

Original Article

Patient delay in initiating treatment after breast cancer diagnosis: A cause for concern

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ABSTRACT

Objectives: Delayed presentation, diagnosis, and treatment negatively impact the survival of breast cancer patients. This study aimed to describe the time to initiation of treatment after breast cancer diagnosis and causes of delay to help identify targets for future interventions.

Material and Methods: A prospective study was carried out on breast cancer patients who had delay initiating two major oncologic treatments (chemotherapy and mastectomy) between July 2018 and June 2021. Data were analyzed by SPSS version 23.0.

Results: Sixty-two of 146 patients (42.5%) delayed initiating oncologic treatments. All patients were females, and their ages ranged from 21 to 70 years, with a median age of 48 years (mean 46.9 ± 10.3 years). Median durations of symptoms at presentation and between diagnosis and commencement of treatments were 6 and 10 months, respectively. The mean lump size at presentation and before treatment were 8.2 cm and 15.4 cm, respectively. Early versus advanced breast cancer was 21 (33.8%) vs. 41 (66.1%) at presentation and 2 (3.2%) vs. 60 (96.8%) before treatment. Major reasons for delayed treatment include the use of alternative therapy (48.4%), financial problems (24.2%), fear of surgery (9.7%), chemotherapy side effects (8.1%), and family interference (4.8%). The length of delay was not affected by the patient's age, marital status, or level of education ($p > 0.05$).

Conclusion: Patients had longer delays in initiating treatments after breast cancer diagnosis. Focusing on causes of secondary patient delay is equally as important as early detection and diagnosis.

Keywords: Breast cancer, Delayed treatment, Intervals, Reasons

INTRODUCTION

Breast cancer is the most common cancer among women worldwide and is a leading cause of cancer-related mortalities.^[1] The incidence of breast cancer is higher in high-income countries (HICs) than the low and middle-income countries (LMICs). However, there is a disproportionately high rate of mortality-to-incidence ratio in LMICs because of late diagnosis and treatment.^[2] According to Espina *et al.*,^[3] presentation intervals longer than six months were documented in most African women, and in the review by Jeddy-Agba *et al.*^[4] in Nigeria, over 70% of patients were diagnosed with advanced-stage disease.

There are two major types of delay: patient delay and system/provider delay.^[5,6] Patient delay is a delay in seeking medical attention after noticing a potential breast cancer symptom, and system delay is a delay within the healthcare system between the first presentation to the time of initiating

treatment.^[5] Recent literature prefer the term “interval” instead of “delays”.^[7-9] The system interval has been further sub-categorized into two: primary care and secondary care intervals.^[10] The primary care interval is between first physician contact and referral, and the secondary care interval is between referral and commencement of treatment. The provider interval is sub-classified into the diagnosis and treatment interval: the diagnosis interval is from the first medical consultation to the confirmation of a cancer diagnosis, and the treatment interval is the time between diagnosis and the beginning of oncologic treatment.^[6]

According to the aforementioned classifications, delays in commencing definitive treatment after the diagnosis of cancer are often blamed on the system and provider, exonerating the patients, notwithstanding reports showing patient-related factors causing delays in diagnosis and treatment in the provider or system interval. A study in southwest and

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northcentral Nigeria identified a cluster of patients who deliberately delayed presentation to specialists after exiting the patient interval.^[9]

To cater for the instance of patient-related delays, the term “secondary patient delay” will represent patient delay within the system or provider interval in this study and will be used henceforth. Further categorization of the causes of delay within the system interval will enable focused intervention and better treatment outcomes. The objective of this study was to describe the time to initiation of treatment after diagnosis of breast cancer as well as causes of delay to help identify targets for future interventions.

MATERIAL AND METHODS

This was a prospective study of patients with histologically confirmed breast cancer managed at Ekiti State University Teaching Hospital (EKSUTH), Ado Ekiti, between July 2018 and June 2021. Patients had delays in the initiation of two major oncologic treatments (chemotherapy and mastectomy). Patients with early disease (stage I and II) and locally advanced breast cancer (stage III), as determined by the American Joint Committee on Cancer (AJCC Cancer Staging Manual, Seventh Edition), were included in this study. Patients who presented with distant metastasis were excluded. All the patients were counseled for chemotherapy and mastectomy. The approval of the study was obtained from the Ethics and Research Committee of our institution (EKSUTH/A67/2018/07/008).

A well-designed proforma was developed and used for the study. Two resident doctors were trained on how to collect information using the proforma, which was pre-tested on five patients at the breast oncology clinic of EKSUTH for modifications, clarity, and validity. Data on patients' sociodemographic variables, including age, religion, occupation, marital status, educational level, and menstrual status were collected. Tumor-specific variables were also collected, including tumor size, lymph node status, and clinical stage.

The data on intervals between breast cancer symptom detection and the time of presentation (SP), between presentation and confirmation of diagnosis (PD), and between diagnosis and initiation of treatment (DT) were collected at different times during the study. The total interval (TI) is the period between the onset of symptoms and initiation of treatment (i.e., SP + PD + DT). Since the primary outcome of this study is on DT interval, we chose a month (30 calendar days) as previously described by Smith and Redondo *et al.*^[11,12] All the patients who failed to commence chemotherapy or have surgery within a month (30 days) of confirmation of breast cancer after being duly counseled for the treatments were included in

this study. Additional information on the tumor size, clinical stage at the commencement of treatment, and reasons for the delay in commencing treatments were sought.

Statistical analysis

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 23.0. and results were presented in simple percentages. Categorical data were compared using Chi-square. Association between patients' age, level of education, marital status, and stage of cancer were compared with the total interval. The level of significance was set at $p < 0.05$.

RESULTS

Sixty-two of 146 patients (42.5%) delayed initiating oncologic treatments during the study. All patients were females and their ages ranged from 21 to 70 years, with a median age of 48 years (mean 46.9 ± 10.3 years). The sociodemographic characteristics of the patients are shown in Table 1. The majority (60%) of the patients were premenopausal.

All patients had breast lumps ranging from 2 to 20 cm (mean 8.2 ± 4.4 cm, median 7.0 cm, interquartile range (IQR) 5.0 – 12.0 cm) at first presentation. Following secondary patients' delay, there was an increase in the size of the tumor with size ranging from 4 to 32 cm (mean 15.4 ± 6.5 cm, median 16.0 cm, IQR 9.75 – 20.0 cm). The AJCC clinical stage at first

Table 1: Sociodemographic characteristics of the patients.

| Socio-demographics | Frequency | Percent |
|--------------------------|-----------|---------|
| Age group (year) | | |
| 21–30 | 6 | 9.7 |
| 31–40 | 10 | 16.1 |
| 41–50 | 25 | 40.3 |
| 51–60 | 16 | 25.8 |
| 61–70 | 5 | 8.1 |
| Gender | | |
| Female | 62 | 100.0 |
| Education | | |
| None | 2 | 3.2 |
| Primary | 8 | 12.9 |
| Secondary | 19 | 30.7 |
| Tertiary | 33 | 53.2 |
| Marital status | | |
| Single | 4 | 6.5 |
| Married | 51 | 82.2 |
| Separated | 1 | 1.6 |
| Widow | 6 | 9.7 |
| Menopausal status | | |
| Premenopausal | 37 | 59.7 |
| Postmenopausal | 25 | 40.3 |
| Occupation | | |
| Employed | 54 | 87.1 |
| Unemployed | 8 | 12.9 |

Table 2: Clinical stage at presentation and commencement of treatments.

| Stage | First presentation (%) | Commencement of treatment (%) |
|-------|------------------------|-------------------------------|
| I | 3 (4.8) | 0 (0) |
| II | 18 (29.0) | 2 (3.2) |
| III | 41 (66.1) | 42 (67.7) |
| IV | 0 (0) | 18 (29.0) |
| Total | 62 (100.0) | 62 (100.0) |

presentation and commencement of treatments are given in Table 2. Early versus advanced breast cancer was 21 (33.8%) vs. 41 (66.1%) at presentation and 2 (3.2%) vs. 60 (96.8%) before treatment. There was tumor progression and stage migration of the disease leading to a reduction in the number of patients with early disease and a concomitant increase in the number of patients with advanced disease.

The right breast was affected in 29 (46.8%), the left breast in 27 (43.5%), and 6 (9.7%) patients had bilateral disease. Fifty-one (82.3%) patients had ipsilateral axillary lymph node involvement at the first presentation.

The durations of the different intervals are shown in Table 3. The duration between diagnosis and treatment was the longest. Various reasons were adduced for the delays in commencing treatments after breast cancer confirmation, as shown in Table 4. About half (48.4%) of the patients delayed

Table 3: Durations of intervals.

| Intervals | Range | Mean (SD) | Median | IQR |
|-------------|----------|-------------|--------|-----------|
| SP (months) | 1–32 | 8.9 (6.9) | 6.0 | 4.0–12.0 |
| PD (weeks) | 1–16 | 4.8 (2.7) | 4.0 | 3.0–6.0 |
| DT (months) | 2–36 | 12.9 (9.2) | 10.0 | 5.8–21.0 |
| TI (months) | 5.0–47.0 | 22.9 (10.7) | 21.0 | 13.0–31.0 |

SP – onset of symptom to presentation, PD – presentation to diagnosis, DT – diagnosis to treatment, TI – between onset of symptom and initiation of treatment (total interval), SD – standard deviation, IQR – interquartile range.

Table 4: Reasons for delays in commencement of cancer treatments.

| Reasons for delayed treatment | Frequency (%) | Percent |
|---|---------------|------------|
| Use of alternative treatment | 30 | 48.4 |
| Lack of money | 15 | 24.2 |
| Fear of surgery | 6 | 9.7 |
| Chemotherapy side effects/death | 5 | 8.1 |
| Family interference | 3 | 4.8 |
| Industrial action (Health workers strike) | 2 | 3.2 |
| Feeling of cure after excision | 1 | 1.6 |
| Total | 62 | 100 |

treatment because they first resorted to spiritual healing, while about a quarter of patients had financial constraints.

There was no significant association between patients' age ($p = 0.17$), level of education ($p = 0.06$), marital status ($p = 0.29$), stage of cancer ($p = 0.23$), and the length of the delay/total interval before initiation of treatments. The longest delay (mean, 27.7 ± 9.5 months) was observed among those who used complementary and alternative medicine (CAM) before commencing conventional therapy, while the least delay (mean, 15.6 ± 4.9 months) was found in those with fear of chemotherapy.

DISCUSSION

The findings in this study showed that patients contributed significantly to delay in initiation of treatment after diagnosis of breast cancer. This is a major cause for concern, considering the initial delay by most patients before presentation. Up to the present time, efforts are more focused on sensitization and awareness campaigns to encourage early presentation and prompt diagnosis with the hope that this translates to early treatment and better survival. Unfortunately, the gains of this process are negated by secondary patients' delay after diagnosis.

The average duration of symptoms before presentation was about 9 months in this study. This finding aligns with previous studies in this center that reported delayed presentations.^[13,14] A time gap of greater than 3 months (90 days) between symptom detection and first medical consultation was regarded as patient delay (6), and a similar time delay was reported as contributing significantly to stage migration by Agodirin *et al.*^[15] in Southwestern and North central Nigeria. Despite the fact that the trend of late presentation has not really changed over time, what is more worrisome is the prolonged period recorded between diagnosis and treatment in this study. According to the review by Unger-Saldaña,^[6] the longest delays occurred between the first medical consultation and the beginning of treatment, termed the provider interval. With the average time to diagnosis of 4.8 weeks in this study, it might be misleading to refer to the period in question as provider interval, as this entirely puts the blame of delayed intervention on the physicians. The term "secondary patient delay" might be more appropriate when there is a timely diagnosis. Clear identification of these intervals is sacrosanct to enable focused intervention. Considering the two long intervals (before presentation and after diagnosis and commencement of treatment) in this study, more attention should be put on addressing the root causes of delays, which perhaps will be as equally important as early detection and diagnosis.

Different factors contributing to delays are resident in the different intervals. In Nigeria and many other developing countries, a combination of poor health education, poverty,

high belief in traditional and faith-based therapies, ignorance of breast cancer symptomatology, fear of mastectomy, inadequate health funding, and lack of screening programs have been found to be responsible for prolonged interval before presentation.^[14,16-19]

In this study, delays in treatment initiation in about half of the patients (48.4%), who also had the longest delay were linked to the use of spiritual healing, food supplements, longevity products, and herbs. These are generally classified as complementary and alternative medicine (CAM). CAM use after breast cancer confirmation in our patients can be explained by our people's sociocultural and religious beliefs and practices and their understanding of cancer as being a "spiritual attack". Greenlee *et al.*^[20] in their study also observed that CAM modalities used, especially dietary supplements, decreased initiation of clinically indicated chemotherapy. Some studies in developed nations reported that the prevalence of CAM use among cancer patients varies from 7% to 83%, and even between reports on the same population.^[21,22] Subsequent researches in Nigeria may focus on describing the prevalence in Nigeria and its implications on cancer care.

A quarter of patients (24%) delayed treatment for financial reasons. The prohibitive cost of conventional antineoplastic agents is still a big challenge as healthcare financing is by way of fees for service or out-of-pocket expenditures.^[14] The Government efforts at subsidizing treatment and involving Non-Governmental Organizations and philanthropists in the care of cancer patients might reduce the financial burden faced by the patients.

Fear of mastectomy is a cause of delayed presentation and also a major reason for absconding treatment after presentation.^[18,23] This is because of the people's erroneous belief that mastectomy often leads to death after the operation. Our study showed that 10% of patients delayed treatment because of fear of mastectomy. Since mastectomy is an integral part of breast cancer management, especially in the developing world, efforts should be made to address the associated fear by giving adequate counseling, allowing patients to express their fears, and dispelling the misconceptions linking mastectomy to mortality. Early introduction of newly diagnosed breast cancer patients to healthy survivors might allay this fear.

Some patients also attributed their delay to fear of chemotherapy vis-à-vis its side effects and perceived "lethality". The attending physician has a major role to play in ensuring that patients are well counseled. While it may not be advisable to mince words in explaining the side effects of drugs, it might be reassuring to patients that the side effects are temporal and mostly reversible.

It is noteworthy that some of the reasons found to be responsible for delay in treatment initiation in this study

have also been previously identified as causes for delayed presentation. This is similar to the findings by Clegg-Lamptey *et al.*^[23] who reported similar reasons for delayed presentation and abscondment during treatment among Ghanaian patients. This underscores the importance of adequate counseling at the time of diagnosis. More efforts should be geared toward addressing the causes of delay before presentation and delay of treatment after diagnosis.

The delay of the appropriate conventional cancer treatment negatively impacts the survival of breast cancer patients.^[24,25] The median duration of commencement of treatments after diagnosis was 10 months in this study. During this period, there was tumor progression and stage migration of the disease with the attendant reduction in the number of patients with early disease and a concomitant increase in the number of patients with advanced disease. According to Flores-Balcázar *et al.*,^[26] initiation of treatment within the first 45 days of diagnosis of breast cancer in women portends better survival, whereas delay decreases survival, especially in women with tumors in more advanced clinical stages. Judging from the upstaging of the disease in this study, it could be inferred that delay will most likely lead to a worse outcome.

In this study, there was no significant association between the common sociodemographic characteristics and delay in initiating treatment after diagnosis. However, in a study in the Northern part of Nigeria, delayed treatment of symptomatic breast cancer was significantly associated with younger patients, elementary or no Western education, and those domicile outside the metropolitan area.^[27] In a Ghanaian study, married women were more likely to abscond from treatment after diagnosis.^[23]

CONCLUSION

In addition to the long patient interval, there was an even longer treatment interval due to secondary patient delays, leading to more stage migration in the treatment interval. Focusing on causes of secondary patient delay is equally as important as early detection and diagnosis.

Ethical approval

The research/study is approved by the Institutional Review Board at Ekiti State University Teaching Hospital, number EKSUTH/A67/2018/07/008, dated 24/7/18.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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