Original Article

Histopathological Spectrum of Benign Lesions of the Breast from a University Teaching Hospital in Northern Nigeria

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Abstract

Background: Benign breast diseases (BBDs) are a term that refers to a heterogeneous group of lesions of the breast that are not malignant. They are more common than malignant breast lesions and are important because of the need to differentiate them from breast cancer and for the increased risk of cancer development associated with some behavior-driven development. **Aims:** The aim of this work was to classify and study the clinicopathological patterns of BBDs as seen in our hospital. **Methodology:** All benign breast lesions diagnosed in our over the study period were studied. Data were extracted from patients' request cards, hematoxylin- and eosin-stained slides, and histopathology reports issued for each of the cases. The data were analyzed and presented in tabular formats. **Results:** Four hundred and fiftyfour cases of BBDs were recorded over the study period. 96% of these cases were reported in the female patient. The mean age of our patients was 29.62 ± 8.86 years with the age group of 21–30 years having the highest frequency. Fibroadenoma (FA) (226 cases) was the most common followed by fibrocystic diseases (FCDs). Four cases of atypical ductal hyperplasia were seen. Lesions of the male breast were seen in 18 patients and all were cases of gynecomastia. **Conclusion:** BBDs are the most common histologically diagnosed breast diseases in our center. FA, and FCDs were the most common BBDs. A relatively low prevalence of premalignant lesions not reflective of the high incidence of breast cancer in our environment was observed. Routine mammographic screen for these lesions is therefore recommended.

Keywords: Benign, breast diseases, northern Nigeria

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Introduction

A wide number of benign and malignant lesions have been reported in the breast, although it is the malignant lesions that mostly grab attention and headlines due to their higher burden in terms of mortality and morbidity.

Benign breast diseases (BBDs) constitute a heterogeneous group of conditions ranging from congenital/developmental, inflammatory, proliferative and benign neoplastic lesions of the epithelium and/or stroma, as well as the nipple/skin covering of the breast.[1]

Worldwide, BBDs are reported to be more common than malignant breast lesions and are important because of the need to differentiate them from breast cancer; the documented increased risk of cancer development associated with some of behavior-driven development (BDD), and the morbidity associated with them.[1]

These lesions have been reported to be common worldwide and are seen more commonly in females than men.[2] Age distribution of BDDs varies among the various entities, but as a group, the incidence has been reported to begin to rise in the second decade of life and peaks in the third and fourth decades.[2] Hormonal influence on the breast has been proposed to be of etiologic significance in the development of these conditions.[1]

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Clinically, patients with BBDs seek medical care mostly because of a palpable mass, a diffuse breast swelling/pain or a nipple discharge. These presenting features often mimic cancer, thereby generating anxiety which is further worsened in our resource constrained setting by a lack of readily available and reliable means of screening/early detection. Furthermore, it has been established that some forms of BDDs are forerunners to the development of cancer as evidence by the multifold increase in cancer risk associated with them.[3]

Although, a sizable number of studies on breast masses had been carried out in Nigeria including a 19-year-old study from our hospital, some of them have a more clinical rather than morphological inclination. Furthermore, the need to observe changing trends, if any, adds to the justification of the index study.

The aim of this work was to classify and study the clinicopathological patterns of BBDs as seen in our hospital.

Methodology

This s a retrospective analysis of all BBDs diagnosed in the Histopathology Department of a university teaching hospital in Northern Nigeria over a 5-year period (January 2015–December 2019).

The cases of interest were extracted from the surgical daybooks of the years under review. Other relevant data were gotten from the pathology request forms filled by the attending physicians and copies of the pathology reports issued on all the cases. The corresponding glass slides for all cases were retrieved from archives. In cases of missing slides, new ones were cut from formalin fixed, paraffin-embedded tissue blocks. Each diagnosis was verified by a consensus of 2 consultant pathologists. All slides examined were 3–5 µm thick sections made from 10% buffered formalin preserved tissue, processed according to standard protocols, and embedded in paraffin wax. The primary stain employed in all cases was hematoxylin and eosin. A few inflammatory lesions were stained with Ziehl–Neelsen and Grocott-Gomori's Methenamine Silver Stains for acid-fast bacilli and fungal organisms, respectively.

Cases for which both the glass slides and the tissue blocks are missing were excluded from the study.

The resulting data were subjected to simple descriptive statistical methods using Microsoft Excel statistical package.

Ethical clearance for the study was obtained from the Health Research Ethics Committee of our hospital.

Results

Four hundred and fifty-four cases of BDDs were recorded in our center over the 5-year study period. They constituted 72.1% of the 631 breast specimens received in the laboratory (malignant to benign ratio was 1:1.4). Four hundred and thirty-six of the cases (96%) were recorded in females, while the remaining 18 cases were seen in male patients giving a male-to-female ratio of 1:24.

Our patients were within the age range of 12–68 with a mean of 29.62 ± 8.86 years. The age group with the highest frequency of BDD was 21–30 years (173 cases), while the least frequency (4 cases) was seen in patients aged 61–70 years. Table 1 presents the age distribution of the patients.

Fibroepithelial lesions, seen in 331 patients (72.91% of cases), constituted the most common category of the lesions seen in our patients. The least common category was lesions of the nipple with 2 cases (0.44%) seen. Table 2 summarizes the frequency distribution of all the lesions seen.

Within the fibroepithelial category of lesions, fibroadenoma (FA) with 226 cases (68.3% of this category) was the most common, followed by fibrocystic diseases (FCDs) (30.21%). Six of these cases of FCDs were high-grade lesions atypical ductal hyperplasia (ADH) with greater propensity for malignant transformation. Five cases of benign phyllodes tumor (1.1% of all BDD) were also recorded within the study period [Table 2]. Figures 1-3 show photomicrographs of FA fibrocystic changes and benign phyllodes tumor respectively.

The mean age for patients with FA and FCDs were 23.2 and 33.6, respectively. Age ranges for patients with FA and FCDs were 14–38 and 18–58 years, respectively. Over half of our patients (53.1%) diagnosed with FA were in the age range of

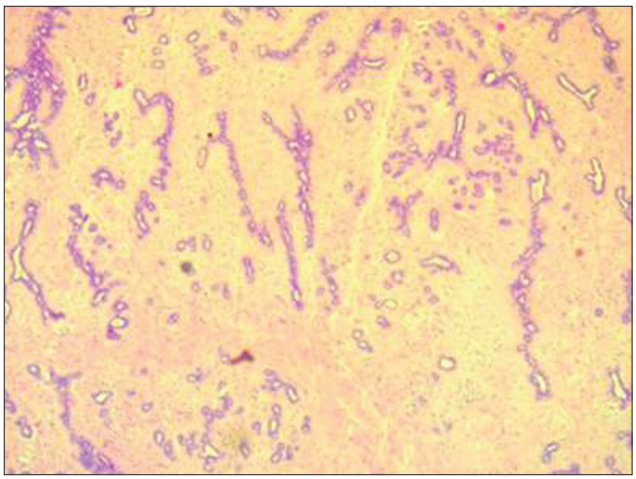

Figure 1: Photomicrograph showing a biphasic tumour composed of proliferating benign ductal elements as well as a proliferating myxoid intralobular stroma (H and E, ×40)

Table 1: Age distribution of patients with benign breast lesions

Age range	Female	Male	Total (%)
11-20	74	2	76 (16.7)
21-30	171	2	173 (38.1)
31-40	166	1	167 (36.8)
41-50	16	6	22 (4.8)
51-60	5	7	12 (2.6)
61-70	4	-	4 (0.9)
Total	436	18	454 (100)

21–30 years, while the age group with the highest frequency of FCDs was 31–40 years (44% of the cases). Table 3 gives the age distribution of the histological entities under the fibroepithelial category of lesions.

Inflammatory diseases of the breast were diagnosed in 43 patients constituting 9.4% of the BBDs seen within the study period. Chronic nonspecific mastitis and fat necrosis were the most common entities seen under this category with frequencies of 14 and 12 cases, respectively. Ten cases of granulomatous mastitis were also seen out of which, 2 cases were confirmed as tuberculous mastitis upon positive staining with Ziehl–Nielsen (ZN) stain, while the remaining 8 cases stained negative to both ZN and fungal stain (Gomori Methenamine Silver).

Fibrous change (8 cases) and pseudoangiomatous stromal hyperplasia (5 cases) were the common stromal breast lesions seen among our subjects. Other lesions diagnosed in this category were fibrolipoma (4 cases) and granular cell tumor (1 case).

Tubular adenoma and intraductal papilloma were the most common benign epithelial lesions of the breast seen among our patients. These two entities constituted 12 (50%) and 6 (25%) of the benign epithelial lesions of the breast, respectively. Most of the patients diagnosed with tubular adenoma were in the 21–30-year age range with a mean age of 29.67 ± 6.69 years [Table 4].

Lesions of the male breast were seen in 18 (4%) of BBD cases. All cases seen in this category were that of gynecomastia. Majority of the cases were seen in patients above 50 years of age, with a mean age of 47.2 ± 5.4 years [Table 5].

Table 2: Frequency distribution of benign breast lesions

Category	Histologic diagnosis	Frequency (%)
Inflammatory lesions	Fat necrosis	12 (2.6)
	Suppurative mastitis	3 (0.7)
	Chronic NS mastitis	14 (3.1)
	Granulomatous mastitis	10 (2.1)
	Lymphocytic mastitis	2 (0.4)
	Duct ectasia	2 (0.4)
	Total	43 (9.4)
Fibro-epithelial lesions	Fibroadenoma	226 (49.8)
	Fibrocystic change	100 (22)
	Benign phylloides	5 (1.1)
	Total	331 (72.9)
Epithelial lesions	Tubular adenoma	12 (2.6)
	Blunt duct adenosis	2 (0.4)
	Intraductal papilloma	6 (1.3)
	Galactocele	3 (0.7)
	Apocrine adenosis	1 (0.2)
	Total	24 (9.7)
Stromal lesions	Fibrous change	8 (1.6)
	Fibrolipoma	4 (0.8)
	Granular cell tumour	1 (0.2)
	PASH	5 (1.1)
	Total	18 (4.0)
Lesions of the nipple	Nipple adenoma	2 (0.4)
Skin lesions	Squamous papilloma	10 (2.1)
	Epidermal inclusion cyst	4 (0.8)
	Dermatofibroma	3 (0.7)
	Keloid	1 (0.2)
	Total	18 (4.0)
Proliferative lesions of the male breast	Gynaecomastia	18 (4.0)
	Grand total	454 (100)

PASH: Pseudoangiomatous stromal hyperplasia

Discussion

BBDs are a group of noncancerous disorders of the breast which can occur in both men and women. The spectrum of lesions belonging to this category includes developmental abnormalities, inflammatory disorders, nonneoplastic proliferations, and neoplastic conditions of the breast.

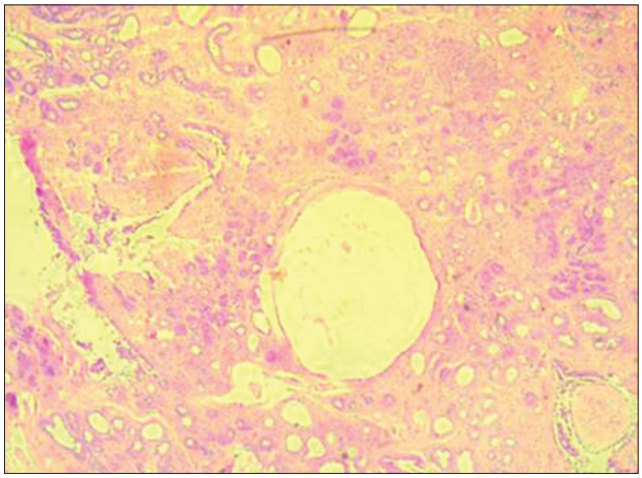

Figure 2: Photomicrgraph showing a lesion composed of areas of adenosis, cyst formation and fibrosis. Mild epitheliosis and apocrine metaplasia are also present

Table 3: Age distribution of fibroepithelial lesions

	Age (years)					Total (%)
	11-20	21-30	31-40	41-50	51-60	
Fibroadenoma	79	120	27	-	-	226 (68.28)
Fibrocystic change	11	23	44	18	4	100 (30.21)
Benign phylloides	-	1	3	-	1	5 (1.51)
Total	90	144	74	18	5	331

Table 4: Age distribution of epithelial lesions

	Age (years)					Total (%)
	11-20	21-30	31-40	41-50	51-60	
Tubular adenoma	-	8	3	1	-	12 (50)
Blunt duct adenosis	-	1	1	-	-	2 (8.33)
IDP	-	3	2	1	-	6 (25)
Galactoceole	1	1	1	-	-	3 (12.5)
Nipple adenoma	1	1	-	-	-	2 (8.33)
Apocrine adenosis	1	-	-	-	-	1 (4.17)
Total	3	14	7	2	-	44

IDP: Intraductal papilloma

Table 5: Age distribution of patients with gynaecomastia

Age	Frequency (%)
11-20	1 (5.6)
21-30	1 (5.6)
31-40	-
41-50	6 (33.3)
50-60	10 (55.6)
Total	18 (100)

In our study, 454 cases of BBD were seen, constituting 71.9% of the 631 breast tissue samples handled in our laboratory over the 5-year study period. This is consistent with a previous report from our center (71.3%)[4] and with other Nigerian reports from Kano,[5] Calabar,[6] and Benin.[7] However, a slightly higher proportion of BBDs (90%) was reported by Adeniji *et al*. from Ife,[8] while Mayun *et al*.[9] reported a bit lower proportion (59.5%) from Gombe, all in Nigeria. In all these reports, meanwhile, BBDs constituted a clear majority of diagnosed breast lesions similar to what was found among Kenyan (72%),[10] and Afro-Caribbean populations in Jamaica (80%).[11] Globally, BBDs are reported to constitute 90% of all breast lesions.[1]

The index study revealed a 96% of BBD cases are recorded in female patients (M: F = 1:24). This collaborates local,[4,7,8] regional,[10] and global[2] reports. It was postulated that the higher breast volume, the more complex architecture, and the repetitive cyclical hormonal influences in the female breast might be contributory to this skewed distribution.[12]

The highest frequency of BBDs was seen among women between the ages of 21–30 years, with the mean age being 29.62 ± 8.86 years. Similar age distribution was reported in Nigeria by Ngadda *et al*.[13] and Imam *et al*.[5] Reports from other centers in Africa,[10,14] and other parts of the world,[15,16] have all revealed a similar pattern.

FA was the most common BBD seen in our study. It constituted 49.8% of the cases. Several previous reports agree with this finding. Notably, Imam *et al*.;[5] Ngadda *et al*.,[13] Echejoh *et al*.,[17] all in Northern Nigeria, as well as reports from other Nigerian[6-8] and African centers[10,14] are all corroborative on this. In all aforementioned studies, FCDs ranked as the most common BBD. Meanwhile, two Nigerian studies from Kano[18] and Ibadan[19]

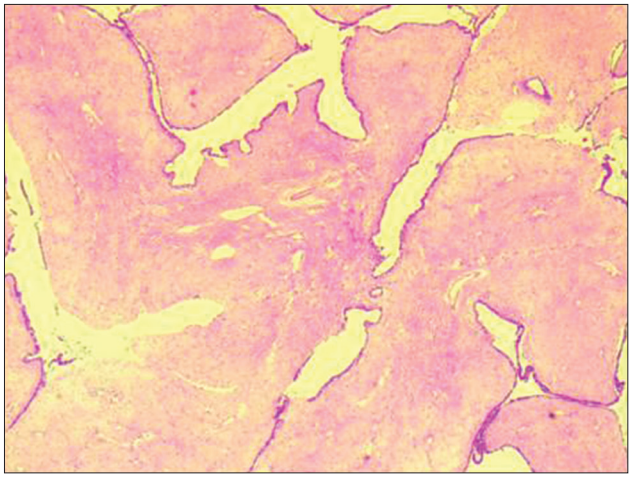

Figure 3: Photomicrograph showing benign ductal elements in a stroma exhibiting leaf like overgrowth. No significant mitotic activity. No stromal atypia (H and E, ×40)

reported a reversed situation in which FA ranked 2nd with FCD in 1st position. However, it is noteworthy that those studies were 19 and 48 years old, respectively. It might be that what we are having now is a changed pattern as postulated by Aisha *et al*.[20]

The mean age of patients with FA was 23.2 years (age range: 14–38 years). Other reports include mean ages of 23.52 years from Uyo,[21] 23.1 years from Bayelsa,[22] and 22.9 years from Benin,[4] Nigeria. Similarly, over half (53.3%) of our patients with FA were in the age range of 21–30 years with a sharp decline in frequency seen from the fourth decade of life upward. This trend is similar to that observed among Nigerians,[5] Africans,[10] and Caucasians.[23]

FCDs consist of a spectrum of morphologic changes comprising varying degrees of cyst formation, adenosis, epitheliosis, apocrine metaplasia, and fibrosis. The fact that these changes spread across the various structural components of the breast justifies its inclusion in the Fibroepithelial category of breast diseases. In the index study, FCDs are the second most common BBD constituting 30.21% of cases. This figure approximates what was reported in a previous from our center[4] as well as reported figures from Kano[5] and Benin.[7] In all these cited Nigerian centers and in other African reports,[10,14] it ranked as the second most common BBD. However, the dominant

patterns reported from Caucasian and Asian populations showed it to be the most common BBD.[24]

The age range and mean age for FCDs in this study were 31–40 years and 33.6 years, respectively. Comparable mean ages of 30 and 39.5 years were reported in Nigeria from Benin[7] and Ibadan[25] centers, respectively. Furthermore, as opposed to FA, our study showed that cases of FCDs continued to show relatively high frequency through the fourth and into the fifth decades of life. This supports the general notion that FCD affects older age groups as compared to FA.[15,16]

Six cases of FCDs (1.8% of BBDs) were high-grade lesions (ADH). Forae *et al*.[26] and Olu-Eddo *et al*.[3] reported 3% and 2.7%, respectively, as proportions of such high-grade FCD lesions. A common trend that we noticed in the course of our current work is that many pathologists do not grade FCD lesions, thereby creating paucity in literature about the relative proportion of the various grades ultimately limiting proper comparison.

Benign phyllodes tumors constituted 1.1% of the BBD cases. The World Health Organization book on breast tumors[15] reported it as constituting <1% of all breast tumors globally. However, local reports from many centers have consistently reported a higher frequency for phyllodes tumor than the global average.[4,5,8,9] Our finding therefore is in synchrony with reported local patterns.

Inflammatory lesions accounted for 9.4% of BBDs. Previously recorded figures in local literature include 8.1%,[7] 4.6%,[8] and 6.0%.[5] Exact documentation of the frequency of inflammatory lesions of the breast from tissue biopsy specimen is problematic in that majority of clinical cases are been treated with Incision and Drainage of Fine Needle Aspiration followed by antibiotic use. Hence, biopsy may not be sent for histology except in suspicious cases. Of the 43 inflammatory cases seen, most were Chronic Nonspecific Mastitis and Fat Necrosis, while 10 cases of Granulomatous Mastitis were recorded. Collaboration with microbiology department for AFB and fungal identification and (or) culture is desirable.

The purely stromal breast lesions seen were Fibrous Change, Pseudoaangiomatous Stromal Hyperplasia, Fibrolipoma, and Granular Cell Tumor. They all together constituted 3.9% of all BBD. Previous reports[5,8,9] have consistently shown this BBD subgroup as not very common in our environment.

Purely epithelial benign lesions of the breast seen in the index study were 12 cases of Tubular Adenoma, and six cases of intraductal papilloma. They constituted 2.64% and 1.32% of BBDs, respectively. This is in keeping with findings of a previous report from our center[4] and with that of other works across Nigeria.[8,9]

All benign lesions of the male breast seen in our study were cases of gynecomastia and most of the patients were above 50 years of age. The frequency and age distribution were consistent reported local patterns.[4,5,7]

Conclusion

BBDs are universally common particularly among women. They are the most common breast disease in Zaria and constituted 71.9% of all breast diseases diagnosed histologically. The peak incidence of this group of diseases is in the third decade of life. FA and FCDs were the most BBDs.

A relatively low prevalence of premalignant lesions, not reflective of the high incidence of breast cancer in our environment was also observed. Routine mammographic screening aimed at early detection of these lesions is therefore highly recommended. Equally, adequate awareness campaign aimed at highlighting the potential malignant transformation in some of these lesions will go a long way in aiding early screening, detection, and follow-up which will help toward lessening the burden of these diseases in our environment.

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Conflicts of interest

There are no conflicts of interest.

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