

Stage and Type of Male Breast Cancer Presented at Mankweng Academic Hospital from 2015–2023

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ABSTRACT

Background: Male breast cancer (MBC) is very uncommon, occurring less than 1% of all breast cancers, and has a worse survival rate compared with that of female patients. Clinical studies on male breast cancer have not been done frequently because of the rarity of the condition. The main aim of this study is to understand the profile of male breast cancer patients treated at Mankweng Hospital.

Methods: A retrospective cross-sectional descriptive quantitative design was adopted to analyze the profile of all patients with histologically confirmed male breast cancer from March 2015 to May 2023 in the Mankweng Breast Oncology clinic.

Results: A total of 17 patients with confirmed MBC were evaluated. Age range 23–80 years. The mean age is 62.5 years, with the majority (76%, 5%) being above the age of 50 years. Early-stage (0, I & II) comprised 6 (35%) and late-stage (III & IV) consisted of 11 (65%) patients. Invasive ductal carcinoma was 14 (82%), Colloid carcinoma 1, Papillary carcinoma 1 and Metastatic Adenocarcinoma 1. Molecular subtype: Luminal A: 7 (43.8%), Luminal B: 8 (50%) & Triple-negative: 1 (6.2%). ER Positive: 15 (93.7%), ER Negative: 1 (6.3%).

Conclusions: The majority (65%) of male breast cancer were diagnosed at an advanced stage, and 76.5% were over the age of 50 years. Invasive ductal carcinoma was the most (82%) common histological type of breast cancer, and the majority (93%) are Oestrogen receptor positive in this study. There is a gap that needs to be filled in terms of public knowledge about male breast cancer. Breast cancer awareness campaigns are also important for men to prevent delayed presentation. Men over 50 years old who notice a change in their breasts should report promptly to a health facility for further assessment.

Keywords: Male breast cancer, molecular subtype, stage.

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1. INTRODUCTION

Male breast cancer (MBC) is very uncommon, occurring less than 1% of all breast cancers [1], and has a worse survival rate compared with those of female patients [2]. Giardano [3] stated that the lifetime risk of MBC is about 1:100 as compared to 1:8 FBC. However, its incidence has increased over the past two decades in both male and female patients [4]. The incidence of MBC in South Africa is the highest in the world, with 1%–3% diagnosed in South Africa [5]. The incidence of female breast cancer was 10172, and male breast cancer was 184 diagnosed in 2019 in South Africa [6]. Mortality of Male breast cancer is usually high because of being diagnosed late [5].

The risk of male breast cancer increases if there is a positive family history, genetic BRCA2 mutations, previous exposure to chest wall radiation, Klinefelter's syndrome, undescended testes, infertility, and older age [3], [5]. There is a high chance of rising breast cancer if a first-degree relative has breast cancer [5]. Clinical studies on MBC have not been done frequently because of the condition's rarity [3], [4]. It has been assumed that sociocultural association with breast cancer is a women's disease [7]. There has been no study on the profile of male breast cancer patients in the Limpopo province. Our study is the first, with the main objective of the study being to understand better the profile and features of male breast cancer (stage, hormonal status, grading and molecular subtype) in Limpopo province, South Africa.



2. METHOD

2.1. Study Approach and Design

The study was a retrospective cross-sectional descriptive quantitative design to analyse the profile of all patients with histologically confirmed male breast cancer within the period from March 2015 to May 2023.

2.2. Study Setting

Breast oncology unit, Mankweng Tertiary Academic Hospital. The breast oncology unit was established in March 2015 in Mankweng Academic Hospital, Limpopo Province, South Africa, and this clinic moved to Pietersburg Provincial Hospital in June 2023.

2.3. Study Population

All male patients with histologically confirmed breast cancer presented within the period of March 2015 to May 2023 in the Mankweng Breast Oncology clinic.

2.4. Inclusion and Exclusion Criteria

All patients with histologically confirmed male breast cancer were included in the study, whereas patients that had missing information in their files were excluded.

2.5. Data Collection and Statistical Analysis

Patients were identified using the register at Mankweng Breast Cancer Clinic, and their relevant records were reviewed to collect the information. The National Health Laboratory Service (NHLS) was used to trace some of the results that were not attached to patient records. The histology of the identified patients was analysed for age, histological type of breast cancer, grading, Ki 67 index, ER (Oestrogen receptor), human epidermal growth factor receptor 2 (HER2), and molecular subtype. Stages of breast cancer were grouped into early (stages 0, I and II) and advanced (stages III and IV). Molecular subtypes of breast cancer are categorised into luminal A (ER+/PR+/HER2-/lowKi-67), luminal B (ER+/PR+/HER2-/+/high Ki-67), HER2-overexpression (ER-/PR-/HER2+) and triple-negative breast cancers (TNBCs; ER-/PR-/HER2-) [8]. In some cases, immunohistochemistry was not done because tissue specimens appeared insufficient. The immunohistochemistry analysis was performed on all patients whose histology reports provided an immunohistochemistry status. The collected data was transferred to an Excel spreadsheet, and from there, it was transferred to Statistica to analyse the data. The patient demographics were summarised using descriptive statistics. Categorical variables were expressed as proportions.

3. RESULTS

A total of 24 male patients with confirmed breast cancer were treated from March 2015 to May 2023, and 17 patients met the inclusion criteria. During this period, 1741 female breast cancer patients were seen. The age range of male breast cancer patients was 23 to 80 years. The mean age of diagnosis was 62.5 years, with the majority being

above the age of 50 years (76.5%). Details are presented in [Table I](#).

4. DISCUSSION

A total of 17 male breast cancer patients were evaluated. The mean age of diagnosis was 62.5 years, with the majority (76.5%) being above the age of 50 years, which is 8–10 years higher compared to female breast cancer in Limpopo from a previous study by Bhuiyan et al. [9]. A South African study by Rattary et al. [10] stated the mean age of male breast cancer diagnosis at 56.8 years. In Korea, MBC usually occurs about ten years later than FBC [4]. Studies from Portugal found that the average age at diagnosis for male breast cancer in Portugal is approximately 5–10 years older than in females, and over 40% of the male patients were aged 70 years or older. This finding is consistent in many studies, including Ferzoco [11] and Garrefa et al. [12].

In this study, a common histological type of breast cancer found Invasive ductal carcinoma (82%), similar to a study by Cardoso et al. [13] conducted on MBC. In many Sub-Saharan African countries, Invasive Ductal carcinoma (IDC) is the most common histological type. A study in Kenya by Matheka and Wasike [14] had similar findings, where 92.3% of the patients were diagnosed with IDC. Another study in southwestern Nigeria found 88.9% IDC, and this follows global trends in MBC across many countries [15]. A similar pattern was seen with the women in Limpopo province, South Africa [16]. Concerning tumour biology with grading in our study, Male breast cancer patients had more grade 2 (70%) and grade 3 30%. It corresponds to Cardoso et al. [13] on male breast cancer, where grade 2 was the majority. It is like female breast cancer in Limpopo from a previous study by Mthembu and Bhuiyan [17], who found that 61% of grade 2 and 29% of grade 3.

Positive family history, BRAC2 mutations, chest wall radiation exposure, Klinefelter's syndrome, exposure to oestrogen in the treatment of prostate cancer, undescended testes, and infertility are the risk factors of male breast cancer [3], [5]. Bevier et al. [18] stated that the risk of breast cancer increases in either gender, both the males and females in the family when the father or mother is affected. However, the risk was marginally higher in the females. In our study, the risk factors were not established in the patients' files, and no genetic studies were done on any of our patients.

Most of the patients presented at an advanced stage of the disease with stage III–IV (65%), and there is no obvious guideline for mammography on how to approach a male breast mass. As a result, this can be directly linked to delayed presentation.

Regarding hormonal receptor status in this study, over 93% of breast cancer patients showed the presence of oestrogen receptor (ER), and 50% had progesterone receptor, which is consistent with other studies [5], [13], [14]. From the literature review, Rudlowski [19] stated that approximately 90% of Hormone expression in male breast cancer is the oestrogen receptor (ER), and 81% is the progesterone receptor. With regards to molecular subtype

TABLE I: PROFILE OF THE MALE BREAST CANCER PATIENTS (N = 17)

Description	Characteristics	Freq.	%
Age	<50	4	23.5%
	>50	13	76.5%
Stage	Total	17	100%
	0	0	
	I	2	11.8%
	II	4	23.5%
	III	10	58.9%
	IV	1	5.9%
Type of cancer	Total	17	
	Invasive ductal carcinoma (NST)*	14	82.3%
	Colloid carcinoma	1	5.9%
	Papillary carcinoma	1	5.9%
	Metastatic Adenocarcinoma	1	5.9%
Grading	Total	17	
	1	0	
	2	7	70%
	3	3	30%
	Not done	7	
Hormone ER	Total	17	
	Negative	1	6.3%
	Positive	15	93.7%
	Not done	1	
Hormone PR	Total	17	
	Negative	8	50%
	Positive	8	50%
	Not done	1	
HER 2	Total	17	
	Borderline	3	18.8%
	Negative	9	56.2%
	Positive	4	25%
	Not done	1	
Molecular type	Total	17	
	Luminal A	7	43.8%
	Luminal B	8	50%
	Triple negative	1	6.2%
	Her2+ Overexpression	0	
	Not done	1	
Total	17		

Note. NST: No special type; ER: estrogen receptor; PR: progesterone receptor; HER2: human epidermal growth factor receptor 2. Stage: The majority of patients presented at an advanced stage III–IV (65%). Molecular subtype: Luminal B was majority (50%).

classification of breast cancer in our research finding, the Luminal B (50%) and Luminal A (44%) molecular subtypes were more frequently similar to male breast cancer in Cardoso et al. [13] and resembling female breast cancer found in Limpopo [17]. Across many studies of MBC and FBC, the commonest subtype is luminal A [20].

A triple assessment is essential to make the diagnosis of MBC. It is similar to female breast cancer, which consists of clinical assessment, imaging and core biopsy [5], [19]. The usual presentation of male breast cancer is a painless lump in a unilateral breast. Other symptoms of nipple retraction, nipple discharge or ulceration may occur [5], [19]. Lumps in males' breasts are simpler to detect due to the smaller breasts [19]. However, men tend to delay seeking help until they have more severe symptoms [5]. It has been presumed that breast cancer is a women's disease [7]. Mammography is helpful for diagnosis [21] but has not been used as a screening tool. Core biopsy is essential for

confirmation of definitive diagnosis of MBC [19]. Mammogram features of MBC include sub-areolar, eccentric masses with well-defined margins and rare calcifications, as reported in some studies; however, in a South African context, microcalcifications are common, as shown in a study by Kaloianova [22].

The treatment of breast cancer in men is the same as the treatment of female breast cancer [23]. Clinical studies on MBC have not been done frequently because of the condition's rarity [3], [4]. The treatment modality of male breast cancer consists of surgery, chemotherapy, radiotherapy and endocrine therapy if the hormonal receptor is positive, which is usually the case in the majority of men diagnosed with MBC [5]. In a previous study by Cardoso et al. [14], the vast majority (95.9%) of M0 patients underwent a (modified) radical mastectomy, with only 4% treated with breast-conserving surgery. In our study, most patients started with neoadjuvant chemotherapy as patients presented at an advanced stage.

Radiation therapy is indicated for men with big tumour size, positive surgical margins and four or more positive lymph nodes. Tamoxifen is the preferred neo-adjuvant and adjuvant endocrine therapy according to the ASCO guidelines and other studies [23], [24] for at least five years as first-line endocrine treatment due to the majority of patients being ER+ and those at high risk for recurrence, able to tolerate Tamoxifen are offered for another additional five years Tamoxifen has been shown to improve survival rates in FBC with ER+. However, it is less when compared to male subjects because many discontinue treatment due to side effects profile, which includes hot flashes, visual disturbances, cognitive changes, and low libido; it is important to understand the toxicities of endocrine therapy, reassure the patient and manage them appropriately [25]. Nonetheless, Ali et al. [26] found that males are more adherent to endocrine therapy than females and showed a 23% risk reduction in mortality risk and improved survival benefit. For patients with contraindications to Tamoxifen, an Aromatase inhibitor is an option; however, it is not as effective as monotherapy and has not been shown to improve survival when compared to Tamoxifen and should be combined with medical or surgical castration. However, the surgical option is a choice of the past [25], [27].

The prognosis of the MBC is worse than the outcome of female breast cancer [2], [28], [29]. Survival rates for male breast cancer are lower due to advanced-stage diagnosis [4], and 5-year survival is about 40% to 65% [19]. According to the Breast Cancer Control Policy, National Department of Health, South Africa, a breast cancer awareness campaign for women over 40 years attending a primary health clinic will have health provider-initiated screening clinical breast exams biannually for Screening and early diagnosis of breast cancer [30]. However, there is no policy for male breast cancer. Though MBCs are rare, breast cancer awareness campaigns are similarly important for men to prevent delayed presentation. In our study, 76.5% of male breast cancer patients were above 50 years old. Awareness messages should be disseminated to men over 50 attending Primary Health Clinics or general medical practitioners. Any man who notices a change in his breast, like a painless lump, nipple retraction, nipple discharge, or ulceration, should report promptly to a health facility for further assessment.

The limitation of the current study is that it was retrospective, and some information was missing to include all patients, and male breast cancer is usually rare in comparison to female breast cancer. We had only 24 cases in 8 years.

5. CONCLUSION

The majority (65%) of male breast cancer were diagnosed at an advanced stage, and 76.5% were over the age of 50 years. Invasive ductal carcinoma was the most (82%) common histological type of breast cancer, and the majority (93%) are oestrogen receptor positive in this study. There is a gap that needs to be filled in terms of public knowledge about male breast cancer. Breast cancer awareness campaigns are also important for men to prevent delayed presentation. Men over 50 years old who

notice a change in breasts should report promptly to a health facility for further assessment.

AUTHOR CONTRIBUTIONS

Both authors equally contributed to the concept, acquisition of data, analysis of data, drafting of the manuscript, and critical revision of important intellectual content.

DATA AVAILABILITY

Data will be made available at a reasonable request.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest in relation to this paper, as well as the published research results, including the financial aspects of conducting the research, obtaining and using its results, and any non-financial personal relationships.

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