



## BREAST DISEASES IN SOKOTO, NORTH-WESTERN NIGERIA

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**ABSTRACT: Background:** The Usmanu Danfodiyo university teaching hospital is a regional tertiary center serving the North-western states of Sokoto, Zamfara, and Kebbi. It occasionally receives patients from neighboring Niger state. In recent times the hospital has recorded an increased number of patients presenting with breast diseases due perhaps to the following factors: increased patient awareness, increased number of trained personnel, improvement in diagnostic facilities, and the referral system. Unfortunately, the majority of the patients with malignant breast diseases present late with attendant poor outcomes. And with the rising patient population and dwindling finances, an idea of the spectrum of breast diseases and its burden in a resource-limited country like Nigeria will greatly enhance policy formulations to meet the challenges of providing quality health care for the people. **Objectives:** (i) To determine the clinical and histo-pathological pattern of breast diseases in Sokoto, Nigeria. (ii) To highlight the most frequently encountered histological subtype of breast lesions in this sub-region. **Methodology:** A prospective recruitment of consecutive patients with breast diseases presenting to the surgical clinic of the Usmanu Danfodiyo university teaching hospital, Sokoto, between 2014 and 2018 was carried out. Data obtained from administered questionnaires included socio-demographic characteristics and histopathological diagnosis. The results were analyzed using the windows SPSS statistics 20.0. **Results:** A total of 1822 patients with breast diseases were seen. This was made up of 1006 (55.2%) benign cases and 816 (44.8%) malignant cases. There was a relative annual increase in the number of cases of breast diseases seen over the five-year study period with 280 cases seen in 2014 and 430 cases seen in 2018. The overall male: female ratio for breast diseases was 1:304. Fibroadenoma accounted for 95.4% (960) of all cases of benign breast lesions seen, followed respectively by fibrocystic disease 1.8% (18), breast abscess 0.8% (8), duct papilloma 0.5% (5), duct ectasia 0.2% (2) and breast tuberculosis 0.1% (1). Fifty-one percent (488) of cases of fibroadenoma occurred between the ages of 11-20 years, while 42.8% (411) occurred between ages 21-30 years giving a mean age range of 21-30 years. Sixty-one percent (11) of fibrocystic disease occurred between ages 30-40 years. Invasive ductal carcinoma was the most commonly diagnosed malignant breast lesion accounting for 98% (800) of all malignant diseases. Invasive lobular carcinoma followed at 1.5% (12). Forty-five percent (362) of invasive ductal carcinoma occurred between the 41-50 year age group. **Conclusion:** Fibroadenoma constitutes 95.4% (960) of benign breast diseases in Sokoto with a mean age range of 21-30 years followed by fibrocystic disease at 1.8% (18). Invasive ductal carcinoma constitutes 98% (800) of malignant breast diseases with a peak age range of 41-50 years followed by invasive lobular carcinoma at 1.5% (12).

**KEYWORDS:** Breast Diseases, Fibroadenoma, Fibrocystic Disease, Carcinoma



## INTRODUCTION

Breast disorders presenting commonly to general surgical clinics may be neoplastic or non-neoplastic, benign or malignant. Neoplastic lesions are by far the chief cause of much anxiety to the patient and the commonest reason for surgical out-patient visitation. In developed countries, presentation tends to be early with the hope of a cure for malignant lesions but the reverse is the case in developing countries where late presentation is the norm [1-3]. Most studies have shown that benign breast conditions are far more common than malignant diseases with benign to malignant (B: M) ratios varying considerably between regions [3-5]. However recent reports from Nigeria revealed that there is an increasing prevalence of malignant breast lesions attributable to factors like 'westernized' lifestyle (increased use of the oral contraceptive pill and hormone replacement therapy, high-calorie low fiber diet, and cigarette smoking), improved diagnostic facilities, increasing awareness and better reporting of the disease [6-8]. Benign breast diseases (BBD) constitute a heterogeneous group of disorders including developmental abnormalities, epithelial and stromal proliferation, inflammatory lesions, and neoplasms [9]. Malignant breast diseases (MBD) on the other hand are predominantly invasive ductal and lobular carcinomas with special-type cancers constituting only 10% [10]. While most reports indicate that breast lumps are predominantly benign and mostly non-proliferative epithelial lesions, there has, however, been increasing recognition of the risk implications of the various forms of premalignant lesions. Researchers widely believe that cancer risk is increased in patients with atypical ductal and lobular hyperplasia [11-13]. Hartmann et al. reported a four- to fivefold increased risk for breast cancer associated with atypical ductal hyperplasia within 10-15 years of diagnosis while Dupont et al. reported a relative risk of 3.1 for subsequent breast cancer in women with atypical lobular hyperplasia [11, 12]. It is therefore important that all breast lumps presenting to the surgical out-patient department be subjected to the triple assessment.

## METHODOLOGY

This was a prospective study in which consecutive patients with breast diseases presenting to the surgical clinic of the Usmanu Danfodiyo university teaching hospital, Sokoto, between 2014 and 2018 were recruited and administered semi-structured questionnaires to obtain socio-demographic information. Biopsies obtained as part of the triple assessment were sent for histopathologic confirmation and results entered into the questionnaire. Immunohistochemistry was not available in this center at the beginning of this study so it was not assessed as part of the study.

### **Histopathologic classification:**

Diseases were grouped into benign and malignant lesions based on the histopathologic diagnosis. The common histologic subtypes were highlighted. Bivariate analysis using the Chi-square test showed a significant relationship between age and breast diseases. P-value of <0.05 was considered significant. Frequencies were presented as absolute values and percentages. Results were analyzed using the windows SPSS statistics 20.0.

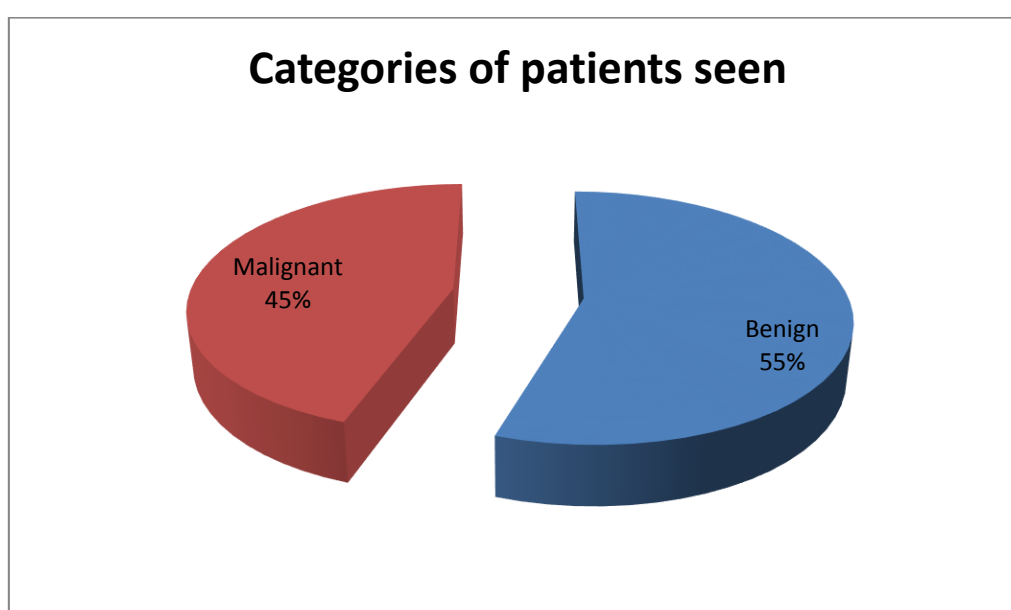
**Inclusion/exclusion criteria:**

All patients with confirmed neoplastic and non-neoplastic breast diseases were included in the study while patients with breast lesions not confirmed by histology were excluded.

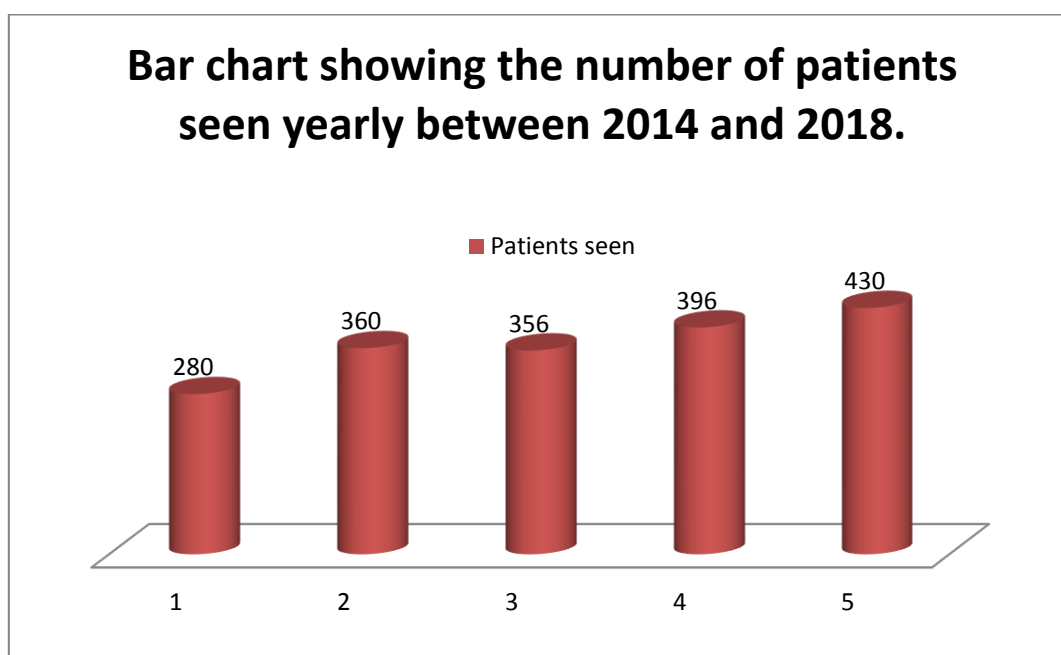
**RESULTS**

A total of 1822 patients with various forms of breast diseases were seen. This was made up of 1006(55.2%) benign cases and 816(44.8%) malignant cases (Figure 1). The Male: Female (M: F) ratio for breast diseases was 1:304. The M: F ratio among benign and malignant cases was 1:502 and 1:203 respectively. The benign breast diseases seen in males were 2 cases of gynecomastia while the malignant diseases seen amongst males were 4 cases of invasive ductal carcinoma. Figure 2 shows a relative annual increase in the number of cases seen over the five-year study period.

Table 1 shows the distribution of benign breast diseases seen in the 5-year period. Fibroadenoma accounted for 95.4% (960) of benign diseases seen, followed respectively by fibrocystic disease 1.8% (18), breast abscess 0.8% (8), duct papilloma 0.5% (5), duct ectasia 0.2% (2) and breast tuberculosis 0.1% (1). 50.8% (488) of cases of fibroadenoma occurred between ages of 11-20 years, while 42.8% (411) occurred between ages 21-30 years, giving a mean age group of 21-30 years and a modal age group of 11-20 years. 61% (11) of fibrocystic disease occurred between ages 30-40 years. Invasive ductal carcinoma was the most commonly diagnosed malignant breast disease accounting for 98% (800) of all malignant lesions. Invasive lobular carcinoma followed at 1.5% (12) while fibrosarcoma and malignant phyllodes tumor followed at 0.25% (2) each (Table 2). The mean and modal age group for invasive ductal carcinoma was 41-50 years while the mean age was 48.2 years (95% Confidence Interval of 43.33 and 53.06). Table 3 showed that malignant breast diseases increase with age while benign breast diseases decrease with age ( $p < 0.0001$ ) thereby disproving the null hypothesis ( $H_0$ ) which assumes that no such relationship really exists.



**Figure 1: Overall categorization of patients seen in the 5 year study period**



**Figure 2: Annual distribution of patients seen between 2014 and 2018.**

**Table 1: Age distribution of benign breast diseases.**

Benign breast diseases		Age group				Total
S/No	Disease	11-20 years	21-30 years	31-40 years	41-50 years	
1	Fibroadenoma	488	411	46	15	960 (95.4%)
2	Duct papilloma	0	1	4	0	5 (0.5%)
3	Duct ectasia	0	0	1	1	2 (0.2%)
4	Phylloides tumour	0	0	4	0	4 (0.4%)
5	Fibroadenosis	7	2	9	0	18 (1.8%)
6	Breast abscess	0	6	1	1	8 (0.8%)
7	Mastitis	1	4	1	0	6 (0.6%)
8	Gynaecomastia	0	2	0	0	2 (0.2%)
9	Breast Tuberculosis	0	0	1	0	1 (0.1%)
	Total	496	426	67	17	1006

**Table 2: Age distribution of malignant breast diseases.**

Malignant breast diseases		Age group							
s/no	Breast disease	11-20 years	21-30 years	31-40 years	41-50 years	51-60 years	61-70 years	71-80 years	Total
1	Invasive ductal cancer	2	22	164	362	177	52	21	800 (98%)
2	Invasive lobular cancer	0	0	4	7	1	0	0	12 (1.48%)
3	Fibrosarcoma	0	0	0	2	0	0	0	2 (0.25%)
4	Malignant phyllodes tumor	0	0	0	2	0	0	0	2 (0.25%)
	Total	2	22	168	373	178	52	21	816

**Table 3: Relationship between breast diseases and age.**

Age group(Years)	Breast diseases		X <sup>2</sup>	P-value
	Benign breast diseases	Malignant breast diseases		
11 -20	496	2	1468.72	<0.0001
21 -30	426	22		
31 -40	67	168		
>40	17	624		
Total	1006	816		

## DISCUSSION

Benign breast diseases (BBD) accounted for 55.2% of all breast lesions in this study with fibroadenoma being the predominant subtype. Most published series show a higher proportion of BBD compared to malignant breast diseases (MBD). Figures from Enugu, Calabar, and Ibadan, Nigeria, showed that BBD accounted for 68.8, 73.4, and 89.4% of all breast lumps respectively [4,5,14]. Olu-Eddo and Ugiagbe in Benin city, Nigeria got 72.5% [15]. Similar figures have been documented in other parts of Africa and the rest of the world [16-18]. Bewtra got 68 % (44) BBD in Kumasi, Ghana [16]. He reported that among the benign breast diseases in all age groups in

Kumasi, fibroadenoma made up 70% of the lesions [16]. Fibroadenoma was the commonest benign breast disease in our study accounting for 95.4% (960) and with a mean age range of 21-30 years. Our figure was higher than most series reviewed [5,7,18-21]. Kathy et al. in PortHarcourt got 51% while Adesunkanmi and Agbakwuru in Ilesha got 91 (46.2%) [19,20]. Adeniji et al. in Ile Ife got 59.1%, Kumar et al. in India got 56.4% while Khanzada et al. in Pakistan got 27% (75/275) [17,18,21]. They all showed a predominance of fibroadenoma in



keeping with works by Oluwole and Freeman which showed a racial predilection of Negroes to fibroadenoma [22].

Fibroadenoma occurs in 25% of asymptomatic women [23]. It is usually a disease of early reproductive life with a peak incidence between the ages of 15 and 35 years. Fibroadenoma is thought to represent a group of hyperplastic breast lobules called “aberrations of normal development and involution.” [23-25]. The lesion is a hormone-dependent neoplasm that lactates during pregnancy and involutes along with the rest of the breast in peri-menopause [25]. A direct link has been noted between oral contraceptive use before age 20 and the risk of fibroadenoma [26]. However, there was no history of contraceptive usage in all the cases reviewed in our study. This perhaps might not be unconnected with the conservative belief concerning its use here. The Epstein-Barr virus is also thought to play a causative role in the development of this tumor in immune-compromised patients [27]. Fibroadenoma commonly presents as a highly mobile, firm, non-tender lesion often described as ‘breast mouse.’ It has been postulated that the tumor might arise from the BCL-2-positive mesenchymal cells in the breast, in a manner similar to that proposed for solitary fibrous tumors [28]. Women with complex fibroadenomas containing sclerosing adenosis and duct epithelial hyperplasia may have a slightly higher risk for subsequent cancer compared to those with simple fibroadenomas [29]. However, the presence of atypia (either ductal or lobular) confined to a fibroadenoma does not lead to a greater risk for long-term breast carcinoma [29,30]. No case of complex fibroadenoma was reported in our study. Fibroadenomas in older women or in women with a family history of breast cancer have a higher incidence of associated carcinoma [23,30]. El Wakeel et al. in their systematic review were able to show that the relative risk of developing breast cancer in patients who had surgically excised fibroadenoma increases in the presence of ductal hyperplasia, complex features within the fibroadenoma, or a family history of breast carcinoma (in a first-degree relative) [23]. The current management of patients with suspected fibroadenoma varies. Some surgeons prefer excision for tissue diagnosis, but conservative management may likely replace surgical treatment in the near future, on the basis of the triple assessment (young age of the patient, findings of benign imaging and clinical characteristics, and benign findings on either FNA cytology or core needle biopsy) [29,31]. Minimally invasive technique such as ultrasound-guided cryo-ablation is an option for the treatment of fibroadenoma in women who wish to avoid surgery [32]. The lesion may simply be observed and followed up periodically in the surgical outpatient department. In our center, most patients are offered excision biopsy as part of the triple assessment. Surgical removal is also recommended for the juvenile variant which may present with a huge solitary mass of up to 20 cm in size [33].

In our study, fibrocystic disease (FD) of the breast was the second most common BBD at 1.8% (18) with a mean age of 30-40 years. Reports from across Nigeria and Ghana showed similar findings [15,21,34-36]. Okobia and Osime in Benin City got 90% benign cases with a benign:malignant ratio of 9:1. Fibroadenoma was the most common benign breast disease in their series followed by fibrocystic disease [35]. Ohene-Yeboah and Amaning in Kumasi Ghana reported that fibroadenoma was 51.0% (159), while the fibrocystic disease was 31.1% (97) [36]. However, this finding is contrary to reports from Caucasian and Asian series where the fibrocystic disease was the most common BBD [37]. Memon et al. in Pakistan reported that fibrocystic change constituted the majority (66.3%) of BBD in their study area, and they concluded that this represented a change in pattern from a previously more prevalent fibroadenoma [38]. Ochicha et al. in Kano also noted that fibrocystic disease was the commonest histological type seen in their study comprising 34.3% (55) of all cases, and with



a mean age of 33 years. This was followed by fibroadenoma with 28.8% and a mean age of 21 years [3]. Synonyms of the fibrocystic disease include fibrocystic changes (FCC), cystic mastopathy, chronic cystic disease, chronic cystic mastitis, Schimmelbusch's disease, mazoplasia, Cooper's disease, Reclus' disease, and fibroadenomatosis. Fibrocystic disease refers to a spectrum of histopathologic changes that are best diagnosed and treated specifically. The term "fibrocystic changes" is now preferred because these histopathologic changes are observed in the majority of patients with the disease [39,40]. FD generally affects premenopausal women between 20 and 50 years of age [41-43]. The mean age range in our study was between 30 and 40 years. FD may be multifocal and bilateral. It commonly presents with pain and tender nodularities in the breast. Although the exact pathogenesis of the entity is not clear, hormonal imbalance, particularly estrogen predominance over progesterone, seems to play an important role in its development [44]. Dupont and Page classified FD as non-proliferative lesions, proliferative lesions without atypia, and proliferative lesions with atypia (atypical hyperplasia) [45]. The majority are non-proliferative lesions. There was only one case of epithelial hyperplasia without atypia in our study. The rest were non-proliferative. Various studies have shown that women with non-proliferative lesions have no elevation in breast cancer risk, whereas women with a proliferative disease without atypia and women with atypical ductal or lobular hyperplasia have a greater breast cancer risk [45,46]. Apart from the histologic features, the age at biopsy and the degree of family history of breast cancer are reported to be the major determinants of breast cancer risk after the diagnosis of benign breast disease [12]. According to Hartmann et al., the risk for breast cancer in young women with a diagnosis of atypical epithelial proliferation is twice the risk observed among women over 55 years with a diagnosis of atypical epithelial proliferation [12]. It was also reported in the same study that family history of breast cancer is an independent risk factor and that strong family history may increase breast cancer risk even in patients with non-proliferative lesions [12]. Most patients with FD respond to danazol, bromocriptine, or tamoxifen but excision biopsy is often advised to exclude malignancy.

In this study, inflammatory breast diseases constituted 1.7% (17) of benign breast lesions. This is lower than reports from Kano, Ibadan, and Benin City, Nigeria with 6%, 4.6%, and 8.15% respectively [3,4,15]. Our figure is however not a true reflection of inflammatory breast disease because most cases are treated conservatively with antibiotics, needle aspiration, and incision and drainage of abscess without biopsies.

Duct papilloma in our study was only 0.5% (5). Echejo et al. in Jos got 2.8% (6) while Khanzada et al. reported 4.7% within 3 years in Pakistan and McFarlane in Jamaica reported 6.7% over a 2-year period [18,34,47]. Duct papillomas are generally not considered premalignant especially the central single types. However, MacGrogan and Tavassoli suggested that papillomas with atypia and surround-tissue hyperplasia are prone to recurrence and therefore may confer certain risks on the individual [48]. They opined that epithelial atypia, even to the extent of low-grade ductal carcinoma (DCIS) has no known prognostic significance or impact on the outcome when it is confined to the central papillomas [48].

In our study, benign phyllodes tumor and gynecomastia were uncommon at 0.4% (4) and 0.2% (2) and peaking at the 4<sup>th</sup> and 3<sup>rd</sup> decades respectively. Studies by Olu-Eddo et al. showed that benign phyllodes tumor constituted 1.8% of benign breast diseases with a mean age of 29.4 years [15]. Gynaecomastia was 2.1% in that study with the mean age at 33.2 years [15]. Benign phyllodes tumor occurs predominantly in middle-aged women between 40 and 50 years in Western countries [49].



Invasive ductal carcinoma was the predominant malignant breast disease in our study at 98% (800). This was followed by Invasive lobular carcinoma at 1.5% (12). The predominant histological type of invasive ductal carcinoma in our study is not different from other findings in the country and elsewhere [50-52]. The study also shows that breast cancer occurs in younger age (mean age 48.2 years) among our women than in Caucasians [50]. Most published works in Nigeria and America reveal that breast cancer in African women occurs a decade earlier than the western average [50,53,54]. African-American women also present at a significantly younger age than their Caucasian counterparts [55,56]. Similarly, black British women presented significantly younger (median age of 46 years), than white patients (median age of 67 years) [57]. The factors responsible for this are not fully understood although it may be due to mutations in the breast cancer genes (BRCA 1 and 2) and their variants [56,58]. Our study however showed that there was an overall increase in the incidence of malignant breast diseases with advancing age. 76.5% of malignant cases occurred above the age of 40 years. This is consistent with most published works in Nigeria and elsewhere [7,59]. Kurian et al. reported that nearly half of all luminal breast cancers occurred after age 70 years across racial/ethnic groups [59].

## CONCLUSION

Fibroadenoma was the most commonly diagnosed benign breast disease in Sokoto at 95.4% (960) and with a peak age range of 21-30 years while invasive ductal carcinoma was the commonest malignant breast disease at 98% (800) and peaking at 41-50 years.

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