## Discussion

MBC is a rare disease, which presents mostly in the latter decades of life. Men have a higher rate of ER positivity, which accounts for good responses with hormonal agents like tamoxifen. Most males present with advanced clinical stage of the disease due to a lack of awareness. Diagnosis is with a mammogram and Fine Needle Aspiration Cytology (FNAC) or core biopsy. All patients should be staged completely to exclude metastasis. The treatment of localized disease is by performing a modified radical mastectomy. Adjuvant therapy is mainly tamoxifen as most are strongly ER positive. Chemotherapy may be useful in node positive and locally advanced disease although more evidence is needed for appropriate regimens. The use of adjuvant RT has not been conclusively proven to reduce local recurrence. The treatment of metastatic disease is mainly hormonal which has shown good survival in some studies versus a poor outlook in others. More research and trials have to be conducted to find out the effect of hormonal agents like aromatase inhibitors.<sup>2</sup>

The most common presenting symptoms in male breast cancer patients are a painless subareolar lump, nipple retraction, and bleeding from the nipple.<sup>10-11</sup> As in women, there is a slight preponderance of left-sided versus right-sided disease.<sup>12</sup> Usually the primary consideration in the differential diagnosis is gynecomastia, which affects approximately 30% of healthy men.<sup>13</sup>

Mammography can be helpful in differentiating gynecomastia from malignant breast disease. The sensitivity and specificity of mammography for the diagnosis of male breast cancer have been reported to be 69% and 87% respectively. Ultrasonography can also be a useful adjunct and provide information regarding nodal involvement. After appropriate local imaging, any suspicious mass needs to be biopsied to confirm the diagnosis.<sup>14</sup>

The extent of disease can be determined from laboratory evaluation, chest radiography, bone scan, and computed tomography scan of the abdomen, as clinically appropriate. Tumor stage is determined using the American Joint Committee on Cancer classification system, which considers tumor size, nodal involvement, and distant metastases.<sup>15</sup>

Sub-Saharan countries with high rates of liver cirrhosis related to schistosomiasis also have higher incidence of male breast cancer.<sup>16</sup>

Approximately 15% to 20% of men with breast cancer report a family history of breast or ovarian cancer. It is estimated that approximately 10% men with breast cancer have a genetic predisposition, and BRCA2 is the most clearly associated gene mutation.<sup>17-20</sup> BRCA1 is also associated associations have also been suggested for PTEN, P53 and CHEK2.<sup>21-24</sup> Other well described risk factors for breast cancer in men include age, race and radiation exposure.<sup>25</sup> At all ages black men have a higher incidence than the white. Black men also tend to have poorer prognostic feature, such as advanced stage, larger tumor size more nodal involvement, and higher tumor grade, compared with their white counterpart.<sup>26</sup> In the present study four patients had positive family history of breast cancer. This supports the mentioned statement.

Other risk factors include hormonal factors, previous breast cancer, and environmental exposures.<sup>27</sup> Cirrhosis of liver, obesity, congenital inguinal hernia, orchiectomy, orchitis, and exogenous estrogen result in an increased circulation estrogen level and, therefore, may contribute to an increased risk of male breast cancer.<sup>28,29</sup> Five Years survival rates for male breast cancer ranges from 36% to 66%.<sup>30,31</sup>

Men with a diagnosis of breast cancer are at increased risk of a second malignancy. In a The Surveillance, Epidemiology and End Results (SEER) data base review that included 4873 men with breast cancer diagnosed between 1973 and 2003, there was 1.9% incidence of second primary male breast cancer. In this study 21% of men with breast cancer developed second non-breast malignancy, the most common reported second malignancies were prostate, colon and genitourinary cancers.<sup>32</sup>

The diagnosis of male breast cancer is generally made on cytology or core biopsy. Male breast tumors tend to be in the areolar region. Mammographically, microcalcifications are less commonly seen in lesions in men than in women<sup>33</sup>, Present study supports the statement as 50% patients had subareolar growth and the affected breast was left breast in 19 (67.8%) patients.

In recent review of male breast cancer, the majority of tumors were invasive ductal carcinoma (85% to 95%) followed by ductal carcinoma in situ (5% to 10%). Invasive papillary carcinoma is more common in males than females accounting for approximately 2% to 4% of breast cancers in men compared to 1% in women. In our study out of 28 patients, 25 had ductal carcinoma. Male breast cancer seems to be more hormone receptor Positive (ER and PgR) than female breast cancer, Paradoxically, HER2 positive also seems higher in male breast cancer than in the female breast cancer.<sup>33</sup>

Most common surgical procedure for male breast cancer is modified radical mastectomy. Axillary nodal involvement is the strongest predictor of both local recurrence and metastatic risk and is present in approximately 50% of men with breast cancer.<sup>34</sup>

In the present study 80% patients underwent Modified Radical Mastectomy (MRM) and 20% simple mastectomy. All the patients were with Positive axillary nodes. Use of adjuvant chemotherapy in male breast cancer is associated with younger age, high tumor grade and axillary node involvement. The main stay of systemic therapy for hormone receptor-positive male breast cancer is hormone therapy. Tamoxifen is the most extensively used and studied. Other hormone therapy includes Luteinizing Hormone Releasing Hormone (LHRH) agonists, orchiectomy, estrogens and progestins.<sup>34</sup>

In our study, 70% of Hormone +Ve patients got Tamoxifen, 20% of patients got Letrozole. Her2 +Ve patients from 12% only 7% got Trastuzumab.

#### Limitations

As it is a rare disease, so the sample size was small. Regular follow was not possible due to lack of awareness.

#### Conclusion

Male breast cancer remains a rare disease, although the incidence is increasing. Due to rarity of the disease sample size of this study is very small and hence it is very difficult to draw any conclusion from this study. Nevertheless, our study shows some correlation of the disease with smoking, positive family history, previous history of radiation. In comparison to female the average of diagnosis is also slightly higher. Like female

breast cancer most of the histologic subtype is duct cell carcinoma. Estrogen and progesterone receptor expression is higher than female breast cancer. Comprehensive, multi center studies are needed to better understand this rare disease.

#### Recommendation

To evaluate response and survival of male breast cancer further study with large and longer period is recommended. As it is a rare disease so, every case should be recorded, reported and included in cancer registry.

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#### Contribution of authors

SMY- Conception, design, manuscript writing, critical revision & final approval.

AAC- Design, critical revision & final approval.

MRH- Manuscript writing, citing references, critical revision & final approval.

AKMI- Manuscript writing, critical revision & final approval.

FA- Citing references, critical revision & final approval.

SUT- Citing references, critical revision & final approval.

#### Disclosure

All the authors declared no competing interest.

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