Characteristics and Treatment of Breast Cancer in Men: A 12-year Single-Institution Review

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Summary

Background: Male breast cancer has a low incidence, hence there are few studies evaluating the disease, and no recent studies from Kenya. **Objective:** The objective of this study was to evaluate the clinical and pathological characteristics, and treatment of men diagnosed with breast cancer. **Methods:** This is a retrospective descriptive study, carried out at a tertiary hospital in Nairobi, Kenya, of men diagnosed with breast cancer between January 2009 and December 2021. Data on the clinicopathological characteristics, treatment, and outcome were collected. Standard descriptive statistics were used to describe the patient characteristics. **Results:** Seventeen male patients were diagnosed with breast cancer, representing 1.40% of all breast cancer patients. Four patients were excluded due to incomplete records. The median age at diagnosis was 68 years (range 28–83). The majority were African Bantu (*n*=11, 84.6%). Most patients presented with clinical T1 (*n*=10, 76.9%) and N0 (*n*=8, 61.5%) disease. Luminal A molecular subtype was the most common (*n*=8, 61.5%). All 11 patients who underwent operative management underwent modified radical mastectomy. **Conclusion:** The rate of male breast cancer was similar to the global rate. The majority of our patients presented with early breast cancer and estrogen receptor-positive disease. Treatment was primarily modified radical mastectomy followed by adjuvant systemic therapy.

Keywords: Male, Breast, Cancer

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Introduction

Male breast cancer is a rare disease accounting for less than 1% of all breast cancers (1). However, the ratio of male-to-female breast cancers has been found to be higher in the African American and African populations at 1.4% and 4.2%, respectively (2).

Data from the Surveillance, Epidemiology, and End Results (SEER) program have shown an increase in the incidence of male breast cancer from 0.85 cases per 100,000 in 1975 to 1.43 cases per 100,000 in 2011 in the general population (3). Patients often present with a firm, painless breast lump and most tumors are >2 cm. Most of the breast cancers in men are invasive ductal carcinomas, while lobular carcinomas account for only 1% compared with 83.6% and 11.8%, respectively, in women (4).

The diagnostic workup of male breast cancer is similar to that of female breast cancer. Men aged >25 years presenting with a breast lump should undergo a mammogram as the initial investigation, with ultrasound recommended if the mammogram findings are

inconclusive or suggestive of cancer (5). The initial imaging of choice for men <25 years is ultrasound (5). Any suspicious mass found on imaging requires a core biopsy to confirm the diagnosis and determine the hormonal receptor and human epidermal growth factor receptor 2 (HER2) status (6). Staging for male breast cancer is the same as female breast cancer (6).

Breast cancer treatment in men is based on studies conducted on female patients, as male breast cancer is uncommon and conducting randomized controlled trials is challenging due to limited patient participation (7). However, male patients are more likely to undergo mastectomy, even for early-stage tumors (T1) (7). Adjuvant radiotherapy follows the guidelines established for women with breast cancer. Men at high risk of recurrence may receive neoadjuvant or adjuvant chemotherapy and targeted therapy for HER2 (8). Since most breast cancers in men are hormone receptor-positive, hormonal therapy, specifically tamoxifen, plays a crucial role in managing breast cancer in men (8).

Breast cancer in men was previously associated with a poorer outcome compared with women. However, retrospective studies that have matched for age, stage, and prognostic factors have found no difference in survival between breast cancer in men and women (9). Men were diagnosed with breast cancer at an older age and were more likely to die of non-breast cancer-related causes (9).

Studies have reported a geographical belt of male breast cancer in Africa where the male-to-female breast cancer ratio is greater than 0.1 (2, 10). This consists of Bantu-speaking countries in Eastern and Southern Africa, including Kenya. However, these studies were based on crude and unreliable data. There are no recent studies in Kenya examining breast cancer in men (2,10).

The primary objective of this study was to evaluate the clinical and pathological characteristics and treatment of men diagnosed with breast cancer at a tertiary hospital in Nairobi, Kenya.

Materials and Methods

This is a retrospective descriptive study carried out at a tertiary hospital in Nairobi, Kenya. Ethical approval was obtained from the institution's research ethics committee.

Men diagnosed with breast cancer between January 2009 and December 2021 were included in the study. Patients who were seen only once and had incomplete clinical and treatment data were excluded from the study. Data were collected on age at diagnosis, stage at diagnosis, histological subtype, receptor status, treatment given, and outcome.

Statistical analysis was carried out using SPSS software (IBM SPSS Inc., Chicago, Illinois, USA).

The demographic and pathologic characteristics were presented using summary statistics. Continuous variables were shown as medians and ranges and categorical variables were shown as percentages and frequencies. The missing data due to loss of follow-up were not analyzed.

Results

In the time period included in the study, there were 1210 new patients diagnosed with breast cancer at our institution and of them, 17 were male (1.40%). Of these, four patients were excluded due to missing data. The median age was 68 years (range 28–83). The majority were African Bantu (n=11, 84.6%), while the rest were Asian (n=2, 15.4%) (Table 1). The most common tumor locations were the lower inner quadrant (n=4, 30.8%) and the lower outer quadrant (n=4, 30.8%) (Table 1). Only three patients (23.1%) had a family history of breast cancer (Table1). However, no genetic testing was done.

Most patients presented with clinical T1 (n=10, 76.9%), while the rest presented with T2 tumors (n=3, 23.1%). Clinical N0 was the most common (n=8, 61.5%). The majority of the patients were at M0 (n=11, 84.6%). Of the two patients with metastatic disease at diagnosis, both had skeletal metastasis. Invasive ductal carcinoma was the most common histological subtype (n=12, 92.3%). Only one patient had invasive lobular carcinoma. Tumor grade 2 was the most common (n=8, 61.5%). Luminal A molecular subtype was the most prevalent (n=8, 61.5%) followed by triple-negative breast cancer (TNBC) (n=2, 15.4%). Only one patient

had luminal B molecular subtype, while none had HER 2-enriched subtype (Table 1).

Table 1. Patient characteristics

	Patient (*N*=13)
Age, median (range)	68 (28–83)
Ethnicity	
African (Bantu)	11 (84.6)
Asian	2 (15.4)
Location	
Lower inner quadrant	4 (30.8)
Lower outer quadrant	4 (30.8)
Periareolar	3 (23.1)
Not specified	2 (15.4)
Family history of BC	3 (23.1)
Clinical T stage	
0	0 (0.0)
1	10 (76.9)
2	3 (23.1)
3	0 (0.0)
4	0 (0.0)
Clinical N stage	
0	8 (61.5%)
1	1 (7.7)
2	3 (23.1)
3	1 (7.7)
Clinical M stage	
0	11 (84.6)
1	2 (15.4)
Histology	
IDC	12 (92.3)
ILC	1 (7.7)
Grade	
1	1 (7.7)
2	8 (61.5)
3	4 (30.8)
Molecular subtype	
Luminal A	8 (61.5)
Luminal B	1 (7.7)
HER 2 enriched	0 (0.0)
TNBC	2 (15.4)
Unknown	2 (15.4)

Abbreviations:BC, breast cancer;HER2,human epidermal growth factor receptor 2;IDC,invasive ductal carcinoma, ILC,invasive lobular carcinoma, TNBC,triple-negative breast cancer.

Table 2. Treatment

	Patient (*N*=13)
Neoadjuvantchemotherapy	2 (15.4)
Surgery (MRM)	11 (84.6)
Adjuvant treatment	
Tamoxifen	7 (53.8)
Herceptin	1 (7.7)
Radiotherapy	4 (30.8)
Chemotherapy	7 (53.8)

Table 3. Outcome

	Patient (*N*=13)
Alive	5 (38.4)
Dead	4 (30.8)
Lung metastasis	1
Brain metastasis	1
Metastasis (site not documented)	1
Non-breast cancer-related	1
Unknown	4 (30.8)

Patients with metastatic disease at diagnosis did not undergo surgery. For the 11 patients who underwent operative management, all underwent modified radical mastectomy. Adjuvant hormonal therapy with tamoxifen was given to seven patients while one received trastuzumab (Table 2).

The median follow-up period was 37 months (interquartile range 5–69). There were four patients lost to follow-up, four patients died, and five were still alive. Of the patients who died, only three were breast cancer-related (Table 3). One had metastasis to the lungs and the other had metastasis to the brain; however, the site of metastasis for the third patient was not documented.

Discussion

Male breast cancer is a rare disease. Our study found a rate of 1.40% of all breast cancers at our institution compared with a global rate of 0.5–1% (1, 11). The majority of our patients (84.6%) were Bantu speakers. This reflects the general demographics of the patients seen at our institution. Although dated studies from sub-Saharan Africa have suggested that there is a higher incidence of male breast cancer in the Bantu-speaking regions, they were based on inaccurate or incomplete

data and therefore, our study may be a more accurate representation of the true picture (2, 10).

The median age at diagnosis in our study was 68 years, which is similar to the global median of 67 years for male breast cancer (12). This is 20 years older than the median diagnosis of breast cancer in women in Kenya (13). It is possible that this is due to male breast cancer being biologically similar to late-onset female breast cancer and its association with non-hormonal risk factors (14).

Although three of our patients had a family history of breast cancer, genetic testing was not available to test for BRCA 1 and 2 mutations. Known risk factors for development of breast cancer in men are family history, BRCA2 gene mutation, and conditions that alter the estrogen-to-androgen ratio such as Klinefelter syndrome (15). Despite these known associations, most men have no identifiable risk factor at diagnosis (15).

A greater number of our patients (61.5%) presented with early breast cancer. This is in keeping with a large retrospective analysis of 1483 male patients diagnosed with breast cancer, which found that most patients (1054, 94.9%) were diagnosed with early disease (16). More than half of these patients (592, 56.2%) had node-negative disease (16). In contrast, some authors have found that male patients are diagnosed later than female patients due to the lack of awareness and screening (17). However, a majority of our patients were diagnosed with early breast cancer compared with a majority of females in Kenya who are diagnosed with advanced disease (18). These differences may be a reflection of our inadequate screening and diagnosis of female breast cancer.

The majority of our patients (61.5%) had luminal A molecular subtype. Male breast cancers are more likely to be estrogen receptor-positive than female breast cancers (90.6% vs. 76%) and the percentage of men with hormone receptor-positive tumors increases with increasing age (19). We found two patients (15.4%) with TNBC, while only one patient (7.7%) had luminal B molecular subtype. This is in contrast to a study examining male breast cancer according to the molecular subtype, which found HER2-positive tumors accounting for 17.8% and triple-negative tumors at 8.9% in black non-Hispanic males in America (20). Two of our patients had missing data on the molecular subtype, and this may have affected our findings.

All 11 patients who underwent surgery underwent modified radical mastectomy, and most received adjuvant hormonal therapy with tamoxifen. Generally, the approach to treatment of breast cancer in men and women is the same. However, male patients are more likely to undergo mastectomy even for T1 tumors (21). This is likely due to the higher tumor-to-breast ratio and lower attention to cosmetic outcomes. Adjuvant radiotherapy is offered according to guidelines developed for women with breast cancer (7). Neoadjuvant or adjuvant chemotherapy and HER2-targeted therapy is offered to men with high risk of recurrence (7). Considering that most breast cancers in men are hormone receptor-positive, hormonal therapy is an important part of the management of breast cancer in men, and tamoxifen is the recommended agent (8).

Although we were not able to run a survival analysis due to the small sample size, we noted that one out of the four patients who died, died from non-breast cancer-related causes, while three died due to metastatic disease. While the survival rate for male and female breast cancer is similar, male patients are more likely to die from non-breast cancer-related causes (22). This may be explained by their older age at diagnosis and increased cardiovascular comorbidities.

The study was limited by a small sample size due to the rare occurrence of the disease and a survival analysis was not possible due to the small sample size. There was missing data due to the loss of follow-up, and genetic testing was not available.

Conclusion

The rate of male breast cancer was similar to the global rate, with the majority of our patients presenting with early breast cancer and estrogen receptor-positive disease. Treatment was primarily modified radical mastectomy followed by adjuvant systemic therapy.

We recommend pooling of data into a regional database and long-term follow-up to provide a greater number of male breast cancer patients to increase the generalizability of the results and provide a more comprehensive picture of male breast cancer.

Incorporation of genetic testing and analysis into future studies will improve the understanding of the role of genetic factors in the development of male breast cancer.

Ethical considerations

The Aga Khan University Research Ethics Committee gave ethical clearance (Reference No. 2021/IERC-95 (v1)).

Author contributions

MW led in the writing of the first draft while WR led in the conceptualization and reviewing and editing the original draft.

Both authors equally contributed to data curation, formal analysis, investigation, methodology and project administration.

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