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Breast Cancer Management at a Tertiary Hospital in Tanzania: Implications for the Implementation of the New Cancer Guidelines

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Abstract

Background
Breast cancer is the second leading cancer among women in Tanzania accounting for about 3,000 cases and 1,300 deaths in 2018 alone. National Cancer treatment guidelines have been developed addressing management of patients with breast cancer. How current practice will need to change to conform to new guideline has not been investigated. Evidence is needed to understand how much changes will be needed to affect changes needed.

Objectives
This study sought to understand how breast cancer patients at Muhimbili National Hospital are investigated and assigned to treatment.

Methodology
A cross-sectional descriptive study was carried out among patients with breast cancer who underwent modified radical mastectomy at Muhimbili National Hospital in 2018. Consent was obtained and patient's demography, clinical characteristics, investigations and treatment assignment was collected. Descriptive statistics were computed where proportions were used for categorical variables and means with standard deviations for age.

Results
A total of 80 patients with mean age of 49.9 (SD 13.5) years were involved. Fine Needle Aspiration Cytology was diagnostic in 19 (23.8%). Immunohistochemistry was not available before surgery and requested only in 60(70%). Regarding clinical status 65 (81.3%) of the patients were clinical stage III disease with only 58 (72.5) receiving neo-adjuvant therapy. None of the patients had mammography or CT scan done.

Conclusion
We have demonstrated that BC management at MNH is not concordant with any known international treatment guidelines. Furthermore, Multi Disciplinary Team approach is critically lacking and needs to be well defined if the new treatment guidelines were to be effective.

Recommendation
Improvement in Breast Cancer Management needs to embrace the concept of Multi Disciplinary Team approach.

Key words: Breast Cancer, Investigations, Treatment Guidelines.

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Introduction

Breast Cancer (BC) is the second prevalent cancer globally contributing to 2,088,849 (11.6%) new cases and is the fourth leading cause of mortality by contributing to 626,679 (6.6%) cancer related deaths worldwide in 2018 alone (1). Early diagnosis of BC coupled with current individualized treatment protocols has been shown to be associated with excellent survival statistics (2). In the United States and many other developed nations, breast cancer treatment has been guided by various guidelines for close to 20 years now with significant improvement in survival (3). In Low and Middle Income Countries (LMICs), BC is still considered a deadly disease partly due to late stage in diagnosis, aggressive disease nature (4,5) and lack of individualized treatment protocols.

In 2018 alone, 3,037 incident cases of BC were reported from Tanzania making it second to cervical cancer among female. Similarly, about 1,300 deaths related to breast cancer were reported (6). This makes breast cancer an important cancer in our society worth addressing to improve livelihood among its sufferers. While cancer treatment in Tanzania is largely “free” of payment (subsidized by the government), how such treatment is directed by evidence has not been studied. Such evidence requires a team approach including the radiologist, oncologists, pathologist and the surgeon.

At the time of this study, there was no existing guideline for the management of breast cancer in Tanzania and decisions were largely made by the surgeon. The role of the multidisciplinary tumor board (MDT) would thus be to decide on adjuvant therapy. This practice has the potential to subject patients to incomplete investigation and hence inadequate treatment, or even denial of targeted therapy to some. This practice at MNH has not been investigated to compare it with any known BC treatment guidelines that are current. Knowing the extent of concordant of the offered therapy to existing guidelines will help address hurdles in the implementation of the just recently launched national cancer treatment guidelines in Tanzania. This study therefore aims to determine how BC patients at Muhimbili National Hospital (MNH) are investigated and assigned to treatment.

Methodology

This was cross-sectional descriptive study, carried out among BC patients at MNH from January to December 2018. MNH is the largest hospital offering cancer surgery in Tanzania, therefore receiving majority of BC patients from all the regions of the country. The hospital has capacity to investigate patients with suspected and confirmed BC by having well equipped pathology laboratory (histology and immunohistochemistry), digital mammogram, CT scan, and MRI among others. The hospital also has ready access of oncology specialist every Tuesday during MDT. The hospital also serves as training center for surgery, oncology, radiology and pathology residents making it an important center for the study. Ethical approval to conduct the study was obtained from Muhimbili University of Health and Allied Sciences (MUHAS) ethics and review committee and separate permission to use MNH patients from the hospital's consultancy and research bureau.

This study only recruited BC patients who were judged by the treating surgeons to be candidates for radical surgery, Modified Radical mastectomy. Patients were recruited after the surgery just before discharge from the hospital after signing an informed consent to participate in the study. Any patient who was being treated by Mastectomy for a recurrent cancer was excluded from the study. Variables collected included patients' demography, clinical information including co-morbidity, stage of the cancer, and whether received neoajuvant therapy. Investigations details included how specimen was obtained: Fine Needle Aspiration Cytology (FNAC) vs open biopsy; CT scan, MRI scan, Mammography, abdomino-pelvic ultrasound, and tissue results as were available. Finally, MDT attendance and its frequency were recorded. A structured questionnaire was used to gather the study variables.

Collected data were checked for completeness, coded and entered into Statistical Package Software for Social scientists (SPSS) version 23 for subsequent analysis. Continuous variables were summarized into means and standard deviations while categorical variables were summarized into proportions. Results are summarized into tables, flow charts, bar graphs and pie charts in the subsequent section.

Results

We included 80 patients with operable or locally advanced breast cancer who had any form of mastectomy (primary surgery) at MNH over a period of ten months. The patients mean age was 49.9±13.5 (27 – 85) years with majority being in the 36 – 55 years' age group. Most of the study patients, 59(73.7%), had low level of education. Furthermore, 29(36.3%) were peasants making it the most common source of living income. Only 27(33.8%) had commodities of which hypertension was the most common among all patients at 14(17.5%). Majority of the patients, 65(81.25%) had stage three diseases with only 22 (27.5%) of all patients receiving neo-adjuvant chemotherapy. (**Table 1**)

Table 1: Demographic and clinical characteristics of female breast cancer patients at MNH in 2018, N=80.

Variable	Frequency (%)
Age	
<35	13 (16.3)
36-55	39 (48.7)
>56	28 (35.0)
Level of Education	
No formal education	13 (16.3)
Primary education	46 (57.5)
Secondary Education and above	21 (26.4)
Occupation	
Peasant	29 (36.3)
Unemployed	20 (25.0)
Employed	24(30)
Others	7 (36.3)
Comorbidity	
HTN	14 (17.5)
DM	4 (5.0)
HIV	3 (3.8)
Others	6 (7.5)
Treatment strategy	
Neoadjuvant Therapy	22 (27.5)
Up front surgery	58 (72.5)
Stage at MRM	
I	1 (1.25)
II	14 (17.5)
IIIA	15 (18.8)
IIIB	50 (62.5)

Table 2: Pathology results reflecting pathology services for breast cancer at MNH in 2018

Report	Frequency (%)
Tissue diagnosis	
FNAC only	19 (23.8)
FNAC + Biopsy	41 (51.3)
Biopsy only	20 (25.0)
Histological subtypes	
Ductal carcinoma	61 (76.3)
Lobular carcinoma	4 (5.0)
Medullary carcinoma	3 (3.8)
Not mentioned	12 (15.0)
Grade of the histological subtypes	
Low grade	8 (10.0)
Intermediate grade	11 (13.8)
High grade	5 (6.3)
Not documented	56 (70.0)
Hormonal testing (ER/PR)	
IHC done	62 (77.5)
IHC not done	18 (22.5)

Figure 1 below represents the investigation path taken to confirm a diagnosis of breast cancer where it can be seen that of the 80 patients, 19 (23.8%) came to our facility with confirmed diagnosis of BC of which 7 (36.8%) were made from FNAC and 12 (74%) from tissue biopsy. Of the remaining patients, 29 had FNAC done at MNH of which a diagnosis of BC was reliably made in 12(41.4%) only and the rest had to be subjected to open biopsy to arrive at a working diagnosis. Open biopsy was therefore the most diagnostic modality of BC where it was done in 61(76.3%) of all the patients. Additionally, it can be seen that FNAC yield rate done outside MNH was low compared to that at MNH, 22.6% vs. 41.4% respectively.

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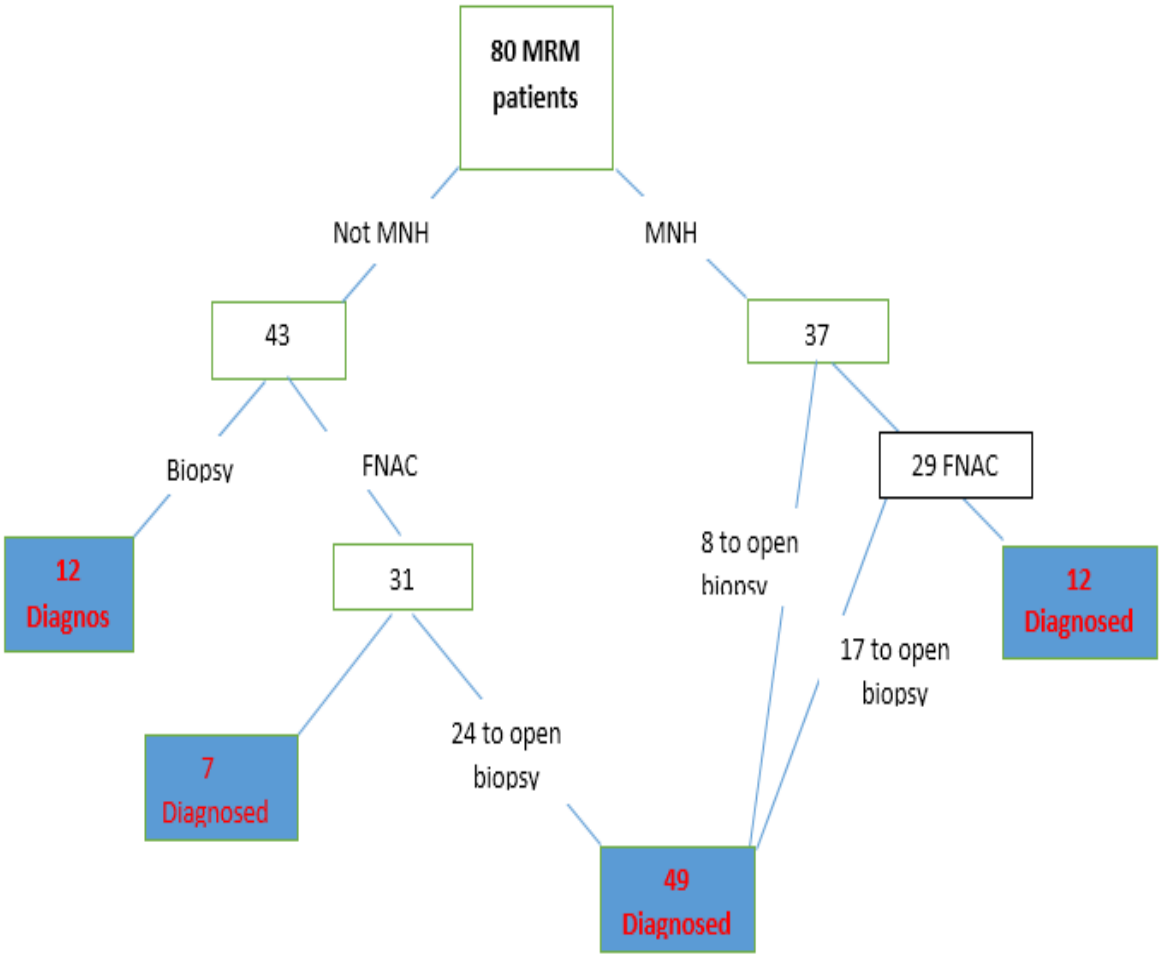

Figure 1: Showing flow chart of diagnostic investigation among 80 breast cancer women who underwent MRM at MNH, 2018

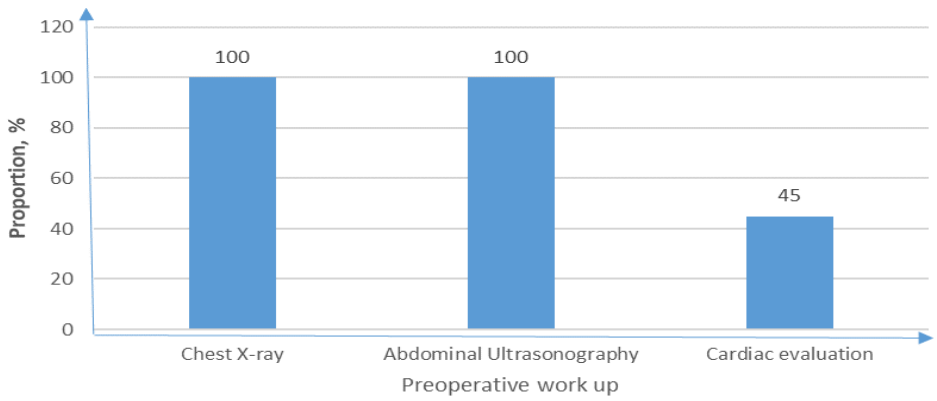

Figure 2: Bar graph showing staging and fitness investigations performed on breast cancer patients prior to surgery at MNH.

From **Figure 2**, it can be noted that evaluations for Metastatic work up for BC patients at MNH employed the use of abdomino-pelvic Ultra sound and plain chest x-ray for all patients. Before treatment 36 (45%) of the patients had cardiac evaluation for fitness done.

Patients to be listed need to appear for surgery panel to check for fitness and availability of slot for surgery. From **Figure 3** below, 58 (72.5%) of the patients did not secure a surgery slot during their first visit. The most cited reason was incomplete investigations as was seen among 20 (35%), followed by unavailability of slot due to full list seen among 19 (33%) and uncontrolled co-morbidities seen among 13 (22%).

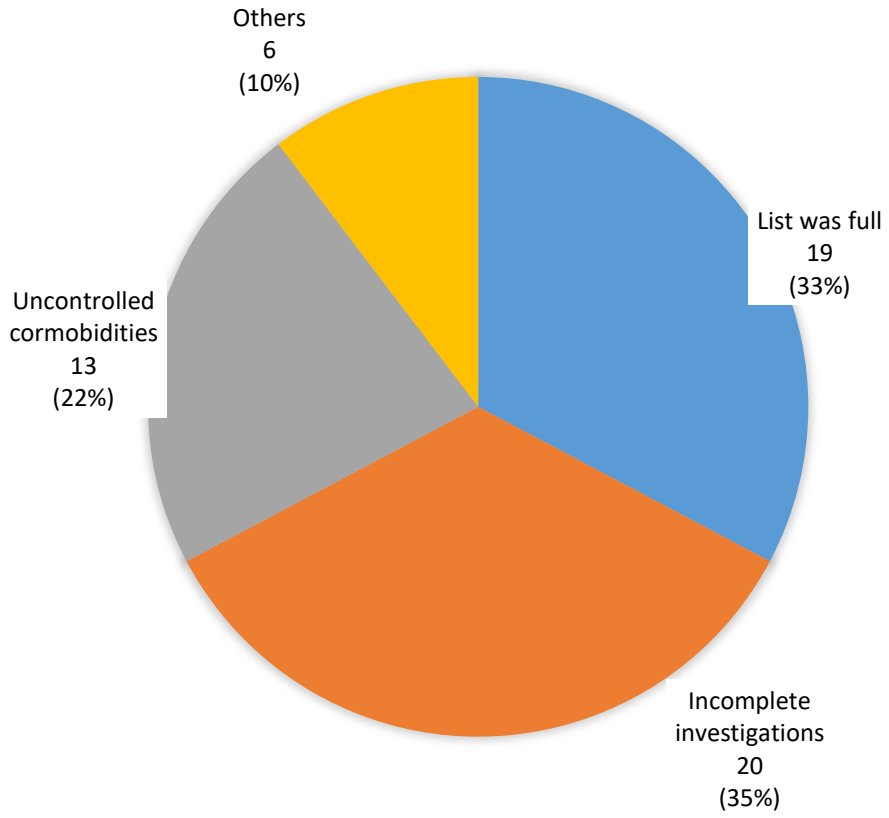

Figure 3: Reasons not to be admitted for Surgery during 1st Panel discussion

Discussion

It is important to have BC histological subtype and molecular subtypes for optimal treatment (7). Histological subtypes were elaborate among our BC patients, but Nottingham Grading was only done to one third of the patients. Furthermore, IHC was done to only 4 in 5 patients but only after mastectomy has been performed. Selections of neo-adjuvant and adjuvant therapy are all guided by the histological and immunohistological subtypes of BC. We will publish soon on IHC results from a larger cohort of BC patients at MNH as a reflection of the country profile. The landmark improvements in BC survival have been noted thanks to proper and detailed characterization of the tumor (8). To patients who can afford, and where treatment plans allow the provision of Trastuzumab, Her-2 receptor status should be determined. However, all patients should have hormonal status determined as targeted therapy are significantly influencing outcomes and shaping the field of cancer therapy (9).

Minimally invasive techniques are recommended globally for obtaining breast specimen for malignancy evaluation pre-operatively (10). This is normally achieved by FNAC under imaging guidance. Under these circumstances, the yieid from such a strategy is promosisng unlike in our case where only just under one quarter of patients had adequate FNAC. The inadequate FNAC rate was much higher than expected rate of 25% (11). Well trainined cytopathologist should handle FNAC specimens incluidng collection to ensure adequate aspirate has been obtained before the patient leaves the premises (12). In the event that FNAC has failed to yield enough aspirate to make a diagnosis, core needle should be the next in line and not open biopsy (13). With Rapid On-Site Evaluation (ROSE), it should be possible for MNH to improve diagnostic accuracy of FNAC and thus avoid delays in issuing results and treatment. The need for open

Metastatic work up is an important component in cancer management as it aides in treatment assignment. In breast cancer, tumor size and nodal status are an important component in deciding which investigations to request. For stage I and II lesions, Chest x-ray and abdominopelvic Ultra sonography might be adequate in many settings. But for stage III BC, thoracoabdominal CT, PET scan and bone scan might be needed. But unless these last three investigations are covered for patients, many will not be able to afford given their low socio-economic status as depicted in this study. Clinicians should be guided by local practice and clinical acumen when ordering CT scan and bone scan which are all available

within the country. Clinical studies comparing local patients staged with CT versus those who are not should be undertaken to define the role of CT scan in the management of locally advanced BC.

In spite of all our BC patients having locally advanced disease at presentation, Mammography (MMG) evaluation still had its place. Traditionally, MMG has been used in the screening set up with myriad of advantages (14). In the setting of a diagnosed BC, bilateral MMG will inform on multi-centricity if Breast conservation following down staging was to be considered. Likewise, existence of contralateral BC can be well identified. (15). None of the BC patients in our series neither had MMG of the affected breast nor of the contralateral breast before FNAC or even after. (16) Even though all patients had mastectomy as treatment modality, the possibility of bilateral BC which occur in about 3% of all patients was not addressed in these patients. Guidelines should be strict on the use of MMG in all patients with breast cancer.

Multidisciplinary panel do exist at MNH, but the whole decision on how patient is managed depends on the treating surgeon. This can be seen with insignificant number of patients receiving neo-adjuvant therapy in the study. For MDT to function well in any setting, all parties might understand their vital roles in the management of BC patient. The radiologist must understand what to report, the pathologist must know what to report, and the clinicians (surgeons and oncologist) must now agree on stage and assign treatment to each patient. There is scientific evidence that MDT has significance in BC management (17,18). Furthermore, lack of standardized care in this setting was demonstrated by the high proportion of patients who failed to secure listing for surgery when they appeared before a listing committee.

Tanzania recently launched its national cancer treatment guidelines addressing BC among other conditions. MNH has the ability to better implement this new treatment guideline, but only if all parties are adequately informed and committed to make it possible. If implemented, it should be possible to document outcome among our patients as various cohort of patients will be treated with significant evidence gatherings. For MNH to improve in its BC patient's care, MDT need to be identified and more research within the team is needed to keep the

team together. Current practice at MNH fall short of any recognized treatment guidelines hence any outcome. Investigations and treatment assignment should by individualized.

Conclusion

We have demonstrated that BC treatment at MNH is not concordant with any known international treatment guidelines. Patients were not adequatley investigated, pathology reports not standardized, and neodajuvant therapy not offered to all that needed it. Furthermore, MDT approach is critically lacking and needs to be well defined if the new treatment guidelines were to be effective.

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Declarations

Authors have nothing to declare.

Competing Interests

The authors have no competing interests to declare.

Authors' contribution

LOA conceived and designed the study, analyzed data, and wrote the manuscript. JMM collected and analyzed data. AHM wrote the manuscript. OVN wrote the manuscript. All authors read and approved the study for publication.

List of Abbreviations

LMICs	Low and Middle Income Countries
MNH	Muhimbili National Hospital
BC	Breast Cancer
MDT	Multidisciplinary Tumor
MUHAS	Muhimbili University of Health and Allied Sciences
FNAC	Fine Needle Aspiration Cytology
MMG	Mammography

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