Clinico-Pathological Evaluation of Breast Cancer in a Nigerian Tertiary Care Center

Obiora Jude Uchendu, Ofunre Ozolua Eboreime[1]

Abstract:

BACKGROUND: Breast cancer (BC) is a major public health concern globally. In Nigeria, it is the most common cancer in females and is often diagnosed at an advanced stage as an aggressive disease.

OBJECTIVE: The study hopes to assess the clinical and morphologic features of BC specimens in Delta State University Teaching Hospital DELSUTH, Nigeria.

METHODS: This is a retrospective cross-sectional study at the Pathology department of a DELSUTH, from January 1, 2014 to March 30, 2020. The age, gender, laterality, histological diagnosis, tumor grade, and year of diagnosis of these BC were analyzed with Microsoft Excel spreadsheet 2007 and presented in tables and figures.

RESULTS: The study comprised 237 BC patients, accounting for 35.5% of total cancer and consisting of 6 (2.5%) males and 231 (97.5%) females with a mean age of 48.21 years. The age group 30–59 years accounted for 80.2% of the cases. The annual incidence rose to a peak in 2019. Bilateral, right breast, and left breast cancer accounted for 6 (3%), 109 (46%), and 122 (51%) cases respectively. Most cases were invasive ductal carcinoma (IDC) (89.9%). Well-differentiate (12.2%), moderately differentiated (19.0%) and poorly differentiated (68.8%) cancer accounted for 12.2%, 19% and 68.8% of the cases respectively.

CONCLUSION: BC constitutes a serious growing but poorly addressed health burden affecting mainly Nigerian young and middle-aged women. Most cases are IDC, and Grade III tumors. There is a need to address the gap in prevention, early diagnosis and quality management of BC in developing countries.

Keywords:
Breast cancer, carcinoma, grade, laterality, morphology

Introduction

Breast cancer (BC) is largely a disease of women with a rare occurrence among men. It is a major public health concern globally, with an estimated 2.1 million newly diagnosed cases, accounting for 11.6%% of all new cancer cases, and 630,000 related deaths, accounting for 6.6% of all cancer deaths, documented in 2018. It is currently the most common cancer among women in most countries with substantial variation from a zenith of 94.2/100,000 population in Australia and New Zealand to a minimum of 25.9/100,000 population in South Central Asian countries.[1]

Although BC is not as common in Nigeria as it is in most developed countries, it remains the most commonly diagnosed cancer among Nigerian women, accounting for about 21.8% of all newly diagnosed cancer cases in this region.[2]

The incidence rate of BC in Nigeria appears to be on the rise, a feature attributed to population growth and aging as well as changing lifestyles. Characteristically the victims are relatively young,

Department of Histopathology, Delta State University, Abraka, Delta State, [1]Department of Surgery, Igbinedion University, Okada, Edo State, Nigeria

Address for correspondence:
Dr. Obiora Jude Uchendu, Department of Histopathology, Delta State University, Abraka, Delta State, Nigeria.
E-mail: ojlinksent@yahoo.com

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with most cases diagnosed at an advanced stage as aggressive disease.[3]

The histopathologist plays a central role in integrated BC care by providing information about the gross specimen, histological stage, grade and diagnosis, hormone receptors expression pattern, and molecular characteristics of BC.[4] This study hopes to assess the epidemiological features of patients with BC and the morphological features of their BC specimens. The study center is the apex hospital of the Delta state where no similar study has been done before.

Materials and methods

Study design
This is a hospital-based descriptive retrospective study.

Setting
The study was conducted in DELSUTH, Nigeria. It is one of the few hospitals with Pathology Service in Delta State.

Study population and sampling strategy
This consists of 237 successive BC specimens (core needle biopsies, excisional biopsies, or mastectomies) submitted for diagnosis to the pathology department of DELSUTH, Nigeria from January 1, 2014 to March 30, 2020. Overall, 446 breast specimens were received during the study period, out of which 237 (53.13%) cases were diagnosed to be BC. These details were extracted from the file copies of the corresponding histopathology reports. Cases with incomplete data or inconclusive diagnoses were excluded from the study.

Data collection
The age, gender, laterality, histological diagnosis, tumor grade and year of diagnosis of these BC cases were accessed for this study. The tumor histologic grading was according to the Nottingham modification of the Scarff-Bloom-Richardson's (SBRs) grading system.[5] In this system, the scoring is based on tubule formation, nuclear pleomorphism and mitotic count, as shown in Table 1.

Data analysis
All our observations were tabulated and analyzed using Microsoft Excel Spreadsheet version 2007 and the statistical summary was presented in tables and figures.

Ethical consideration
Ethical approval (reference number HREC/PAN/2019/056/0338) for this study was granted by the hospital committee on ethics before its commencement.

Results

The study incorporated a total of 237 BC patients, comprising 6 (2.5%) males and 231 (97.5%) females. The age range and mean age for the females were 25–81 and 47.93 years respectively while that of the males were 35–84 and 59 years respectively. The mean age for the combined gender is 48.21 years.

The yearly trend of diagnosed BC cases is shown in Table 2 as 13.1%, 16.9%, 14.8%, 11.8%, 19.4%, 20.3% and 3.8% of the patients were diagnosed in 2014, 2015, 2016, 2017, 2018, 2019 and 2020 respectively.

The laterality of BC is depicted in Figure 1, with BC diagnosed on both breasts, right breast and left breast in 6 (3%), 109 (46%) and 122 (51%) cases respectively.

Figure 2 shows the age and sex distribution of BC patients. The number of patients within the age groups of 20–29, 30–39, 40–49, 40–59, 60–69, 70–79, and 80–89 years were 2 (0.8%), 66 (27.9%), 60 (25.3%), 64 (27.0%), 34 (14.3%), 9 (3.8%) and 2 (0.8%) respectively. Of the six male BC cases, two cases fell within the age of 40–49 years while four cases occurred singly through the 30–39, 60–69, 70–79 and 80–89 years age-groups respectively.

The distribution of BC according to the histological types is shown in Table 3. All male BC cases were invasive ductal carcinomas (IDCs) while female BC cases consist of DCIS (2 [0.9%]), IDC of no special

Table 1: Modification of the Scarff Bloom and Richardson's grading system

Parameters	Scores	Histopathological features
Tubule formation	1	Majority of tumors (>75%)
	2	Moderate degree (10%-75%)
	3	Little or none (<10%)
Nuclear pleomorphism	1	Small, regular, uniform cells
	2	Moderate increase in size and variation
	3	Marked nuclear variations
Mitotic counts	1	0-9 mitoses/10 hpf
	2	10-19 mitoses/10 hpf
	3	20 or >mitoses/10 hpf

Table 2: Yearly trend of breast cancer in Delta State University Teaching Hospital

Year	Number of cases (*n*=237), *n* (%)
2014	31 (13.1)
2015	40 (16.9)
2016	35 (14.8)
2017	28 (11.8)
2018	46 (19.4)
2019	48 (20.3)
2020 (1st quarter)	9 (3.8)
Total	237 (100)

type (NST) (207 [89.9%]), lobular carcinoma (4 [1.7%]), mucinous carcinoma (7 [3.0%]), medullary carcinoma (4 [1.7%]), metaplastic carcinoma (4 [1.7%]) and papillary carcinoma (3 [1.3%]).

Table 4 shows the distribution of BC cases into well differentiated (12.2%), moderately differentiated (19.0%) and poorly differentiated (68.8%) cancer.

Figure 3 shows classic photographic images of IDC NST, lobular carcinoma, mucinous carcinoma, medullary carcinoma and papillary carcinoma, encountered in this study.

Discussion

The study showed that BC is relatively common (35.5% of the total cancers) with an incidence about 38 cases per annum. Although the trend shows striking variation, there seems to be an overall gradual increase from 13.1% of the total cases in 2014 to 20.3% of cases in 2019. This is in line with recent studies that demonstrated increasing incidence of BC in Nigeria.[6,7]

In this study, BC represents 35.5% of cancers cases in this center. Within the Nigerian cancer space, our report is higher than the 14.1%, 19.4%, 21.0%, 22.4% and 29.0% reported in Kano,[8] Sokoto,[9] Benin City,[10] Ilorin,[11] and Port Harcourt[12] respectively, but lower than 38.0% and 40.9% reported in Lagos[13] and Ogun State,[14] respectively. Report from Ghana showed that BC accounted for 16.0% of all cancer.[15] Reports have also shown that BC is much more common in Europe and America than in our region.[1,16] It is, however, alarming that in all recent reports in Nigeria, BC has remained the most common of all cancer. Most recent literature agrees
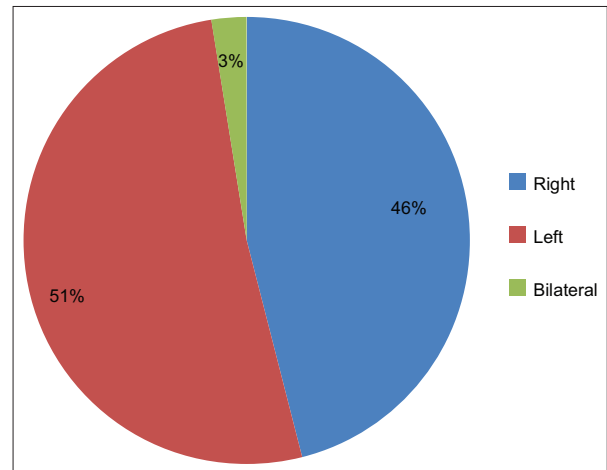

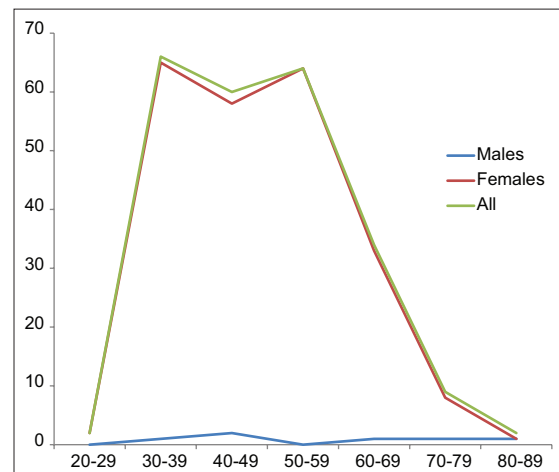**Figure 1:** Laterality of breast cancer. BC: Breast cancer

Figure 2: Age and sex relationship of patients with BC. BC: Breast cancer

Table 3: Incidence of histologic types of breast cancer

Histologic type	Gender		Number of all cases, n (%)
	Male, n (%)	Female, n (%)	
DCIS		2 (0.9)	2 (0.8)
IDC NST	6 (100)	207 (89.6)	213 (89.9)
Lobular		4 (1.7)	4 (1.7)
Medullary		4 (1.7)	4 (1.7)
Metaplastic		4 (1.7)	4 (1.7)
Mucinous		7 (3.0)	7 (3.0)
Papillary		3 (1.3)	3 (1.3)
Total	6 (100)	231 (100)	237 (100)

DCIS: Ductal carcinoma *in situ*, IDC NST: Invasive ductal carcinoma of no special type

Table 4: Histological grading of breast tumor based on modified Scarff Bloom and Richardson's system

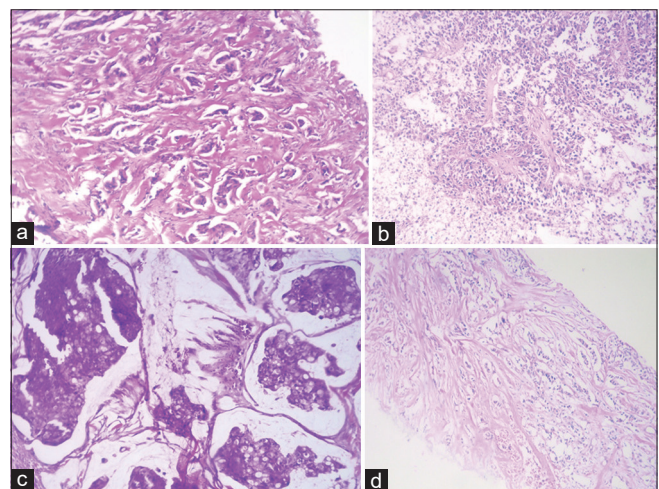| Degree of differentiation	Nottingham grade (score)	Number of cases, n (%)
Well	I (3-5)	29 (12.2)
Moderately	II (6-7)	45 (19.0)
Poorly	III (8-9)	163 (68.8)
Total		237 (100)

Figure 3: The histological variants of BC (×10 magnification). (a) Invasive ductal carcinoma NST. (b) Papillary carcinoma. (c) Mucinous carcinoma. (d): Invasive lobular carcinoma. BC: Breast cancer, NST: No special type

that BC incidence in Nigeria is consistently increasing,[6,7] probably as a result of increasing risk factors such as alcohol use, physical inactivity, obesity, and reproductive factors that increase estrogen exposure such late age at first childbirth, reduction of breastfeeding time, early menarche, late menopause. This underscores the heavy burden of BC among women and by implication, the related mortality and socioeconomic dynamics. This calls for urgent intervention to prevent BC and to mitigate the effect on BC patients and the society at large.

In this study, male BC patients accounted for 2.5% of the cases. Our report is higher than 1.5% and 2.0% in Nnewi[17] and Enugu[18] respectively but lower than 2.8%, 3.0%, 3.7%, 4.0%, 4.6%, 5.2%, 8.6%, and 8.9% in Benin City,[19] Calabar,[6] Maiduguri,[20] Gombe,[2] PortHarcourt,[12] Zaria,[21] Jos,[22] and Osogbo[23] respectively. In a meta-analysis across 22 African countries, male BC accounted for 3.2% of the total BC cases.[24] In India, male BC accounted for about 0.4% of all BC.[25] Among Caucasians, male BC accounts for 2% of all BC cases.[26] The male breast is a rudimentary organ and consists predominantly of fibrous tissue and fat and with scanty poorly-developed ducts and lobules.[26] It has been established that BC occurs predominantly at the level of ducts and lobules which may account for a substantial difference in incidence in both genders.[26] Difference in the endogenous estrogen in males and females may also partly contribute to this disparity. More endogenous estrogen exposure in females implies more cell division and consequently more DNA copying error with consequently increased BC risk among females.[26]

Our study showed that BC is uncommon before the age of 30 years, representing 0.8% of the total cases, which is lower than 3.7% in Benin City,[27] and 10.7% in Kano.[28] Our observation is also lower than 6.4% reported in Tanzania.[29] In US, studies show that BC among women younger than the age of 30 years account for 0.65% of all BC.[30] Rarity of BC below the age of 30 years is however a general observation although it seems than BC below the age of 30 years in more common in African than in Caucasian population.[26] It has however been shown than BC at early age is more likely associated with familial risk factors such as BRCA1, BRCA2 and TP53 mutations.[3]

We observed a near-flat slope in the age-incidence curve from 30 to 59 years with this age group accounting for about 80% of all cancer cases. This incidence is in line with a comparative review across Africa which showed that BC among this age group accounted for 81% of the cases.[31]

We also observed that 54% of patients were below the age of 50 years. Our observation is equal to the incidence reported in both a hospital-based study in Ile-Ife[3] and a population-based study in Ogun state[14] respectively but lower than 63%, 69%, and 70% reported in Nnewi,[17] Calabar[6] and Ibadan[32] respectively. In Ghana, women younger than 50 years accounted for 50%–61% of BC cases[33] while in Malawi 55% of BC patients were below the age of 50 years.[34]

Another interesting observation is that the mean age for females with BC in our study is 47.9 years. This is intermediate between the mean age of 42.0 years, 44.2 years, 44.9 years, and 45.5 years reported in Kano,[28] Makurdi,[35] Calabar[6] and Port Harcourt[12] respectively and 48.0 and 49.2 years in Ogun State[14] and Ibadan respectively.[32] Similarly, in Ghana case series, the mean ages for BC fell between 33.6 and 50.3 years,[33] while in Malawi, the mean age for BC patients is 48.6 years.[34] An average age of 54.6 years for females with BC was reported in a Meta-analysis across Africa.[24]

In contrast, mean age of 67 years was documented among Caucasian female BC patients, while African-Americans females and Black women in UK presented with BC at a much younger ages of 46 years.[16,26] The striking difference may be as a result of differences in inheritance of BC genes. It is however not surprising that BC incidence is low after the age of 60 years in our region, given the prevailing young population structure.[36]

In this study, we observed striking gap between the mean age for females and males with BC, with males with BC having a mean age of 59 years. Sahabi and Abdullahi in Kano[37] reported a lower mean age of 49.7 years, while Ezeome et al.[18] in Enugu and Olu-Eddo and Mohoh[19] in Benin city reported a higher mean age of 60.5 and 64.4 years respectively. The disparity in age of presentation may in part be attributed to the late presentation of male BC patients, who are generally unaware of such cancer.

We observed that 97% of the total BC cases were unilateral while the remaining 3% occurred bilaterally. Our observation is lower than the 99.2% observed in both Warri[38] and Benin city,[39] and 99.4% in Gombe,[40] but lower than the 93.4% observed in Lagos.[41] In a study in India, 99% of the BCs were unilateral disease.[42] Bilateral BC can arise either as metastatic disease from a preexisting BC on one breast or an entirely distinct cancer. Where it is a metastatic disease, it may correlate with advanced disease or late presentation.[26,43] Several reports have confirmed that prognosis of bilateral BC is worse than that of unilateral disease,[43] probably because they are usually advanced diseases.

BC was 5% more common on the left than in the right breast in our report. Our observation was higher than

3.4% difference reported in Warri,[38] but lower than 7.6% and 42.8% difference reported in Benin City[39] and Gombe[40] respectively. In Egypt,[44] South Africa,[45] Pakistan[46] and USA,[47] 7.28%, 10.6%, 18% and 5% excess of left BC were respectively observed. Three hypotheses have been proposed to explain the excess of left BC. Anatomically, the left breast has more tissue than the right breast and this could explain the proportionately more duct-lobular units and therefor higher cancer risk. More females are right handed and are more comfortable to feeding their infants on the right breast. This has protective effect on BC and therefore may reduce cancer risk on the right breast. Thirdly, it is easier to examine the left breast and therefore easier to self-detect left breast lumps or cancer.[45]

Based on the knowledge of the anatomy of the breast, two major cancers can develop from the breast, namely the carcinomas (from the ducts and lobules) and the sarcomas and Phylloides tumors (from the connective tissue stroma). Studies have however shown that almost all BC are adenocarcinoma.[26] All cases in our study were also adenocarcinoma. Some investigators in Nigeria also reported only carcinoma among their BC case series,[14] while in some others, 0.5%–2.3% BC were of varying proportions of sarcomas, malignant phylloides and lymphomas.[38,40,48]

In this study, IDC NST was the mostly observed histological variant of BC, accounting for 89.9% of the total BC. This is higher than 59.5%, 68.6%, 70%, 74.9%, 75.0%, 82.8%, 83.5% and 85.3% reported in Kano,[28] Warri,[39] Maiduguri,[48] Benin City,[39] Lagos,[41] Zaria,[21] and Makurdi[35] respectively but lower than 90.1% reported in both PortHarcourt[12] and Uyo.[49] In Tanzania and India, IDC NST accounted for 91.5% and 88% of BC, respectively.[29,42] In general, IDC NST is the most common histological variant worldwide.[26] In our series, we encountered only five special types, namely lobular, metaplastic, mucinous, medullary and papillary carcinoma.

The prognostic heterogeneity of BC has always fascinated both the clinician and pathologist. The Modified SBR grading system is one of the prognostic parameters utilized in the management of BC, and has been useful in guiding the clinician to his choice of adjuvant systemic therapy. The key elements in this system namely the mitotic rate of the tumor, nuclear size and pleomorphism and the extent of tubule formation are each assigned the score of 1–3, and the final grade generated from summation of these individual scores. Three levels of differentiation are recognized in this grading system namely: well differentiated (Grade I/score 3–5), moderately differentiated (Grade II/score 6–7) and poorly differentiated (Grade III/Score 8–9).[5] In this study, we encountered mostly poorly differentiated BC, which accounted for 69.8% of the cases, while moderately differentiated and well-differentiated BC accounted for 19% and 12.2% of the total cases, respectively. Grade III tumors were also the most common type of BC encountered in both Warri and Port Harcourt.[12,38] In a review of BC in Ghana, about 50%–76% were Grade II disease, while in Tanzania, over 56.4% were Grade III disease.[29,33] In India, as high as 80% of BC in referral centers were Grade III disease, while Grade II tumors were more common in private hospital.[50] Strikingly, studies have shown that Black-American women often present with high grade disease, while American and British women often present with disease of lower grades.[16,51] In a report of comparative analysis of tumor grade in Africa and Finland, Grade III accounted 45.1% and 15.8% of all BC in the respective regions.[52] This is probably the reason for our tumor's highly aggressive disease and consequently have poor prognosis.

Limitations of the study
The study is a hospital-based study and therefore do not capture the overall community incidence. There are also cases of disruption of service during industrial actions and this may affect the significance of this study.

Conclusion

BC accounts for 35.5% of all cancers with rising incidence during the study. It affected 231 (97.5%) females and 6 (2.5%) males, with mean age of 48.2 years and most patients were within 30–59 years. Most cases were IDC, Grade III cancer and were more on the left than the right breast. There is need for a strong political will to fund breast prevention, early diagnosis and management strategies.

Data availability
The raw data used for this study are available at the archives of Pathology department of the institution. Derived data supporting the findings of this study are available from the corresponding author on request.

Disclaimer
The views expressed in the submitted article are ours and not an official position of the institution.

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Conflicts of interest

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