

Delay among Patients Presenting with Advanced Breast Cancer at Muhimbili National Hospital: A Cross-Sectional Survey

Larry O. Akoko^{1*}, Elisia P. Mpango², John M. Mtei³, Caspar Haule⁴

¹Department of Surgery, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania

²Department of Surgery, Amana Regional Referral Hospital, Dar es Salaam, Tanzania

³Neurosurgery Unit, Muhimbili Orthopedic Institute, Dar es Salaam, Tanzania

⁴Department of Surgery, Muhimbili National Hospital, Dar es Salaam, Tanzania

***Corresponding author:**

Dr. Larry O. Akoko

Muhimbili University of Health and Allied Sciences

P.O. Box 65001

Dar es Salaam, Tanzania

Email: akokole12@gmail.com

Abstract***Background***

Breast cancer is the second most common cancer among Tanzanian women. Advanced disease at presentation is not uncommon among our patients with reasons for such late presentation being unknown. Late presentation is costly to treat compared to early disease presentation, and further carries dismal outcome. Understanding factors related to late presentation will help formulate strategies to downstage the disease through early intervention. This study therefore sought to understand the factors related with late presentation among patients presenting with advanced breast cancer in Tanzania.

Methodology

This was an analytical cross-sectional hospital-based study that involved patients with advanced breast cancer at Muhimbili National Hospital during the period of study from February 2018 to January 2019. Delay was considered as presenting beyond three months following suspicion of breast mass. Socio-demographic variables and clinical presentation times at various facilities were determined. Descriptive and comparative statistics were computed.

Results

A total of 185 patients with a mean age of 48.4 years were involved in the study. Delay in seeking medical attention was noted in 76% of the patients with advanced breast cancer with young age, rural residency and lack of formal education showing significant association with delay in presentation. A mean of 125.7 days was spent before finally arriving for definitive care at Muhimbili National Hospital.

Conclusion

This study has recognized existence of late presentation following detection of breast mass among patients with advanced breast cancer in Tanzania. Studies to address delay among breast cancer patients are needed given the anticipated cost effectiveness.

Key words: Delay, Advanced Breast cancer, Stage 3 and 4, Breast, Late Presentation.

Background

According to global cancer statistics, Breast cancer (BC) is an important health problem among women in Tanzania by being the second most common cancer contributing to 3,037 (12.1%) cases and 1,303 deaths in 2018 alone (1). Over the years, breast cancer outcome has shown improvement globally, with such improvement depending on early stage at diagnosis and access to therapy (2). Access to therapy has also been associated with good outcome, distant disease survival of 74% at 2 years, among patients with late stage disease at presentation (3). Other studies from Africa have similarly demonstrated late stage at presentation among African patients (4).

At Muhimbili National Hospital (MNH), a tertiary hospital in Tanzania where comprehensive management of cancer is available, hospital registry shows that 1 in 3 of female surgical admissions is due to breast cancer, majority of which present at an advanced stage (5, 6). With patients travelling long distances to reach the hospital, it is possible that geographical and logistic barriers play a role rather than tumor biology. We sought to understand the time interval from first suspicious diagnosis to the arrival at a definitive treatment center. Understanding the presence of a delayed presentation is important in designing patient navigation pathways to facilitate early diagnosis, an approach recommended in national policy. This study therefore seeks to understand whether there is delay in arriving in hospital for treatment and to assess the possible factors related to such a delay at MNH.

Materials and Methods***Study design***

This was an analytical hospital based cross-sectional study conducted over a period of one year, from February 2018 to January 2019.

Study setting

It was carried out at MNH, a teaching hospital to Muhimbili University of Health and Allied Sciences (MUHAS), located in the commercial capital of Dar es Salaam. The hospital serves as a public national referral hospital of last resort, being at the Apex of healthcare delivery with comprehensive services. The hospital is also convenient for cancer services as diagnostic capacity is available in house and easy referral for chemotherapy and/or radiation services at Ocean Road Cancer Institute which is about two miles away.

Study population

The study involved female patients with a diagnosis of breast cancer attended during the study period. The inclusion criteria included having a histological confirmation of breast cancer, clinical stage three or four disease, provided informed consent to participate in the study and age 18 years or older. Patients with a recurrent breast cancer or progression following treatment were excluded from the study.

Sample size and study protocol

A sample of 185 was estimated to be able to detect a 14% delay, previously found by Ermiah, E. et al (7) in Libya at type 1 error of 20% and power of 80%. A pretested data capture tool was used to collect patients' variables which had included: socio-demography and time spent since first diagnosis to arrival at definitive point of care. Patients were asked when they first felt the mass on the breast to when they reported to any health facility for care. Data was collected by performing direct patients interviews and their case notes for documented evidence of diagnosis and stage. Patients were then consecutively recruited to when the sample size was attained. Collected data was coded and entered into SPSS for analysis where proportions were used for categorical variables and means (and standard deviation) for continuous variables. Delay was considered to be present when time lapse of three months or more was present from initial diagnosis at local facility to arrival at the definitive treatment center. Chi square test was used to analyze potential association between socio-demographic characteristics and delay or no delay in coming to the treatment center and statistical significance was based on a p-value of <0.5%. Results were then summarized into tables and figures as presented in the next section.

Results

A total of 185 women with a confirmed diagnosis of breast cancer with either clinical stage 3 or 4 were recruited into the study. The patients had a mean age of 48.4 ± 14.9 (15 – 82) years with majority being in the age group of between 30 – 49 years and 50 – 69 years by 76 (41.1%) and 71 (38.4%), respectively. Rural area of residence had the greatest number of cases as was seen in 146 (78.9%), while with regards to employment status, most were either petty traders or peasants as was seen among 85(45.9%) and 73 (39.5%) respectively. The level of education achieved by the majority was primary certificate 120 (64.9%) while 42 (22.7%) had not attained any education certificate. Most of the breast cancer patients were

married, 102 (55.1%), with the rest being single, divorced or widowed as was seen among 24 (13%), 29 (15.7%) and 30 (16.2%) respectively. (Table 1)

Table 1: Baseline characteristics of patients with clinical stage 3 or 4 breast cancer at MNH in 2018, n= 185

Variables	Frequency, (%)
Age grouping	
≤ 29	17 (9.2)
30 – 49	76 (41.1)
50 – 69	71 (38.4)
≥70	21 (11.4)
Area of Residency	
Urban	39 (21.1)
Rural	146 (78.9)
Occupation status	
Employed	16 (8.6)
Petty Traders	85 (45.9)
Peasant	73 (39.5)
Unemployed	11 (5.9)
Level of Education	
None	42 (22.7)
Primary	120 (64.9)
Secondary and above	23 (12.4)
Marital Status	
Single	24 (13)
Married	102 (55.1)
Divorced	29 (15.7)
Widowed	30 (16.2)
Clinical Stage of disease	
Stage 3	39 (21.1)
Stage 4	146 (78.9)

The time spent before seeking medical consultation at any level after noticing a breast lump was also assessed: the mean time to consultation was 117.2 ± 62.1 days, ranging from 7 – 300 days with the majority seeking first medical attention between three to six months by 126 (68%) and only 45 (24%) had reported within the first three months of symptoms.

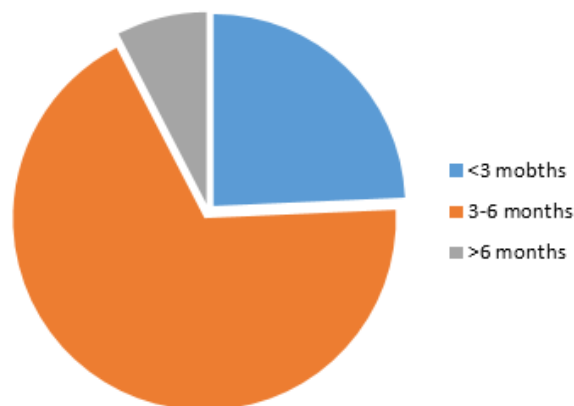


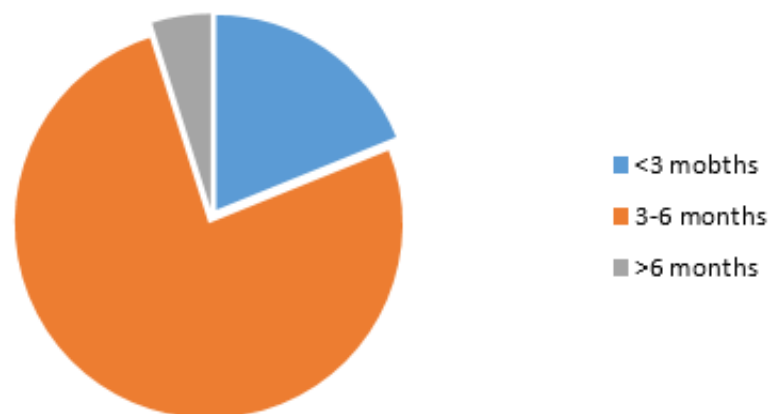
Figure 1: A pie chart showing time before seeking medical attention at any facility since symptoms began among breast cancer patients with late stage at presentation at MNH in 2018.

Delay in seeking advice was taken as presenting beyond three months of symptoms hence 140(76%) all breast cancer patients had delayed presenting to hospital. **Table 2** presents the association between the baseline factors and delay or no delay and the assessment of levels of significance of each. Delayed presentation was observed in all socio-demographic categories though with varying degrees. Regarding education status 22.3% more patients who lacked formal education compared to those with formal education had delay in seeking further care, and this finding was statistically significant (p , 0.003). Rural residency had 46.2% more women who delayed compared to those residing in urban, a very significant finding (p , 0.001). Looking at age, women who were below the age of 50 years had 21.9% more delays compared to older women, and this was significant (p , 0.009). Being employed in the informal sector had 10% more delays, but the difference was not statistically significant. Marital status had no influence of seeking medical attention.

Patients usually have to undergo a referral path to reach definitive level of care where investigations and treatment can be offered. Mean time from consultation at any facility to reaching MNH was found to be 125.7 ± 42.5 days (ranging from 7 – 240 days) with majority presenting between 3 to 6 months 141(76.2%) while only 35(18.9%) presented within three months, as shown in **Figure 2** below.

Table 2: Factors associated with delay in seeking medical attention among breast cancer patients

Variable	Total	% Delayed	P-value
Education			
No formal	42	92.9	0.003
Formal	143	70.6	
Residency			
Urban	39	46.2	0.001
Rural	146	83.6	
Employment			
Formal	100	71.0	0.118
Informal	85	81.0	
Marital status			
Single	83	73.5	0.533
Married	102	77.5	
Age Range			
< 50	93	83.9	.009
>50	92	67.4	

**Figure 2: A pie chart showing time from initial consultation at any facility to arrival at MNH in months among patients with late stage breast cancer in 2018.**

In order to assess the level of knowledge on crucial breast cancer aspects that may affect delay in seeking treatment, the participants were asked a series of questions whose responses have been presented in **Table 3** below. It was noted that the majority of our patients had good knowledge on some of the basic facts about the disease that should have brought them early to hospital: majority believed it was a curable disease (94.1%), that early detection would improve survival (87%) and that it can present with painless lump and could be inherited as was reported by 63% each. Only 7% thought it could be treated by traditional medicine.

Table 3: General Assessment on facts and myths regarding Breast Cancer among patients

Variable	Frequency (%)
Breast cancer is curable	174 (94.1)
Early detection can improve outcome	161 (87.0)
Presents with painless lump	118 (63.8)
Can be Inherited	117 (63.2)
Breast cancer can be cured by traditional medicine	13 (7)

Discussion

Though breast cancer is a superficial disease that should be 'easy' to detect, late presentation is not uncommon in our practice. This study was solely carried out among women with advanced BC at MNH, which receives patients from the whole of Tanzania. Tanzania has more than 120 culturally diverse ethnic groups, a fact that might hide significant reasons that affect health seeking behavior (8, 9). We sought in this study to expose the patient's related factors that affect how they navigate the health system from their place of domicile to tertiary treatment centers. This study did not compare these potential factors with women who present with early stages of the disease. This means our study cannot address whether what we are seeing is a delay or advanced and aggressive disease biology.

This study has demonstrated that delay in seeking further care is prevalent among Tanzanian women whereby 2 in 3 had delayed presenting to hospital after being suspicious

of a breast symptom. This finding is not surprising as there are similar reports from other countries like Libya and Rwanda (10, 11). This is unlike High Income countries (HICs) where patients present within the first month of suspicion (12, 13). In Tanzania, cancer patients receive free of direct payment services but only after a diagnosis of cancer has been confirmed. This definitive diagnosis can only be made after pathological evaluation of submitted specimen, which is only available in tertiary level hospitals in Tanzania. This makes several factors; socio-cultural and rural residence to potentially affect access to pathological services.

Women from rural residence locations were significantly more in patients with advanced BC compared to those with urban residence. This differs from a finding from a regression meta-analysis from Africa that revealed late BC presentation is neither influenced by region nor rural vs urban residency among black race (14). They further documented average younger age at diagnosis compared to patients from High Income countries similar to our findings on age. Increased community awareness programs and navigation strategies have the potential to downstage the disease by early identification. Such strategies employing the use of trained lay personnel have been shown to be able to identify patients in the communities and facilitate early referral for treatment in Sudan (15). Similar study in a Tanzanian village had yield significant down staged tumors when community navigators screened and referred suspicious cases for further investigations (16). For community detection and early diagnosis to be effective, assurance of the diagnosis and treatment are two important events (17). Likewise, since low level of education has been found to be significant factor in late stage disease and presentation delay, additional communication strategies are needed in rural communities.

Advanced BC was noted in both age groups, but significant young population (mean age 48 years) compared to western patients who are at an older age. However, age specific incidence rates of BC have not differed significantly from those in the West (18). Advanced BC in this younger age group need to be explored biologically to determine aggressiveness and inform early detection and treatment strategies. Understanding the disease in this age group will inform screening age, and resources needed to achieve that at lower level facilities.

Knowledge regarding BC early detection, treatment and its outcomes when diagnosed early was noted to be good in this study. But why the same BC patients still presented late is still unknown. A qualitative study among all women with various stages of BC is needed to understand factors that hinder early treatment seeking behavior. Late presentation of BC is usually accompanied with dismal results, and which might have negative reinforcement to the community on outcome of BC. Early detection positively impacts on BC treatment, especially where resources are scarce (19). Treating early cancer is simpler and more cost effective than treating advanced stage disease (20). Population of BC survivors can be explored as a potential workforce to help mobilize local resources to help with early diagnosis of BC in Low- and middle-income settings.

Conclusion

This study has recognized existence of late presentation following detection of breast mass among patients with advanced BC in Tanzania. Lack of formal education, residing in a rural residence and younger age were significantly associated with delay in seeking hospital treatment among this patient population in Tanzania. Studies to address delay among breast cancer patients are needed given the anticipated cost effectiveness.

Ethical approval and consent to participate

Ethical approval to conduct this study was obtained from MUHAS IRB and a separate hospital permission to use patients from the hospitals research and consultancy bureau was obtained. A written informed consent was obtained from all participants. There was no monetary compensation for participation. Treatment was fast tracked for all the patients as per the treating physician's management plan. Patients were interviewed in private rooms to ensure confidentiality of information offered. Additionally, data was de-identified during entry into the analysis software to maintain confidentiality.

Author's contribution

LOA designed, conducted and wrote the manuscript. EPM designed the manuscript, collected data and performed initial analysis; JMM wrote the manuscript; OVN wrote and critically reviewed the manuscript. All the authors have approved the manuscript for publication.

Acknowledgements

We highly acknowledge MNH for allowing access to their patients; we thank all the study participants, the Ministry of Health for their financial support and everyone else who was involved in assisting completion of the study.

List of abbreviations

BC	Breast Cancer
MNH	Muhimbili National Hospital
HIC	High Income Countries
MUHAS	Muhimbili University of Health and Allied Sciences
IRB	Institutional Review Board

Reference

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. **Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries.** CA CANCER J CLIN 2018;68:394–424 <https://doi.org/10.3322/caac.21492>.
2. Allemani C, Weir HK, Carreira H et al. **Outcome of Global surveillance of cancer survival 1995–2009: analysis of individual data for 25 676 887 patients from 279 population-based registries in 67 countries (CONCORD-2).** Lancet. 2015; **385**: 977-1010.
3. Kantelhardt E, Zerche P, Mathewos A, et al. **Breast cancer survival in Ethiopia: a cohort study of 1,070 women.** Int J Cancer. 2014;**135**: 702-709.
4. Islami F, Lortet-Tieulent J, Okello C et al. **Tumor size and stage of breast cancer in Cote d'Ivoire and Republic of Congo—results from population-based cancer registries.** Breast. 2015; **24**: 713-717.
5. Khan MA, Shafique S, Khan MT, Shahzad MF, Iqbal S. **Presentation delay in breast cancer patients, identifying the barriers in North Pakistan.** Asian Pacific J Cancer Prev. 2015;**16**(1):377–80.
6. Rambau P, Chalya P, Manyama M, Jackson K. **Pathological features of Breast Cancer seen in Northwestern Tanzania: a nine years retrospective study.** BMC Res Notes [Internet]. 2011;**4**(1):214. Available from: <http://www.biomedcentral.com/1756-0500/4/214>.
7. Ermiah E, Abdalla F, Buhmeida A, Larbesh E, Pyrhönen S, Collan Y. **Diagnosis delay in Libyan female breast cancer.** BMC Res Notes. 2012 Aug **21**;5:452. doi: 10.1186/1756-0500-5-452.
8. Pace LE, Mpunga T, Hategekimana V, Dusengimana J-M V., Habineza H, Bigirimana JB, et al. **Delays in Breast Cancer Presentation and Diagnosis at Two Rural Cancer Referral Centers in Rwanda.** Oncologist. 2015.
9. Benbakhta B, Tazi M, Benjaafar N, Khattabi A, Maaroufi A. **Determinants of patient and health system delays for women with breast cancer in Morocco, 2013.** 2015; BMC Res Notes. 2012 Aug **21**;5:452. doi: 10.1186/1756-0500-5-452.
10. Ermiah E, Abdalla F, Buhmeida A, Larbesh E, Pyrhönen S, Collan Y. **Diagnosis delay in Libyan female breast cancer.** BMC Res Notes. 2012 Aug **21**;5:452. doi: 10.1186/1756-0500-5-452

11. Odongo J, Makumbi T, Kalungi S, Galukande M. **Patient delay factors in women presenting with breast cancer in a low income country** Cancer. BMC Res Notes. 2015
12. Molinié F, Leux C, Delafosse P, Ayrault-Piault S, Arveux P, Woronoff AS, et al. **Waiting time disparities in breast cancer diagnosis and treatment: A population-based study in France.** Breast. 2013.
13. Reyes-Gibby C, Spitz M, Wu X, Merriman K, Etzel C, Kurzrock R, et al. 31st Annual Meeting * American Society of Preventive Oncology, Houston, Texas * March 2-4, 2007. Cancer Epidemiol Biomarkers Prev. 2007.
14. Jedy-Agba E, McCormack V, Adebamowo C, dos-Santos-Silva I. **Stage at diagnosis of breast cancer in sub-Saharan Africa: a systematic review and meta-analysis.** Lancet Glob Health. 2016; 4: e923-e935.
15. Abuidris DO, Elsheikh A, Ali M et al. **Breast-cancer screening with trained volunteers in a rural area of Sudan: a pilot study.** Lancet Oncol. 2013; 14: 363-370.
16. Ngoma T, Mandeli J, Holland JF. **Down staging cancer in rural Africa.** Int J Cancer. 2015; **136**: 2875-2879.
17. Nelson AM, Milner DA, Rebbeck TR, Iliyasu Y. **Oncologic care and pathology resources in Africa: survey and recommendations.** J Clin Oncol. 2016; **34**: 20-26.
18. Corbex M, Bouzbid S, Boffetta P. **Features of breast cancer in developing countries, examples from North-Africa.** Eur J Cancer. 2014; 50:1808-1818.
19. Anderson BO, Braun S, Lim S, Smith RA, Taplin S, Thomas DB, Global Summit Early Detection Panel. **Early detection of breast cancer in countries with limited resources.** Breast J. 2003 May-Jun; 9 Suppl 2():S51-9.
20. Carlson RW, Anderson BO, Chopra R, Eniu AE, Jakesz R, Love RR, Masetti R, Schwartzmann G, Global Summit Treatment Panel. **Treatment of breast cancer in countries with limited resources.** Breast J. 2003 May-Jun; 9 Suppl 2():S67-74.)