

Prevalence of Benign Breast Lesions, Epithelial Proliferations with or Without Atypia in Calabar-A Retrospective Review.

ABSTRACT.

AIMS: The aim of this study is to find out the prevalence of benign breast lesions and proliferative lesions which are associated with increase risk of breast cancer. This is aimed at influencing the hospital policy on mammographic screening.

Study Design: Descriptive retrospective study involving a trend analysis of benign breast lesion, proliferative analysed in the surgical pathology unit of the University of Calabar Teaching Hospital between 1st of January 2012 to October 31st 2014.

Place and Duration of Study. Pathology department of the University of Calabar Teaching hospital. The study was carried out between March and April 2019.

Methodology: Descriptive retrospective study of trend analysis of benign and proliferative breast lesions over the period with literature review.

Results: Two hundred and seventeen 217 patients consisting of seven males and two hundred and ten females with a female: male ratio of 1:0.04. Mean age was 26.4 ± 10.0 years, ranging from 10 to 70 years, with 21-30 (94, 43.5%), as the predominant age and less than 21 years (70, 32.4%) as the second common age group. Seventy four percent of (74%) of the breast lesions were benign non proliferative lesions while 26% were proliferative breast lesions. Of the proliferative lesions, five or 8.9% of the proliferative or 2.33% of the lesions were atypical ductal hyperplasia's which have a high risk of progression to cancer.

Conclusion: Proliferative breast lesions and the premalignant lesions of the breast are not commonly reported in Calabar. An upscale of population screening and mammographic services may improve their yield which will help prevent some invasive breast cancers.

Keywords: *Proliferative, Benign, Breast, Calabar.*

1 INTRODUCTION:

The discovery of a breast lump in Calabar-Nigeria as it is everywhere evokes such deep anxiety in the patients and relations, young and old alike(1). Myths about breast cancer still abound among Nigerians, uneducated and educated, because according to Anyanwu et al missed opportunities for breast cancer education fuel them(2). The generally young populations in sub-Saharan Africa are reflected in the low mean ages of breast cancer patients for instance, 44 years was reported by Anyanwu et al South east Nigeria, 49 years by Ikeri et al in Lagos Nigeria(3) and 46 years by Anakwenze et al in Botswana (4). There is a high rate of surgical treatment for breast lesions. The low per capita presence of ancillary radiological diagnostic tools and pathology service, means that many of these lumps are not properly investigated before surgery. So, lesions that should ordinarily be managed conservatively end up being removed surgically.

41 Previous studies of benign breast lesions in Nigeria reported a preponderance of fibroadenoma,
42 followed by Fibrocystic disease and inflammations such as acute and chronic mastitis in females and
43 in males gynaecomastia(5-14).This compares favourably with other sub-Saharan African studies(15),
44 and reports from other tropical settings(16).In the western world fibroadenoma or fibrocystic disease
45 followed by radial scar/complex sclerosing lesion as well as atypical ductal hyperplasia and usual
46 ductal hyperplasia were the common lesions (17).The risk stratification of benign lesions regarding
47 association with breast cancer ranges from low, in non-proliferative types to intermediate in the case
48 of benign epithelial proliferations(18-23).In the case of fibroadenomas Ben Hassouna et al reported
49 four cases of breast cancer arising from fibroadenoma(24).Although in two of these cases, the
50 fibroadenomas were complex, with cystic areas, adenosis, apocrine metaplasia,whereas the other
51 case had fibrocystic dysplasia and lobular neoplasia in adjacent parenchyma(24) Among the benign
52 epithelial proliferations in which fibrocystic disease typifies, Cheng et al reported that a single breast
53 lump may present with heterogenous histology, sometimes, the components may bear different risk
54 profiles(25).This kind of expression they term Heterogenous benign breast disease HBBD(25).

55 The current concept presupposes that ductal epithelial proliferations are a direct precursor to breast
56 cancer(26),and the spectrum ranges from usual ductal hyperplasia, through atypical ductal
57 hyperplasia to carcinoma in situ and invasive carcinoma(26).While at the usual ductal hyperplasia
58 stage the cell is still benign, it has however taken the committed step towards malignancy(27, 28).It
59 will then progress through atypical ductal hyperplasia stage to cancer(27, 28).Although the Nurses
60 commissioned study concluded that the extent of atypicality did not directly correlate with the
61 transformation to cancer(29),as one would expect.The risk of association of atypical lesions of the
62 breast were further demonstrated in a study by Anastasiadis et al in Greece who found that in frozen
63 section examination of breast specimens , fibroadenosis tended to occur with benign breast lesions
64 while atypical ductal hyperplasia tended to occur with breast cancer(30).

65 2 MATERIALS AND METHODS.

66 A trend analysis of benign breast lesions diagnosed at the department of Pathology University of
67 Calabar Teaching Hospital between 1st of January 2012 to October 31st 2014 was carried out.Data
68 extraction form comprised of Demographic, clinical and pathologic reports of these patients.Extracts
69 comprised of, age,sex, symptoms type and duration, laterality of the lesions and diagnostic procedure
70 as well as histological diagnosis. Only formalin fixed paraffin embedded breast tissue obtained by
71 incision biopsy, excision biopsy and core needle biopsy were included in the study. Special stains and
72 hormone receptor assays were not included in the study. Two hundred and seventeen (217) benign
73 breast lesions were diagnosed during this period. Two were subsequently treated as missing data
74 because they had no specific diagnosis other than they being called benign lesions. The data was
75 fed into IBM spss statistical data package version 21.0.The data was entered according to the
76 classes of benign breast diseases proposed by Page et al 1985 which recognised proliferative and
77 non proliferative benign lesions as the two broad groups(31)

78 3 RESULTS

79 Data was obtained from 217 subjects consisting of seven males and two hundred and ten females
80 with a female: male ratio of 1:0.04. Mean age was 26.4 ± 10.0 years, ranging from 10 to 70 years,
81 with 21-30 (94, 43.5%),as the predominant age and less than 21 years (70, 32.4%) as the second
82 common age group (table 1).

Table 1: Sociodemographic characteristics of subjects (N=217)

Variable	Frequency	Percentage
Sex		
Male	7	3.2
Female	210	96.8
Total	217	100
Age groups		
<21	70	32.4
21-30	94	43.5
31-40	29	13.4

41-50	19	8.8
51-60	1	0.5
61-70	3	1.4
Total	216	100

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84 Table 2 shows that most of these breast diseases (166, 89.3%) occurred on the right (87, 46.8%) or
85 left (79, 42.5%) sides, with approximately one-tenth (20, 10.8%) occurring on both sides (table 2).
86 Painless lump (167, 85.6%) was the commonest presenting complain. Two subjects (1.0%) each, had
87 bloody and non-bloody nipple discharge. Mean duration of presenting complain was 21.2 ± 30.5
88 months, ranging from less than one to 240 months.

Table 2: Morphologic and clinical presentation of benign breast disease and,proliferative disease,with or without atypia (N=217)

Variable	Frequency	Percentage
Side of breast		
Right	87	46.8
Left	79	42.5
Both	20	10.8
Total	186	100
Presenting complain		
Painless lump	167	85.6
Painful lump	23	11.8
Bloody nipple discharge	2	1
Non-bloody nipple discharge	2	1
Multiple symptoms	1	0.5
Total	195	100

89

90 Histologic findings consisted breast disease without proliferative activity (159,74.0%)(table 3),the
91 proliferative lesions comprised of of benign epithelial proliferations, proliferative without atypia and
92 proliferative with atypia (56, 26.0%) (table 3). Of the fibrocystic disease, unqualified fibrocystic change
93 (38, 86.4%) was the commonest of the benign epithelial proliferative forms. Intraductal papilloma (5,
94 71.4%) was the commonest proliferative lesion without atypia, while atypical ductal hyperplasia (5,
95 100%) was the only form of proliferative lesion with atypia. Fibroadenoma (121, 76.1%) was the
96 commonest form of benign breast disease without proliferation. All the cases of gynecomastia (7,
97 4.4%) were found in males.

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Table 3: Histologic types of benign and proliferative breast diseases seen at UCTH (N=215)

Histology	Frequency	Percentage
Benign breast diseases (n=159)		
Fibroadenoma	121	76.1
Gynecomastia	7	4.4
Periductal mastitis	4	2.5
Lipoma	4	2.5
Fat necrosis	4	2.5
Tubular adenoma	3	1.9
Juvenile papillomatosis	3	1.9
Granulomatous mastitis	3	1.9
Granulation tissue	2	1.3
Benign phylloides	2	1.3
Mastitis	2	1.3
Lymphocytic mastitis	1	0.6

Granular cell myoblastoma	1	0.6
Lactating adenoma	1	0.6
Myofibroblastoma	1	0.6
Total	159	100
Benign epithelial proliferative diseases (n=44)		
Fibrocystic change (unqualified)	38	86.4
Duct ectasia	3	6.8
Blunt duct adenosis	2	4.5
Mild epithelial hyperplasia	1	2.3
Total	44	100
Proliferative Without Atypia (N=7)		
Intraductal papilloma / papillomatosis	5	71.4
Sclerosing adenosis	1	14.3
Moderate ductal hyperplasia	1	14.3
Total	7	100
Proliferative with atypia (n=5)		
Atypical ductal hyperplasia	5	100
Total	5	100

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100 The mean age of patients with proliferative disease was 33.3 ± 9 and this was statistically significant
101 when compared to the mean age of the non proliferative group, 24.0 ± 9.1 , table 4.

**Table 4: Relationship between mean age and histomorphologic characteristics
(N=215)**

Variable	mean age \pm SD	t-test	p-value
Proliferative disease	33.3 ± 9.2	6.52	0.00
Benign non proliferative disease	24.0 ± 9.1		

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103 **4 DISCUSSION:**

104 Benign non proliferative lesions of the breast were the commonest lesions 159(74.0%) in females in
105 our study. Of these lesions Fibroadenoma (76%),is the commonest benign non proliferative
106 lesion,mirroring other Nigerian studies(14, 32-36). Other benign lesions in the female breast in our
107 study were Periductal mastitis,lipomas,fat necrosis,tubular adenoma,Juvenile papillomatosis,
108 granulomatous mastitis , granulation tissue, benign phyllodes,acute mastitis, lymphocytic
109 mastitis,granular cell myoblastoma,lactating adenoma and myofibroblastoma all of which account for
110 less than 30 %.Baum,M reviewed the impact of these lesions on the patients and concluded that the
111 cost lies on the anxiety that they may be cancerous and the cosmetic deformity from multiple
112 biopsies that often accompany them(1).Surgical treatment of these benign lesions tends to be
113 common in our setting and diagnosis commonly relies on clinical assessment alone.Egwuonwu et al
114 in south east Nigeria studied the reliability of clinical diagnosis of fibroadenoma in women 25 years
115 and below,and reported a high sensitivity of 93.3%but a low specificity of 58.8%(37).In this age group
116 non operative management of fibroadenoma may be an option if the other factors are favourable. And
117 in adolescents well investigated, conservative management of small sized fibroadenoma is
118 recommended (38, 39).Equally imaging in this age group differs from adults because of the rarity of
119 cancer in this age(38).A few fibroadenomas may show proliferative activities, however both non
120 proliferative and proliferative types of fibroadenomas are associated with low risk of breast cancer(40,
121 41).

122 The proliferative lesions comprising of benign epithelial proliferations(BEP), proliferative breast
123 diseases without atypia and proliferative breast diseases with atypia accounted for 26% of the
124 cases.BEP comprised of Fibrocystic disease(unqualified)(17.7%),others are duct ectasia, blunt duct
125 adenosis and mild epithelial hyperplasia. The frequency of fibrocystic disease in this study compares
126 with some Nigerian series,for example 16.5% was reported by Adeniji et al in South-West
127 Nigeria(5),Anyikam22.9% in South -East Nigeria(8).Our results were lower than some Nigerian
128 series, for instance Adesunkanmi reported 42.2% in South-West Nigeria(6).This is equally lower than
129 reports in western and Afro Caribbean literature(42),where it is often reported as the commonest
130 BBD(43, 44).Lesions in this group do not just attract a passing interest, because there are
131 documented low risk of association with breast cancers(45).There is a tendency however to lump
132 these lesions with all proliferative lesions in one basket with a heard risk of 1.5 to 3.0% when the
133 generalizing term of fibrocystic disease is used (43).

134 In our review, proliferative lesions without atypia were 7(3.3%), with individual lesions being;ductal
135 papilloma/ papillomatosis, sclerosing adenosis and moderate ductal hyperplasia.Radial scar or
136 complex sclerosing lesion was a notably absent in our series.These lesions are reported to pose
137 level two risk (1.5% to 1.7%) of breast cancer(40, 46, 47),which is inferior to the level three risk
138 posed atypical proliferative lesions.The only proliferative lesion with atypia in our series is Atypical
139 ductal hyperplasia which were 5(2.3%). These lesions are rated level 3 in the risk scale with risk of
140 about 4-5%(47).It is now thought that many breast cancers arise through a multistep process which
141 takes them through ductal epithelial hyperplasia through atypical ductal hyperplasia, then carcinoma
142 in situ before becoming invasive cancer(28).It is our belief in conclusion that as more and more
143 screening mammography and other radiological tools are employed, the harvest of the high risk
144 proliferative lesions will increase thereby preventing many invasive cancers.

145

146 **CONCLUSION:**

147 Benign breast lesions are diagnosed frequently as they should be in Calabar. But the high risk atypical
148 lesions and the premalignant lesions are not frequently diagnosed. This is not unconnected to the lack
149 of mammographic screening of the population. If this is routinely done it might help in reducing the
150 incidence of invasive breast cancer.

151 **CONSENT:** Not applicable.

152 **ETHICAL APPROVAL:**

153 Ethical approval was granted by the institutional ethical review board.
154

155 **COMPETING INTEREST:**

156 The authors declare no competing interest
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158

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