Original Research Article

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.

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

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

2 MATERIALS AND METHODS.

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

3 RESULTS

Data was obtained from 217 subjects 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 (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

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

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

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

The mean age of patients with proliferative disease was 33.3 ±9 and this was statistically significant 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 ± SD	t-test	p-value
Proliferative disease	33.3 ± 9.2	6.52	0.00
Benign non proliferative disease	24.0 ± 9.1		

4 DISCUSSION:

Benign non proliferative lesions of the breast were the commonest lesions 159(74.0%) in females in our study. Of these lesions Fibroadenoma (76%),is the commonest benign non-proliferative lesion, mirrowing other Nigerian studies(14, 32-36). Other benign lesions in the female breast in our study were Periductal mastitis,lipomas,fat necrosis, tubular adenoma, Juvenile papillomatosis, granulomatous mastitis, granulation tissue, benign phyllodes, acute mastitis, lymphocytic mastitis,granular cell myoblastoma,lactating adenoma and myofibroblastoma all of which account for less than 30 percent.By comparison fibrocystic disease,followed by fobroadenoma and complex sclerosing lesions are commoner in reports from the developed world(17).Although the rate of non prolifrative lesions(37)(67%),in a fifteen year Mayo clinic cohort study in the United states, compares with our findings. Baum,M reviewed the impact of these lesions on the patients and concluded that the cost lies on the anxiety that they may be cancerous and the cosmetic deformity from multiple biopsies that often accompany them(1).Surgical treatment of these benign lesions tends to be common in our setting and diagnosis commonly relies on clinical assessment alone.Egwuonwu et al in south east Nigeria studied the reliability of clinical diagnosis of fibroadenoma in women 25 years and below, and reported a high sensitivity of 93.3%but a low specificity of 58.8%(38).In this age group non operative management of fibroadenoma may be an option if the other factors are favourable. And in adolescents well investigated, conservative management of small sized fibroadenoma is recommended (39, 40).Equally imaging in this age group differs from adults because of the rarity of cancer in this age(39).A few fibroadenomas may show proliferative activities, however both non proliferative and proliferative types of fibroadenomas are associated with low risk of breast cancer(41, 42).

The proliferative lesions comprising of benign epithelial proliferations (BEP), proliferative breast diseases without atypia and proliferative breast diseases with atypia accounted for 26% of the cases.BEP comprised of Fibrocystic disease(unqualified)(17.7%),others are duct ectasia, blunt duct adenosis and mild epithelial hyperplasia. The frequency of fibrocystic disease in this study compares with some Nigerian series,for example 16.5% was reported by Adeniji et al in South-West Nigeria(5),Anyikam22.9% in South -East Nigeria(8).Our results were lower than some Nigerian series, for instance Adesunkanmi reported 42.2% in South-West Nigeria(6).This is equally lower than reports in western and Afro Caribbean literature(43),where it is often reported as the commonest BBD(44, 45).Lesions in this group do not just attract a passing interest, because there are documented low risk of association with breast cancers(37, 46).There is a tendency however to lump these lesions with all proliferative lesions in one basket with a heard risk of 1.5 to 3.0% when the generalizing term of fibrocystic disease is used (44).

In our review, proliferative lesions without atypia were 7(3.3%), with individual lesions being;ductal papilloma/ papillomatosis, sclerosing adenosis and moderate ductal hyperplasia.Radial scar or complex sclerosing lesion was a notably absent in our series.These lesions were comparatively fewer than 30% reported in the 15 years mayo clinic cohort study(37).One hopes that benign epithelial proliferations(fibrocystic disease),were not included in the non-proliferative lesions reported in the Mayo clinic study.These lesions are reported to pose level two risk (1.5% to 1.7%) of breast cancer(41, 47, 48),which is inferior to the level three risk pose by atypical proliferative lesions. The only proliferative lesion with atypia in our series is Atypical ductal hyperplasia which were 5(2.3%).this number is slightly less than 4% reported in the Mayo clinic cohort study.(37).In terms of breast cancer risk these lesions are rated level 3 in the risk scale with cumulative risk of about 4-5%(48).It is now thought that many breast cancers arise through a multistep process which takes

them through ductal epithelial hyperplasia through atypical ductal hyperplasia, then carcinoma in situ before becoming invasive cancer(28).It is our belief in conclusion that as more and more screening mammography and other radiological tools are employed, the harvest of the high risk proliferative lesions will increase thereby preventing many invasive cancers.

CONCLUSION:

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

CONSENT: Not applicable.

ETHICAL APPROVAL:

Ethical approval was granted by the institutional ethical review board.

COMPETING INTEREST:

The authors declare no competing interest

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