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ORIGINAL ARTICLE

PATTERN OF POST-TREATMENT METASTATIC SUBSITES IN BREAST CANCER PATIENTS IN A TERTIARY HEALTHCARE CENTRE IN NIGERIA

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ABSTRACT

Introduction: *Managing breast carcinoma in Nigeria is challenging as a large proportion of these patients present at advanced stage of their disease. Our study aims at determining the pattern of post-treatment metastasis in the University of Benin Teaching hospital.*
Methods: *A retrospective review of records of breast cancer patients seen over a five-year period (January 2013 to December 2017) was conducted. Relevant information was extracted and analyzed with statistical package for social science software 21.*
Results: *A total of 292 patients with carcinoma of the breast were seen at the University of Benin Teaching Hospital. Metastases developed in 113(38.7%) patients post-treatment with taxane-based therapy within 2 years. Majority of patients were aged 30-59years (77.4%). Moderately differentiated carcinoma was the main histologic diagnosis (62.8%). The pattern of metastases was commonly to the loco-regional sites (39.5%), bone (16.9%), lungs (10.6%), brain (6.3%) and liver (4.4%) while multiple sites were (15.0%) and of these, 51.3% developed the metastasis within 10 – 12months. Within a period of 2 years, 60.2% had stable disease.*
Conclusion: *Our study showed loco-regional site as the commonest metastatic sub-site in this region with bony metastasis being the commonest distant spread. These occur commonly within the first one year post-treatment. Careful evaluation of these sites during follow-up is advocated to ensure early detection and appropriate management. This study also showed a significant survival of patients at 2 years following taxane-based therapy. We therefore advocate that taxane-based therapy should be the main stay of treatment of breast cancer patients.*
Keywords: *Metastatic breast cancer; pattern of metastasis; breast; taxane.*

INTRODUCTION

Breast cancer is the most common cancer in women worldwide. It accounts for 12 percent of all cancers diagnosed yearly, and a major cause of cancer-related death in women worldwide (1).

Approximately 1.68 million new cases of breast cancer were diagnosed and 520,000 deaths from breast cancer recorded globally, in 2012 (1). The lifetime risk of developing invasive breast cancer is about 1 in 8 American women and 1 in 100 men (2).

In Nigeria, breast cancer accounts for 29.7% of 818 cancer cases seen annually. This makes it the most common cancer with a substantial increase in its incidence in recent times (3, 4).

Breast Cancer peaks a decade earlier in Nigerian women than in Caucasian women (5). This disease is aggressive and unpredictable in Blacks: some patients present with early stage disease and succumb to widespread metastasis within six months to one year; some patients survive longer despite presenting with advanced disease (5). There are disparities concerning breast cancer in blacks in contrast to the Caucasians with peculiar characteristics of breast cancer among blacks (6).

Breast cancer incidence in Nigeria is rising: 13.8-15.3 per 100,000 in 1992; 33.6 per 100,000 in 2000 (7). It was estimated that 7000 - 10,000 new cases would develop in 2005, and most of these patients presented with advanced disease (7, 8). A lot of advocacy and health enlightenment has been instituted, leading to an overall 5-year survival rate of 89% which is a dramatic improvement over the 63% rate recorded in early 1960s. The 5-year survival rate is dependent on the stages of breast cancer: 99% for localized disease; 85% for regionally advanced disease (spread to regional lymph nodes), and 26% for distant metastasis (stage 4) (9).

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There is paucity of data as regards metastatic sub-sites and time to metastasis in our locale hence the need to determine the pattern of metastatic sub-sites post-treatment- the aim of our study.

MATERIALS AND METHODS

This study was conducted at the Radiotherapy and Surgery Departments of University of Benin Teaching Hospital (UBTH) Benin, Edo State, the premier tertiary referral center in South-South Nigeria and it provides radiotherapy and surgical services for neighboring states. It was a retrospective review of all patients that had metastasis following treatment (post-treatment) for breast cancer between January 2013 and December 2017.

Post-treatment refers to all patients who had metastasis following modified radical mastectomy, taxane-based chemotherapy and External beam irradiation. All patients had 3 - 4 cycles of neo-adjuvant taxane-based chemotherapy and 4 – 6 cycles of adjuvant taxane-based chemotherapy. These were included in the study. Data obtained include the socio-demographics, menopausal status, parity of the patient, metastatic sub -sites and time to metastasis post-treatment.

All the patients had routine investigations as follows: Abdominopelvic Ultrasound, a Chest X-ray, Liver Function Test, a Bone Scan and Computerized Tomography scan as appropriate. Clinico-pathological features of the patients: site of the disease (left, right or both breast), Stage, Histological subtypes, Histological grade, Hormone receptor status, Metastatic sub sites, Status within two years following treatment

All the patients had late-stage disease.

Diagnosis of post-treatment metastatic lesions was made from clinical and radiological evaluation. Following diagnosis of post-treatment metastatic disease, triple negative patients received further adjuvant platinum-based chemotherapy while hormone receptor positive patients received hormonal therapy. Her2/Neu positive patients were managed with trastuzumab and cytotoxic chemotherapy where affordable, otherwise they received further cytotoxic chemotherapy alone.

The protocol of this study was in accordance with the World Medical Association Declaration of Helsinki.

The data obtained were analyzed using the IBM Corporation Statistical Package for the Social Sciences (SPSS) statistics for windows, version 21.0. Armonk, New York, United States of America.

RESULTS

Two hundred and Ninety-two patients were seen during the study. Of these, 113 (38.7 %) had metastatic disease post-treatment with taxane-based chemotherapy and external beam irradiation.
Peak age at presentation was 40-49 years (31.1%). (Figure 1)

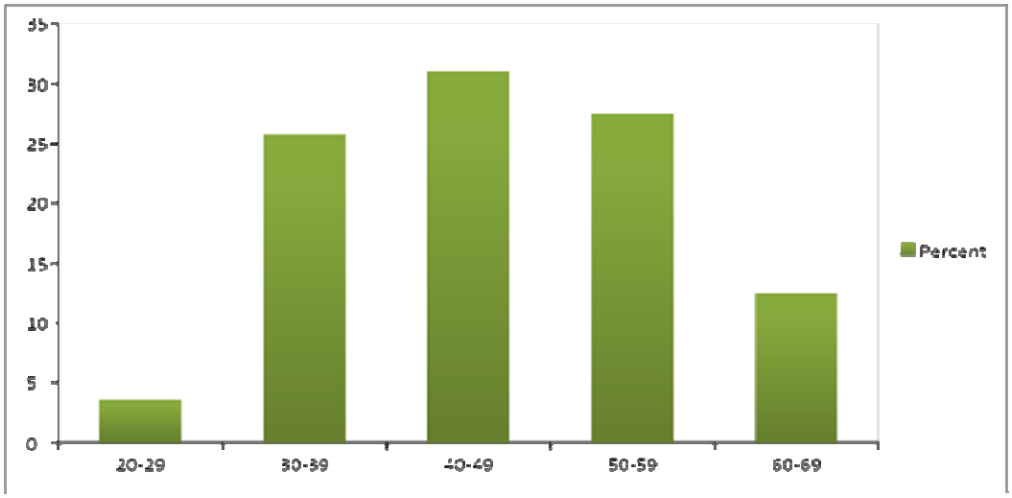

Figure 1: Age distribution of metastatic breast cancer patients, University of Benin Teaching Hospital, 2013-17.

Mean age at presentation was 44.51years. Most patients in this study were premenopausal (54.0%), multiparous (73.5%) with tertiary education (53.1%). (Table 1)

Table 1: Patients' characteristics, University of Benin Teaching Hospital, 2013-17.

Sex	Frequency	Percent
Male	1	0.9%
Female	112	99.1%
Menopausal status		
Premenopausal	61	54.0%
Postmenopausal	52	46.0%
Parity		
Nulliparity	15	13.3%
Primipara	7	6.2%
Multiparity	83	73.5%
Grandmultiparity	8	7.1%
Educational Status		
None	4	3.5%
Primary	12	10.6%
Secondary	37	32.7%
Tertiary	60	53.1%

Invasive ductal carcinoma of the breast was the commonest histologic variant, accounting for 95.6% of the metastatic disease. Most of these carcinomas were moderately differentiated (62.8%). (Table 2)

Table 2: Site of Cancer, histologic types and grade of differentiation, University of Benin Teaching Hospital, 2013-17.

Site of cancer	Frequency	Percent
Right breast	49	43.4%
Left breast	52	46.0%
Bilateral	12	10.5%
Histologic types		
Invasive Ductal Carcinoma	108	95.6%
Medullary Carcinoma	2	1.8%
Papillary Carcinoma	2	1.8%
Invasive Lobular Carcinoma	1	0.9%
Grade of differentiation		
Well differentiated	10	8.8%
Moderately differentiated	71	62.8%
Poorly differentiated	32	28.3%

The Immunohistochemistry report of the study participants were as follows: ER +ve 27.4% (31), PR +ve 7.0% (8), ER/PR +ve 34.5% (39) and Triple negative (ER +ve, PR +ve and Her2/neu +ve) 28.3% (32). Triple positive, Her2/neu positive only and PR +ve/ Her2/neu +ve were 0.9% (1) respectively. Cumulatively ER positivity was 61.9%.

Distant metastasis occurred in 60.7% of patients. Bone was the commonest distant site (16.9%). Ipsilateral axillary nodes were the commonest locoregional site (27.5%). Metastasis to multiple sites was found in 15.0% of patients in this study. (Figure 2)

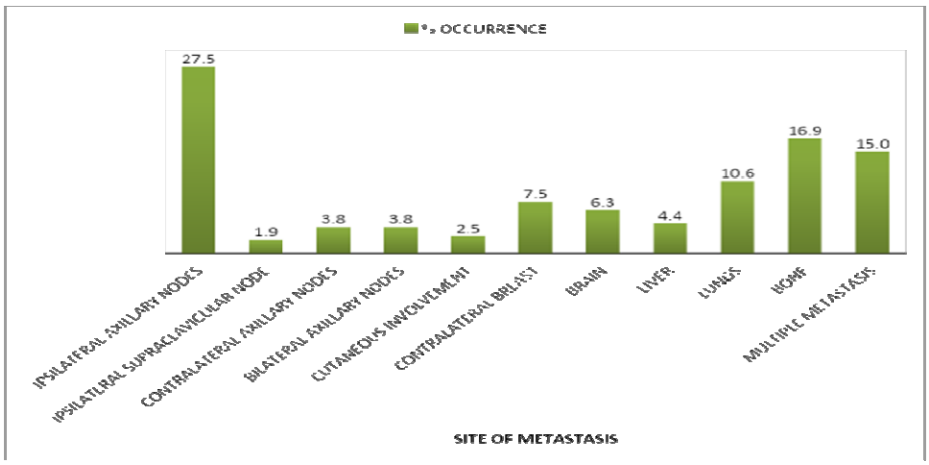

Figure 2: Pattern of metastasis, University of Benin Teaching Hospital, 2013-17

Most (51.3%) of the patients in this study, developed metastasis within 10-12 months while 28.3% developed metastasis within 22 – 24 months. (Figure 3)

Majority of the patients were alive at 2 years; 12.4% were disease free, 60.2% had stable disease while 7.0% died. (Fig 4)

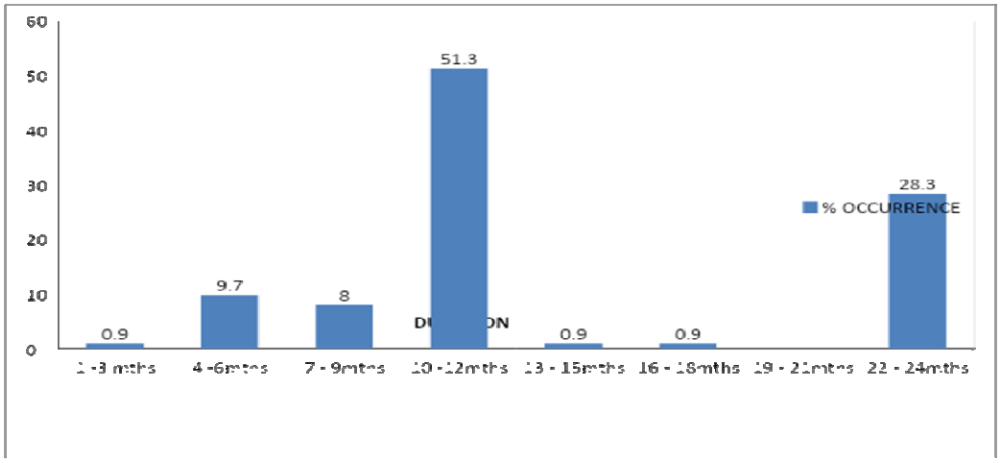

Figure 3: Time to metastasis, University of Benin Teaching Hospital, 2013-17

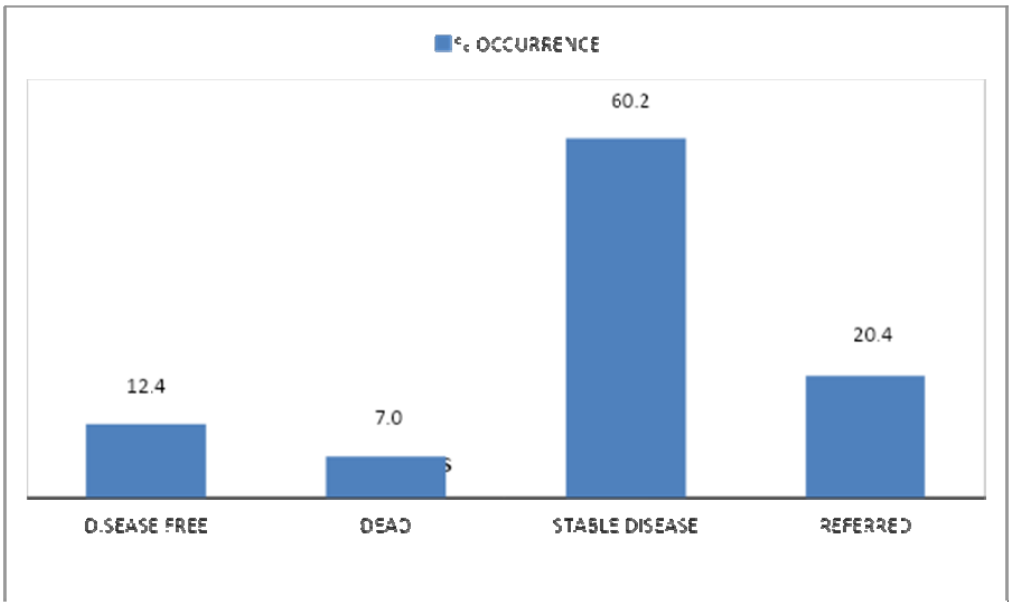

Figure 4: Status after two years, University of Benin Teaching Hospital, 2013-17

DISCUSSION

Breast cancer can metastasize to any part of the body and this was the cause of death in most of the patients with this disease (10). Our study showed that 113 (38.7%) of the patients seen within the study period had metastasis post treatment; this is higher than that reported by Thompson where 10 -15% had distant metastasis within 3 years of diagnosing the primary tumor (11). Most (53.8%) of our patients were between the ages of 30 and 50 years with mean age of 47 years. This is comparable to the works done by Adebamowo et al and Rahman GA et al; where most patients were young, pre- and peri-menopausal (12,13,14). Breast cancer in the young is known to be more aggressive, more likely to recur after treatment loco-regionally or at distant sites and associated with shorter disease free survival and higher mortality, than in older women. (15).

In our study, invasive ductal carcinoma of the breast was the commonest histologic variant and accounted for greater than 50% of the metastatic disease. Most of these carcinomas were moderately differentiated .This is in tandem with other studies that showed invasive ductal carcinoma of the breast as the most common histologic type (16, 17, 18). The histologic subtype and grade have a substantial influence on the development of metastasis and survival in patients with breast cancer (19). The pattern of immunohistochemistry in our study- estrogen positivity of 61.9% and triple negativity of 28.3% - is comparable to previous studies done in Nigeria (20, 21).

There is a high proportion of distant metastasis (60.7%) in this study and this is in contrast to reports by Ikpatt OFR et al (19) and Tesfamariam A et al (22) which showed a high proportion of loco-regional disease. In this study, bone was the commonest distant site (16.9%). Varying incidence of bone metastasis have been reported in Nigeria; Ketiku K documented 19.6% in Lagos and Elumelu TN et al reported 24.1% in Ibadan (23, 24).

In Zaria, Nigeria, 72.0% of all bone metastasis seen were primarily from Breast cancer (25).

Lung metastasis accounted for (10.6%), and liver (4.4%); which is lower than that found by Tesfamriam et al (22). In Ile Ife, Adesunkanmi et al, reported a higher incidence of lung metastasis (20.3%) (26), while in Uganda 42 % of their patients had lung metastases (27). These discrepancies may be due to difference in study designs.

In our study, brain metastasis accounted for 6.3%. Clegg-Lamptey JNA et al and Lee YT reported a comparable incidence of brain metastasis in their studies (28, 29). Brain CT scan, MRI or PET scan either singly or in combination are required for the diagnosis of brain metastasis. Most of our patients are unable to afford CT scan or MRI by the time they develop brain metastasis. Majority of these patients are terminally ill patients and require palliative care, thus, there is the need to weigh the cost against the benefit of these diagnostic tools.

Metastasis to multiple sites was found in 15.0% of patients in our study, this increases their risk of death from the disease. Most deaths from the disease are accounted for by distant metastasis rather than the primary tumor (30).

Most (51.3%) of the patients in this study, developed metastasis within 10-12 months, so a close follow up during this period is required for early detection of metastasis and appropriate treatment.

Majority of the patients were alive at 2 years; 12.4% were disease free while 60.2% had stable disease, 7.0% died but 20.4% were referred back to their primary physicians based on proximity to their place of abode and need for care by close relatives.

Taxane-based chemotherapy was used in this study and we recorded 60.2% of a stable disease at 2 years. Extended survival with taxane-based chemotherapy in metastatic breast cancer has been reported (31, 32).

Limitation of the study

Metastatic lesions were not subjected to pathological evaluation in this study. Diagnosis of metastasis was made based on clinical and radiological features of the lesions.

Follow up of patients was a challenge. Patients needed to be supported to get Taxane for completion of treatment.

Conclusion

The report of this study is a reflection of the disease pattern in this region where the commonest metastatic sub-sites is loco-regional with bony metastasis occurring as the commonest distant spread.

These occur commonly within the first one year post-treatment.
During follow up, these sites should be carefully evaluated to ensure early detection and appropriate management.

This study also showed a significant survival of patients at 2 years following taxane-based therapy. We therefore advocate that taxane-based therapy should be the main stay of treatment of breast cancer patients.

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Conflict of interest

The authors declare that they have no conflicts of interest in this study.

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