

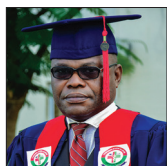


Original Article

Breast cancer metastasis patterns in Yenagoa, Nigeria

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ABSTRACT

Objectives: The objective of this study was to study the characteristics and patterns of metastatic breast cancer in Yenagoa, Nigeria.

Material and Methods: This study was a retrospective hospital-based study using a standardized data form for the capture of relevant information with definite exclusion criteria. Information gathered was captured in an Excel spreadsheet and subjected to statistical analysis. Subjects were 78 female patients diagnosed with breast cancer.

Results: The mean age of the study population was 47.86 years. About 64% had 1–4 children while 26% had more than five children. The most common findings on general clinical examination were anemia (43.6%), cachexia (39.7%), and hepatomegaly (11.5%). On breast examination, the most common findings were axillary lymphadenopathy (87.2%), nipple changes (67.9%), peau d'orange (64.1%), skin nodules (64.1%), and chest fixity (60.3%). About 29.5% of patients had evidence of pulmonary metastasis, 19.2% had liver metastases, and 25.6% had spread to multiple sites. Central nervous system and spinal spread were found to be commoner in younger patients (<48 years).

Conclusion: Most of the patients presenting in the hospital had evidence of metastasis. This has been found to be due mostly to delay in hospital presentation due to a complex combination of patient and healthcare-related factors. Measures for improving the dire statistics are proffered.

Keywords: Breast cancer, Metastasis, Delayed presentation, Complications, Spread pattern

INTRODUCTION

Breast cancer is the most common malignancy in women.^[1,2] In 2018, over 2.09 million new cases were diagnosed worldwide resulting in more than 600,000 deaths. At least, 4.4 million women are living with breast cancer.^[1,2] Age-standardized incidence rates in Nigeria range from 43.6 to 56.7/100,000 with age-standardized mortality rates of 16.7–20.0/100, 000.^[1] Even in early-stage breast cancer, 20–30% of patients already have distant metastases and at least 90% of mortalities in breast cancer have been found to be due to the complications of metastatic or recurrent disease.^[3,4]

This study aims to determine the sites of breast cancer metastasis in our environment to improve the allocation and deployment of resources and efficiently manage complications that are common in our area.

The most common sites for metastasis of breast cancer are the bones, liver, lungs, and brain.^[3] There has been extensive research done on why these tissues are most commonly involved in distant spread. Several theories are extant and have contributed immensely to understanding this process:^[4]

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Growth factor theory

This holds that tumor cells in the blood or lymphatics invade organs at a similar frequency but only those that find favorable growth factors can multiply. Transferrins, for example, are iron-transferring ferropoteins needed for cell growth that have additional mitogenic properties beyond their iron-transporting functions. Increased concentrations of transferrin are found in the lungs, bone, and brain and are associated with elevated levels of transferrin receptors on metastasizing tumor cells.^[5]

Adhesion theory

Endothelial cells lining the blood vessels in certain organs express adhesion molecules that bind tumor cells and allow extravasation.

Chemokine theory

Chemokines secreted by the target organ can enter the circulation and selectively attract tumor cells which express receptors for these chemokines. Breast cancer cells preferentially metastasize to the liver, bone marrow, lymph nodes, and lung. These organs secrete CXCL12-C-X-C motif chemokine 12 (CXCL12) which is the ligand for the C-X-C chemokine receptor 4 (CXCR4) which is enriched on breast cancer cells.^[5]

Pre-metastatic niche theory

Bone marrow-derived progenitor cells expressing vascular endothelial growth factor (VEGF) receptor 1 and very late antigen 4 (VLA-4) are prompted by the primary tumor to establish sanctuaries for the tumor cells before their arrival.^[5]

Six steps can be defined in cancer metastasis:^[6,7]

- Detachment: Tumor cells will detach from the primary tumor and acquire motility while losing the ability to adhere to neighboring cells
- Invasion: The detached cells break through the basement membrane and migrate through surrounding tissues until they eventually reach a blood or lymphatic vessel
- Intravasation: This occurs in the blood or lymphatic circulation either directly in the tumor neovasculature or indirectly in lymphatic channels
- Transport and arrest
- Extravasation: Migration into tissues through the vascular endothelium
- Invasion of the target organ.

MATERIAL AND METHODS

Design

This study was a hospital-based retrospective study.

Setting

The study was carried out at the Federal Medical Center Yenagoa, a 400-bed hospital serving as the only tertiary health facility for the 1.2 million people of Bayelsa State.

Yenagoa is the capital of Bayelsa state with a population of approximately 250,000 people.

They are served by private clinics run by general practitioners but a lot of people patronize tradomedical practitioners, patent medicine stores, and new generation churches for their ailments.

Duration

This study duration was from January 2022 to –December 2022.

Population

All patients diagnosed with breast cancer in the hospital within the specified time period.

Study inclusion criteria

The following criteria were included in the study:

- Patients with breast complaints are seen in the hospital through the general outpatient, surgical outpatient, and emergency departments
- Patients who had a comprehensive history and physical examination carried out including clinical staging, laboratory investigation, and imaging
- Patients who were seen or reviewed by a senior registrar or consultant
- Patients with histologically confirmed breast cancer
- Patients with properly documented treatment records.

Study exclusion criteria

The following criteria were excluded from the study:

- Patients with incomplete and poorly documented medical records
- Patients who were unable to pay for biopsy and histological analysis
- Patients who were unable to carry out staging investigations such as chest X-ray, abdominal ultrasound scan, and skeletal survey.

Ninety-one patient records were retrieved but only 78 were entered in the study because 13 were ruled out by the exclusion criteria.

Methods

Patient registries in the general outpatient, surgical outpatient, and emergency departments were retrieved and examined for patients with breast-related complaints and diagnoses within the specified time period.

Patient case notes were then recovered and subjected to the inclusion and exclusion criteria listed above with a selection of patients found suitable.

Investigations carried out on these patients included:

- Full blood count
- Liver function tests
- Excisional, incisional, or tru cut biopsy
- Chest X-ray
- Spinal X-rays
- X-ray of long bones
- Abdominal ultrasound scan.

Data analysis

Sociodemographic and other information were obtained from patient records using a structured pro forma. Retrieved data were entered into Microsoft Excel and exported to IBM Statistical Package for the Social Sciences version 21 for statistical analysis.

Data were tested for normality using Kolmogorov–Smirnov Statistics before the selection of statistical methods. Comparison between proportions employed Fisher's exact test. $P < 0.05$ was considered statistically significant.

RESULTS

[Table 1] shows that the mean age of the study population was 47.86 years.

About 80% of patients reached menarche between 12 and 14 years, 64% had 1–4 children, and 26% had more than five children.

[Table 1] also outlines the laterality of breast cancer in the patients studied.

The most common findings on general clinical examination were anemia (43.6%), cachexia (39.7%), and hepatomegaly (11.5%).

On breast examination, the most common findings were axillary lymphadenopathy (87.2%), nipple changes (67.9%), peau d'orange (64.1%), skin nodules (64.1%), and chest fixity (60.3%).

This is a testament to the general late presentation in this cohort.

[Figure 3] shows that 29.5% of patients had evidence of pleural metastases, 19.2% had liver metastases, and 25.6% had spread to multiple sites.

[Table 2] shows that there was a statistically significant difference in the pattern of spread according to age, with the central nervous system and spinal spread being more common in younger patients.

[Table 3] shows that 22.8% of patients did not undergo abdominal ultrasound scans. This was due to either financial constraints or the scanning machine being out of service at the time of the request.

About 61.5% of patients had a normal abdominal scan, 6.5% had hepatomegaly or hepatic nodules, and 3.84% had evidence of pleural effusion.

Table 1: Characteristics of patients presenting with breast cancer.

Variables (n=78)	Frequency (n)	Percentage
Age in years		
16–25	0.00	0.00
26–35	14.0	18.0
36–45	28.0	35.9
46–55	22.0	28.2
56–65	11.0	14.2
66–75	3.00	3.80
Mean age (SD): 47.86±10.84		
Age at menarche		
9–11 years	9	11.5
12–14 years	63	80.8
15–17 years	6	7.7
Parity		
Para 0	7	9.0
Para 1–4	50	64.1
≥Para 5	21	26.9
Side affected		
Left	23	29.5
Right	24	30.8
Both sides	31	39.7

SD: Standard deviation

Table 2: Pattern of spread by patient age.

Spread	n	Mean Age±SD
Pleural effusion		
Yes	23	45.6±10.0
No	55	48.8±11.1
		$t=1.16; P=0.249$
Liver spread		
Yes	15	45.6±10.0
No	63	48.8±11.1
		$t=1.16; P=0.249$
Bone spread		
Yes	5	38.8±4.7
No	73	48.5±10.9
		$t=1.97; P=0.053$
CNS spread		
Yes	5	39.0±6.8
No	73	48.6±10.8
		$t=2.13; P=0.036^*$
Spine spread		
Yes	9	40.8±6.3
No	69	48.9±11.0
		$t=2.26; P=0.026^*$

*Statistically significant. SD: Standard deviation

Table 4 shows that sixty-nine patients (88.5%) had invasive ductal carcinoma as a histological diagnosis while 48 patients (61.0%) were premenopausal. Sixty-nine patients (88.5%) had invasive ductal carcinoma as a histological diagnosis while 48 patients (61.0%) were premenopausal.

Figure 1 shows findings on general examination. 43.6% of patients had anaemia, 39.4% were cachexic, 11.4% had

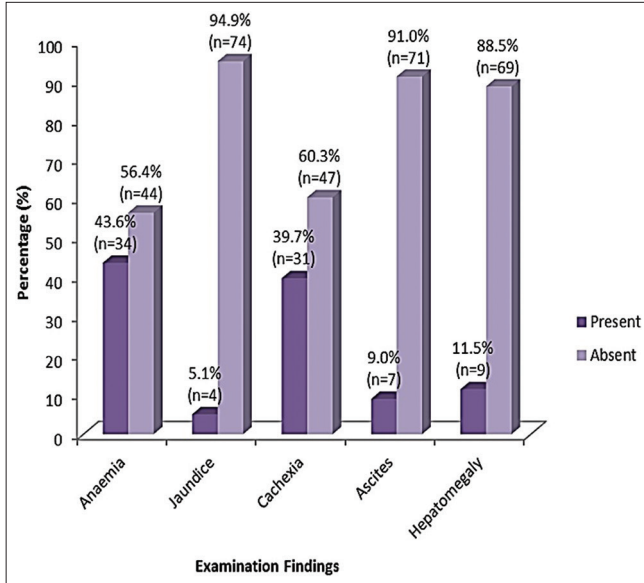


Figure 1: Findings on general examination.

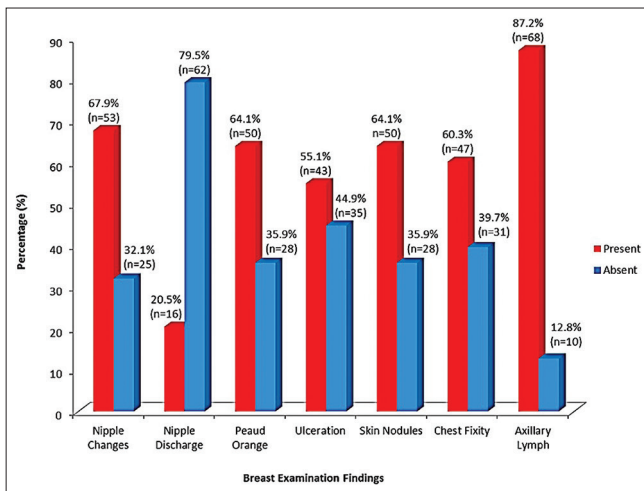


Figure 2: Findings on breast examination.

developed hepatomegaly, 9.0% ascites while only 5.0% had jaundice.

Figure 2 shows that on breast examination 87.2% of patients had already developed axillary lymphadenopathy. 67.9% had nipple changes and 64.1% of patients had peau d'orange and skin nodules. 60.3% had fixity to the anterior chest wall and 55.1% developed breast ulceration.

Only 20.5% of patients were found to have nipple discharge.

DISCUSSION

The mean age of the study population was 47.86 years with 53% falling into the childbearing age group. About 61% of the studied patients were premenopausal.

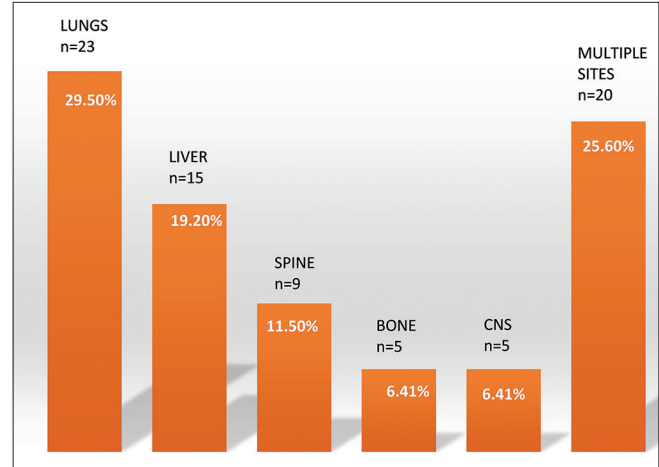


Figure 3: Sites of metastasis.

Table 3: Findings on abdominal ultrasound.

Abdominal ultrasound findings	Number	%
Scan not done	22	22.8
Normal scan	48	61.5
Hepatomegaly/nodules	05	6.40
Pleural effusion	03	3.84
Total	78	100

The most common findings on general clinical examination were anemia (43.6%), cachexia (39.7%), and hepatomegaly (11.6%). These are all pointers to the advanced stage at the initial presentation.

In addition, breast examination revealed axillary lymphadenopathy (87.2%), nipple changes (67.9%), peau d'orange (64.1%), skin nodules (64.1%), and chest fixity (60.3%).

There was no significant laterality in the breast cancer with 30.8% involving the right and 29.5% on the left. This differs from the findings of Mokone-Fatunla *et al.* in South Africa where left-sided breast cancer was more common.^[8] The confounding factor in our study, however, was the fact that both breasts were involved in 39.7% of patients.

The most common sites of metastasis were the lungs (29.6%), liver (19.2%), and multiple sites (25.6%). This is different from the studies of Wu *et al.* which showed the bones to be the most common site, followed by lung, liver, and brain.^[9-11]

Liver metastasis (19.2%) was higher than the 5.2% reported by Hoe *et al.* in Southampton.^[12-14] It is important to note that 22.8% of patients were unable to carry out abdominal ultrasound scans due to financial constraints or challenges with the machine. There, thus, exists the possibility that liver metastases might be higher than reported.

Our study showed a statistically significant occurrence of spinal and central nervous system spread in patients younger

Table 4: Histological types of breast cancer and distribution in premenopausal and menopausal patients.

Variables	Premenopausal	Menopausal	Total
Ductal carcinoma <i>in situ</i>	1	0	1
Inflammatory breast carcinoma	1	0	1
Lobular carcinoma <i>in situ</i>	1	0	1
Mucinous carcinoma	1	0	1
Mixed invasive ductal and mucinous carcinoma	1	0	1
Invasive lobular carcinoma	4	0	4
Invasive ductal carcinoma	39	30	69
Total	48	30	78

than 48 years. This is in keeping with the findings of Tsukada *et al.*^[15,16] and Warrior *et al.*^[17]

The main implication of these findings is that a majority of our patients fall into the young, childbearing group and present late in the hospital. This has an adverse effect on outcome. Similar demographic and temporal presentations were found by Olayide *et al.* in Lagos,^[18] Agbo *et al.*,^[19] and Ezeome in Enugu.^[20]

Limitations of the study include the fact that it is a retrospective study. The relatively small sample size is also a further limitation influenced by reduced hospital attendance in the immediate post-COVID period. A larger prospective study is planned in the future during which funding will be sought to enable more imaging and staging investigations to be done.

CONCLUSION

Late presentation remains the bane of cancer treatment in Nigeria. The situation is particularly dire in Yenagoa, Bayelsa State where non-hospital treatment is the norm. Eventual hospital presentation revealed that most of these patients had already developed metastases to the lungs liver and other organs. Most of these metastases resulted in mortalities. The concept of palliative care is not well developed in our center and many others in Nigeria.

Recommendations

Creation and development of awareness is key to urgently addressing these issues and will require a coalition of government and non-governmental agencies. Initiatives to promote awareness of breast and other cancers should

emphasize the importance of early presentation in hospitals. Public enlightenment programs should emphasize the importance of breast self-examination and screening. Legislation may be required to criminalize the treatment of such cases outside a hospital setting.

Subsidized health-care programs will benefit patient access to investigations and treatment. While emphasis should be on prevention and early diagnosis, budgetary provision for the development of palliative care programs for cancer patients should be made.

Acknowledgments

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Ethical issues

The approval of the Research Ethics Committee of the Federal Medical Center Yenagoa was obtained.

Declaration of patient consent

Patient consent not required as patient's identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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

The author(s) confirms 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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