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Histological Type and Tumour Grade in Nigerian Breast Cancer: Relationship to Menarche, Family History of Breast Cancer, Parity, Age at First Birth, And Age at Menopause

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***Abstracts: Background**: The high burden of disease due to breast cancer has continued to have its toll on global health, without exception to Nigeria. The menace of late presentation, with resultant poor survival rates, may be better contained, with improved understanding of the disease characterization in our local settings.*
***Objective**: to determine the distribution of tumor grades and histologic types of breast cancer, in Calabar*
***Methodology**: retrospective study of eighty-one (81) cases, with use of hospital records*
***Results**: Most of the patients were young, with a mean age of 45.06 years, and 30-39 years being the commonest age group (38.3%). They were mostly non-menopausal (72.6%) urban residents (72.2%). As in similar local and international studies, invasive ductal carcinoma was the most prevalent histologic type (85.2%). Grade 3 tumors were most prevalent (66.7%), while grade 1 tumors were least commonly seen (9.9%), with no significant difference in tumor grades across the various socio-demographic and notable risk factors.*
***Recommendations And Conclusion**: high prevalence of late stage presentation in our young women is a cause of public health concern, with urgent need for early detection, especially through wide coverage of breast cancer education and screening programs. In-depth interviews, with further case-control studies using larger samples, is required for better understanding of the determinants of tumor grades and histologic types, towards disease prevention and effective health service delivery.*
Keywords: Histological Type, Grade, Breast Cancer.

I. Introduction

Breast cancer is a very common cancer in Nigeria [1], and is now being described as an emerging epidemic [2].Change in demographics, with resultant increase in life expectancy is thought to be one of the factors responsible for increased prevalence of breast cancer in Nigeria[3].So far not so much has changed about the Nigerian breast cancer patient, who presents late for treatment with very advanced stage disease, tends to be younger, with a very dismal outcome [4,5]. Added to the problem, is the lack of knowledge of the true incidence of breast cancer in Nigeria, due to non availability of functional systematic cancer registries, except for a few institution-based centers [2].

Whereas many Nigerian studies have examined the histological type of breast cancers prevalent in Nigeria histological grade is seldom written about [4, 6, 7, 8, 9, 10, 11,12]. Just as it is reported worldwide, the prevalent histological type in Nigeria is invasive ductal carcinoma, no special type (nos), the relative frequency ranges from 65% to 83.1% [4, 5, 6, 7]. Ikpatt and Ndoma Egba in their study of 129 cases of breast cancer in Calabar, reported that majority of the cases (57%) were of high grade (grade 3)[12]. In the same vain, Fregene et.al., who reviewed the similarities of breast cancer between African Americans and Africans, found that the relative frequency of grade 3 breast cancers ranged from 37 to 54% [13].

Prolonged reproductive life span characterized early menarche and late menopause are reported as risk factors for breast cancer [14,15] ,however the protective factors of late menarche and early menopause are reported to be associated with breast cancers with poor prognosis [16, 17].
Family history of breast cancer [18, 19, 20], never being pregnant and increasing age at first birth [21, 22] have been severally reported to be associated with increased breast cancer risk whereas increasing parity, lower age at first birth are associated with reduced risk[23, 24, 25]

This study, being a retrospective study has limited itself reporting in the simplest form data on breast cancer in Calabar, the hope is that subsequent researches will clarify the statistical and scientific reasons for this observations.

II. Materials and Methods

A retrospective cohort of 81 female breast cancer patients, attending the University of Calabar teaching hospital surgery clinic and the surgical Pathology clinic between 1st January 2005 and 31st December2009 was studied. Patients' data were accessed through the hospitals' central records department after obtaining the institutions' ethical permission. Similarly patients' histology and pathological case histories were obtained from the departmental manual and electronic data. From these files the demographic information and the relevant reproductive histories were extracted as follows: age of patient at cancer diagnosis, age at menarche, age at menopause, parity and number of pregnancies, age at first full term pregnancy, duration of lactation, oral contraceptive use and family history of breast cancer. Each of these case histories were matched with the corresponding histological diagnosis and the tumour subtype as well as the grade. Cases included in the study are those in which at least three of the stated reproductive characteristics were documented, while those excluded included male breast cancers and cases where these three parameters were not documented.

III. Results

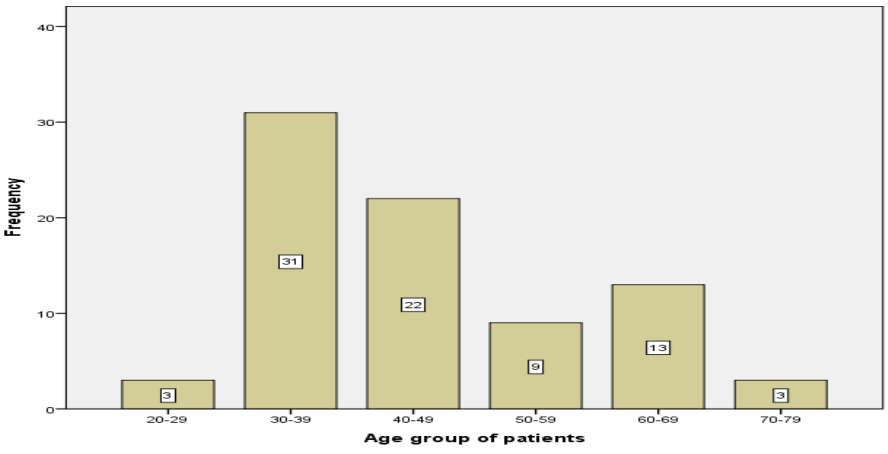
Eighty-one (81) breast cancer cases were seen at the University of Calabar Teaching Hospital, between 2005 and 2009. They were all females, who were predominantly urban residents (72.2%), and mostly civil servants (28.2%), farmers (19.2%), or business traders (16.7%). The mean age of the patients was 45.06 years, ranging from 23 to 76 years, with most of the patients being less than 50 years old (69.1%). 30-39 years, was the commonest age group (38.3%)), followed by 40-49 years (27.2%), with the disease being relatively uncommon at less than 30 years and more than 70 years of age (3.7% respectively) (See figure 1). The mean age at menarche was 13.82 years, ranging from 11 to18 years, with two-thirds of them (66.7%), experiencing menarche when they were 14 – 16 years old. Only 15.8% (12) of the patients admitted to using oral contraceptive pills, with most of the users (72.7% (8)), only using them for 1 to 5 years. Most of the patients (86.1%) were parous, with a mean parity of 3.7 children ranging from 0 to 12 children. For the parous patients, the mean age at first pregnancy was 20.93 years, with most of them (93.0%) having their first child at less than 30 years of age, and 18-24 years being the commonest age group at first pregnancy (51.2%). All the parous patients practiced breastfeeding, with mean breastfeeding duration of 12 months ranging from 6 to 30 months, and with most of them (91.5%) breastfeeding for at least 7 months.

About a quarter of the patients (27.4%) were menopausal, with a mean age at menopause of 50.30 years ranging from 44 to 56 years, and 46-50 years being the commonest age group at menopause (50.0%). Only 13.9% (10) of patients admitted to having positive family history of breast cancer, most of which were of first degree relatives (90.0%).

Invasive ductal carcinoma was the commonest histologic type of breast cancer seen (85.2%), being comparable to similar local and international studies (see table 4). This is distantly followed by medullary carcinoma (3.7%), mucinous (2.5%), pleomorphic (2.5%), and intraductal comedocarcinoma (2.5%). Invasive lobular/invasive ductal, metaplastic and squamous cell carcinomas were the rarest histologic types seen in the study population (1.2% respectively). (See table 1).

66.7% (54) of patients presented with grade 3 disease, followed by grade 2 disease (23.5%), with grade 1 disease being least commonly seen (9.9%) (See figure 2, table 2). The grade of disease was not seen to be significantly different amongst the different age groups, place of residence, parity, family history, non-menopausal status and histologic types (see table 3).

Figure 1: Age Distribution



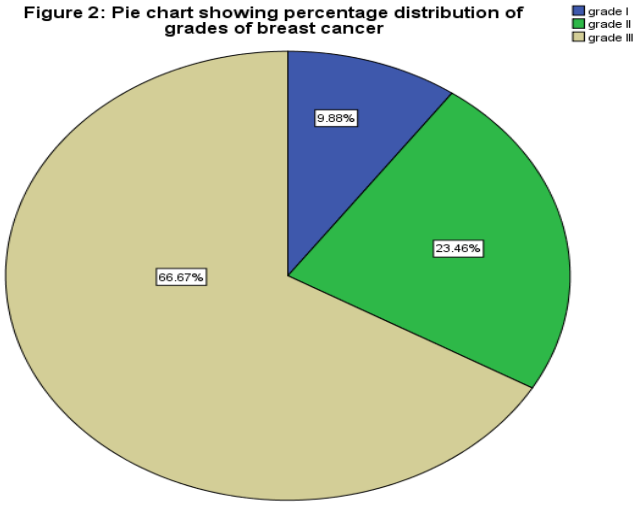


Table 1: Distribution of histologic types of breast carcinoma

Type	Cases	%
Invasive ductal carcinoma	69	85.2
Medullary carcinoma	3	3.7
Muscinous carcinoma	2	2.5
Pleomorphic carcinoma	2	2.5
Intraductal comedocarcinoma	2	2.5
Invasive lobular/ductal carcinoma	1	1.2
Metaplastic carcinoma	1	1.2
Squamous cell carcinoma	1	1.2
Total	81	100.0

Table 2: Distribution of grades of breast cancer at presentation

Grade	Cases	%
I	8	9.9
II	19	23.5
III	54	66.7
Total	81	100.0

Table 3: Frequency distribution of breast cancer grade by age group, residence, family history, parity, non-menopausal status, and histologic type (n = 81)

Variable	Grade I n (%)	Grade II n (%)	Grade III n (%)	Total n (%)
Age group				
< 50 years	6 (10.7)	13 (23.2)	37 (66.1)	56 (100)
> 49 years	2 (8.0)	6 (24.0)	17 (68.0)	25 (100)
Extended age group				
20-29 years	0 (0.0)	0 (0.0)	3 (100)	3 (100)
30-39 years	2 (6.5)	9 (29.0)	20 (64.5)	31 (100)
40-49 years	4 (18.2)	4 (18.2)	14 (63.6)	22 (100)
50-59 years	1 (11.1)	2 (22.2)	6 (66.7)	9 (100)
60-69 years	1 (7.7)	3 (23.1)	9 (69.2)	13 (100)
70-79 years	0 (0.0)	1 (33.3)	2 (66.7)	3 (100)
Residence				
urban	6 (10.5)	11 (19.3)	40 (70.2)	57 (100)

rural	2 (9.1)	7 (31.8)	13 (59.1)	22 (100)
Family history				
yes	0 (0.0)	5 (50.0)	5 (50.0)	10 (100)
no	8 (12.9)	11(17.7)	43 (69.4)	62 (100)
Parous status				
nulliparous	1 (9.1)	3 (27.3)	7 (63.6)	11 (100)
parous	7 (10.3)	15(22.1)	46 (67.6)	68 (100)
Non-menopausal status				
yes	5 (9.4)	13 (24.5)	35 (66.0)	53 (100)
no	2 (10)	4 (20)	14 (70)	20 (100)
Histologic type				
invasive ductal carcinoma	6 (8.7)	17 (24.6)	46 (66.7)	69 (100)
other histologic types	2 (16.7)	2 (16.7)	8 (66.7)	12 (100)

Table 4: Comparison with similar local and international studies

Author/Year/Location	Cases	Predominant age group (yrs)	Predominant histologic type	Common Grade/ Stage
Jeje EA/2010/Lagos[6]	43	31 - 40	infiltrating ductal carcinoma (83.1%)	-
Nggada HA/2008/Maiduguri[7]	169	40 - 49	invasive ductal carcinoma (82.6%)	-
Gogo-Abite M/2005/Port-Harcourt[8]	269	-	invasive ductal carcinoma	**FG3 (53%**
Clegg-Lamptey J/2007/Ghana[26]	158	40 - 49	invasive ductal carcinoma (85.8%)	-
El-Hawary AK/2012/Egypt[27]	274	-	invasive ductal carcinoma (83.2%)	-
Obose A/2007/Jordan[28]	184	-	invasive ductal carcinoma (82.1%)	-
Shirley SE/2008/Jamaica[29]	278	-	invasive ductal carcinoma (69.5%)	-
Mamoon N/2009/Pakistan[30]	822	-	invasive ductal carcinoma (81%)	**FG2 (64%)**
Sariego J/2009/USA[31]	811,652	-	invasive ductal carcinoma	-
Kwong A/2011/Hong Kong[32]	7449	**40-50 / 75-85**	invasive ductal carcinoma (81.8%)	**FG2 (43.5%)**

IV. Discussion

Invasive ductal carcinoma (IDC nos) was the commonest histologic type of breast cancer seen (85.2%), being comparable to similar local and international studies (see table 4) [6, 7, 8, 26, 27, 28, 29 30, 31, 32]. This is distantly followed by medullary carcinoma (3.7%), mucinous (2.5%), pleomorphic (2.5%), and intraductal comedocarcinoma (2.5%). Invasive lobular/invasive ductal, metaplastic and squamous cell carcinomas were the rarest histologic types seen in the study population (1.2% respectively).Outside IDC(nos) the other histological types were so few it was not possible statistically to analyze the associations and make inferences .

The most important observation we made was the age of occurrence of breast cancer in this environment; the mean age of the patients was 45.06 years, range 23 to 76 years, with most of the patients being less than 50 years old (69.1%). 30-39 years, was the commonest age group (38.3%)), followed by 40-49 years (27.2%).This is similar to results of local and regional studies, for example, 31-40 years in Lagos Western Nigeria6,40- 49 years in Maiduguri, North Eastern Nigeria[7], 40- 49 years in Ghana [26] while being different from figures reported in Hong Kong 40-50/75-85years [32], Maryland, United States 62 years (median age for all histological types)[33].

In countries with substantially mixed blacks and Caucasians such as South Africa and the United States ,variation is seen in both incidence and average age of occurrence between black women and Caucasian women, and in all instances features of breast cancer in black women in Diaspora mirrors that of women in the home continent. [13, 33, 34] . This would suggest that breast cancer in women of African ancestry shares a common a

theme. This study with its limited scope cannot explain the reason for the variation in behavior between cancer in black women and women of other races, neither will it explain the similarities between breast cancers in African women and women of African American ancestry.

Several studies have documented the peculiarities of African breast cancer patients, some of these are in reproductive factors which include; later age of attaining menarche for example, 14.7 yrs in rural black, 13.9yrs in urban blacks v 12.6 yrs in white women ,in South Africa [35]. Early age at first child birth and prolonged lactation ,which are protective of breast cancer [33], paradoxically are said to be risk factors aggressive breast cancers in Women of African descent [16, 17]. Genetic factors are also reported to be peculiar in African and African American women with breast cancer [36] perhaps accounting for why some features like proliferative activities are more in African breast cancers versus Caucasians, such differences in proliferation were noticed in Nigerian v Finish samples[37]. In our study no correlation was found between the histological type and, parity, family history age at menarche or menopause perhaps due to our small sample. This is contrary to studies showing that reproductive factors may determine histological types[38, 39, 40] and biological behavior [17, 41].

The grade of disease was not seen to be significantly different amongst the different age groups, place of residence, parity, family history, non-menopausal status and histologic types (see table 3). Majority of the tumours, 66.7% (54) were reported as high grade tumours, this is similar to earlier reports by Ikpatt et. al., who reported 57%[12] and Fregene et. al., who found a range of 37 to 54% in their review [13].It is important to note that most of our breast cancers occur in the age group less than 50 years (69.1%), this is the age group where the tumours are reported to be more aggressive [42, 43, 44, 45], an observation that needs to be studied thoroughly in this environment, using case controlled studies to unravel the scientific reason.

It is also reported that early age at first birth <20 years, more than three live births, which is common in Africa is associate with high stage and high grade breast cancer. Grade as a prognostic factor was recognized long ago[46], however our study does not include follow up of these patients so we cannot correlate the observed tendency for our tumours to be of high grade to actual prognosis.

V. Conclusion

Invasive ductal carcinoma (nos) is the commonest type of histological pattern in this environment. Breast cancer occurs at an earlier age in our women than in Caucasian women and most tumours are of high grade with reproductive risk factors that appeal to differ from those reported for Caucasian women. Case controlled studies need to be carried out in a wider spectrum of our patients to be able to make far reaching generalization.

CONFLICT OF INTEREST: The authors declare no conflict of interest.

AUTHOURS CONTRIBUTION:

Dr Ebughe and Dr Ugare retrieved the patients folders.

Dr Ebughe collated the case histories and entered them into Excel.

Dr Ogban reentered the information in SPSS and analyzed the work.

Dr Ebughe wrote the paper.

All the authors read the papers and made contributions,

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