

Age Prevalence and Management of Breast Fibroadenoma At a Nigerian Tertiary Hospital: A Five Year (2016-2020) Analytical Review

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Abstract

Background: Fibroadenomas are one of the most common benign tumors of the breast in women between 18-39 years of age. In the adolescent population, the overall incidence of fibroadenoma is 2.2% and accounts for 68% of all breast masses. It feels like a smooth lump in the breast. It is painless and moves easily when touched.

Method: Following the consecutive percutaneous needle or excision surgical biopsy all breast masses were grossed and processed according to the standard histological tissue processing techniques. 241 of 1038 breast tissues were diagnosed of fibroadenoma in the Nigerian tertiary hospital.

Result: Out of 82% of histology specimen received for the period of five years, 13% were excised breast masses and 5% was confirmed positive for fibroadenoma. Out of this 5% of positive cases from 2016 to 2020, there was a slight and irregular interval of 1-4% increase each year. The prevalence of fibroadenoma was mostly seen in youths of ages 18-39 years having 75%, followed by adolescence of ages <18 years with 22% and lastly older adults of ages 40-59 years with 3%. The cause of this prevalence is not confirmed but with the current view of fibroadenoma cases in this study it can be predicted that there might be subsequent increase of cases in of this specific age group in the future. The slight annual increase indicates that breast fibroadenoma across the varying age groups underwent varying degrees of somatic mutations and harbored mutations in the exon (exon 2) of the mediator complex subunit 12 (MED12) gene of the stromal cells of the breast which led to the excessive proliferation.

Conclusion: The data presented showed high prevalence of fibroadenoma cases in ages 18-39 annually which indicates that these individuals in this age group experienced rapid instability of the estrogen or progesterone hormone either due to childbearing, abortion, or genetic hormonal abnormalities. This suggests that there might be increased rates of abortion occurring among this age group in Nigeria or lack of proper postnatal care in Nigeria tertiary hospitals. More clinical investigations need to be carried out to confirm these suspected reasons in Nigeria.

Keywords: Breast Fibroadenoma, Prevalence of fibroadenoma in Nigeria, Cases of Fibroadenoma in ages 18-39 years.

1. METHODS

Aim, Design and Setting of The Study: This study was to provide an update on the prevalence of fibroadenomas in females between ages 18-39 years in a Nigeria tertiary hospital within the period of five years (2019-2020) and ways of managing its prevalence in the female population.

Following the consecutive percutaneous needle or excision surgical biopsy all breast masses were grossed and processed according

to the standard histological tissue processing techniques. Clinical data was collected (upon approval) from the information unit of the department of clinical pathology and analyzed using statistical tools. The data collected includes the number of histology samples received, the number of breast tissue samples received in five years, the number of positive cases reported for breast fibroadenoma and the age range of individuals who were reported to have breast fibroadenoma cases.

This study was conducted at the department of Clinical Pathology, Histopathology and Cytology unit, at the tertiary hospital in Nigeria.

2. Materials

Mammography was performed with screen-film (Mammomat 3000, Siemens Medical Solutions) previously until digitalized mammography (LoRad, Hologic) was installed and used for improved results. Sonography was performed using a linear transducer (7-12 MHz, ATL 3500, Phillips Medical System). Clinical data on the patients, including, the patients age was retrieved retrospectively from imaging reports and files. Imaging studies were initially read by one of four experienced breast imaging radiologists. A single pathologist reviewed pathologic samples for all patients in study.

3. Methods

Women presenting to the breast imaging center was screened according to standard guidelines. All women receive a physical examination by a gynecologist. Women younger than 40 years begin their screening with sonography. Those older than 40 years undergo mammography, and women in this group with dense breasts, palpable masses or findings on mammography also undergo sonography. Mammography is indicated when sonography shows a suspicious finding or when there is a palpable mass/lesion that is not seen on sonography. MRI is performed for some women at high risk of the disease.

Evaluation of breast fibroadenoma was performed, including palpability, general appearance on mammography and assessment according to the mammographic BI-RADS categories and general sonographic appearance with assessment according to the sonographic BI-RADS categories. The diagnosis for patients in this study was achieved by core needle biopsy using a 14-gauge cuttle needle under sonography guidance or excisional surgical biopsy of palpable lump. At pathology, fibroadenoma was diagnosed according to the accepted definition of a benign tumor arising from the epithelium and stroma of the terminal duct-lobule unit. The histologic hallmark of fibroadenoma is concurrent proliferation of glandular or stromal elements. In addition, core, and excisional biopsy pathologic findings for the breast fibroadenomas obtained were grossed and histologically processed according to the standard tissue processing techniques.

The excised breast mass was fixed in 10% Neutral Buffered Formalin for 48hrs following grossing at 3-5mm in diameter. Subsequently, they were dehydrated in graded concentration of ethanol (ascending grades), cleared in xylene, and embedded in paraffin wat for sectioning. After that, sections of about 3-5mm in thickness were obtained using the Hertz rotary microtome (Leica RM2255, Cambridge Mode) and mounted on glass slides. Staining of the section was according to Hematoxylin and Eosin technique and Periodic Acid Schiff technique and was examined using Swift® binocular microscope with an inbuilt lightening system (Olympus, England). All histopathology changes observed in kidney, liver and small intestine sections were observed by the pathologist.

Protocols for Hematoxylin and Eosin:

- a. Deparaffinize tissue slides in xylene.
- b. Hydrate in decreasing grades of alcohol (100%, 95%, 90%, 70%).
- c. Stain in Coles hematoxylin 3-5minutes
- d. Rinse in distilled water
- e. Differentiate in 1% HCL in 70% alcohol, briefly (5seconds).
- f. Rinse in distilled water, Blue in Scott's water for 5 minutes.
- g. Counter stain with 1% eosin solution for 2 minutes.
- h. Rinse in distilled water, Dehydrate in increasing grades of alcohol (70%, 90%, 95%, 100%), rinse in water. Clear in xylene. Mount with synthetic medium. Observe under the microscope.

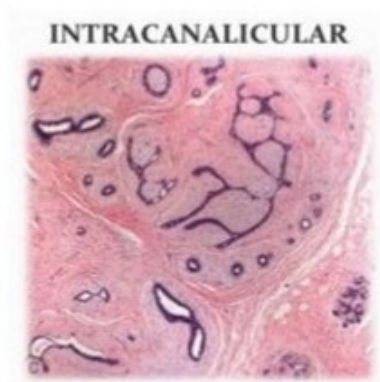
Protocol for Periodic Acid Schiff technique:

- a. Deparaffinize tissue slides in xylene.
- b. Hydrate section in decreasing grades of alcohol (100%, 95%, 90%, 70%).
- c. Rinse in water, oxidize sections in 1% Periodic Acid Schiff for 5 minutes.
- d. Wash sections thoroughly in running tap water, place in Schiff reagent for 15minutes.
- e. Wash in lukewarm water for 5 minutes, counter stain nuclei with Erlich's hematology for 1minute.
- f. Wash sections in water for 5minutes, dehydrate sections in increasing grades of alcohol (70%, 90%, 95% and 100%). Clear sections in xylene, mount in synthetic medium.

4. Photomicrography



Well circumscribed, lobulated contours, white-gray color, lobulations bulge above the cut surface, slit-like spaces



Mainly cellular stroma with distorted duct



Mainly fibrous stroma with normal duct

Figure.1.1: A photomicrograph showing the normal and abnormal cellular components of the breast in fibroadenoma cases of ages <18 years and 18-39 years.

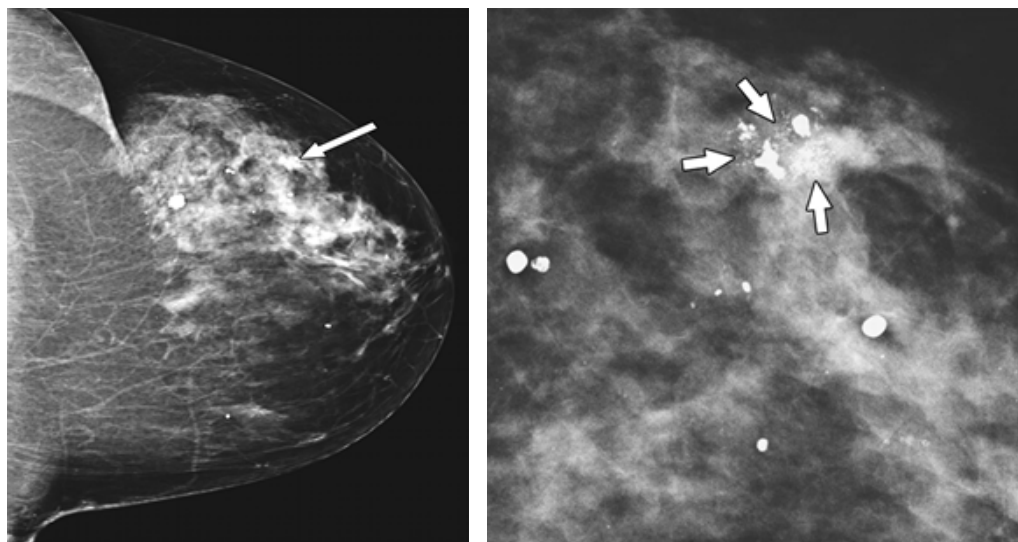


Figure 1.2: A radiograph showing calcified cellular components of the breast in complicated/complex fibroadenoma cases of ages 40-59.

5. Statistical Analysis

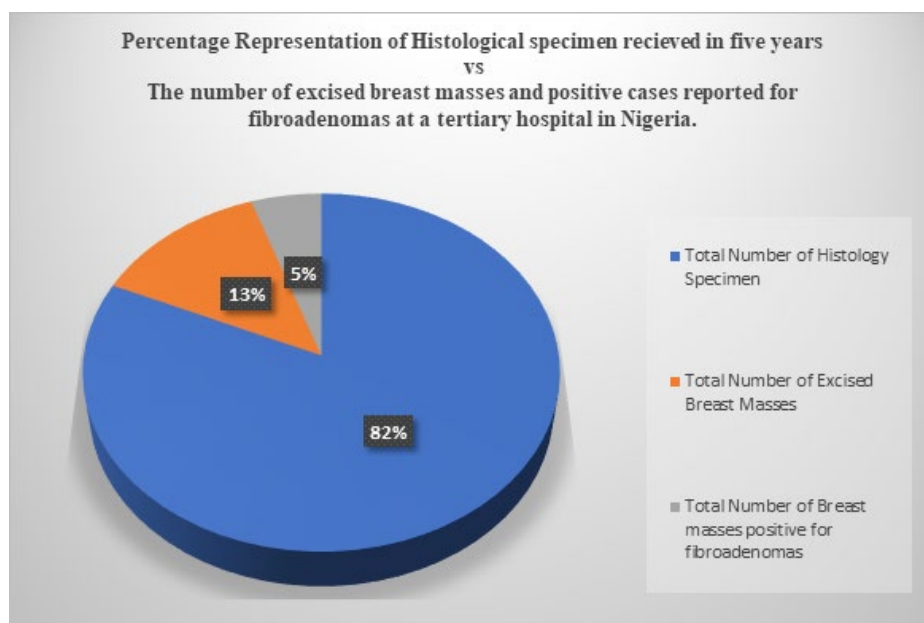
The relationship between age and pathologic diagnosis were evaluated using the students *t* test. A value for *p* of less than 0.05 was considered significant.

Years	2016	2017	2018	2019	2020
Number of Histology Samples	1283	1315	1421	1680	791

Table 1: Number of histology specimen received at the tertiary hospital in Nigeria.

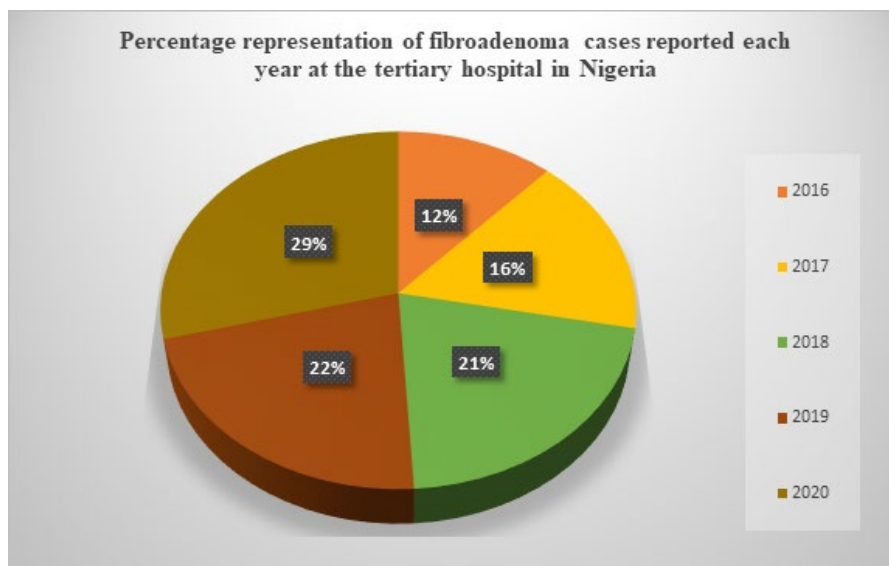
Years	2016	2017	2018	2019	2020
Number of Histology Samples	133	210	218	219	258

Table 2: Number of excised breast masses received at the tertiary hospital in Nigeria.



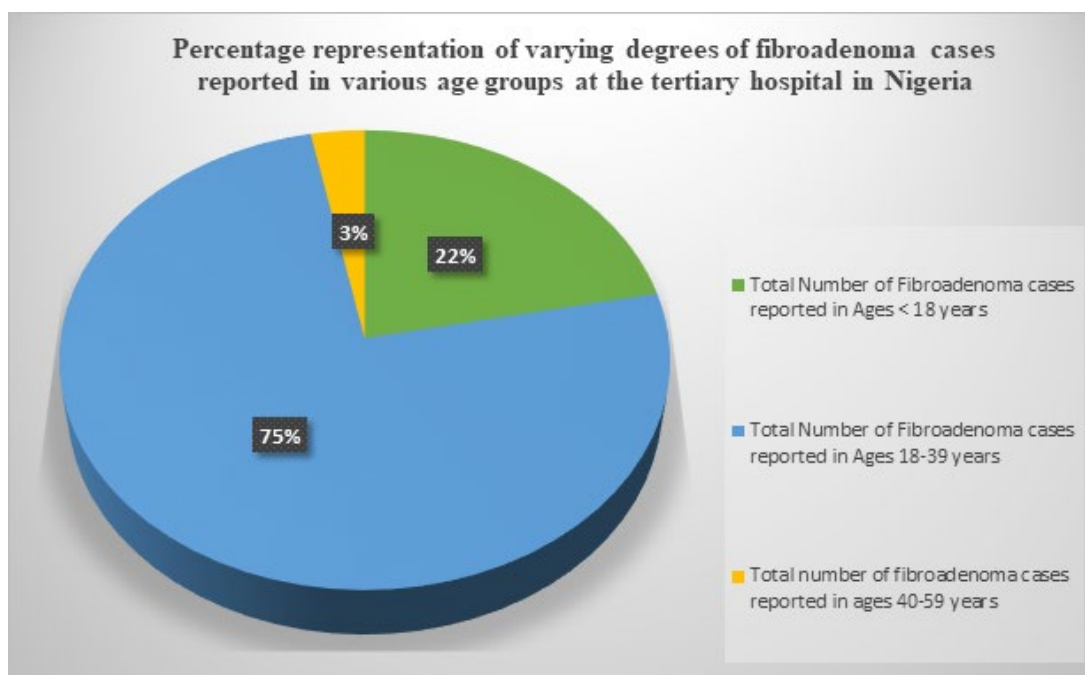
Years	2016	2017	2018	2019	2020
Number of Histology Samples	133	210	218	219	258

Table 3: Number of fibroadenoma cases reported each year at the tertiary hospital in Nigeria.



Year:	Age Group:		
	<18	18-39	40-59
2016	7	34	1
2017	11	48	2
2018	16	48	4
2019	17	54	6
2020	19	57	7

Table 4: Range of fibroadenoma cases reported in various age groups at the tertiary hospital in Nigeria.



6. Conclusions

After the processing of breast tissues, specimen slides were produced and viewed using a low-powered microscope. The slides above represent the images seen under the microscope. The first slide represents an image of an unhealthy and distorted breast-tissue duct (fibroadenoma). While the second slide (on the right) represent a healthy and normal breast-tissue duct (none fibroadenoma).

The microscopic examination of the breast biopsy revealed a benign tumor composed of a bi-plastic proliferation of both stromal and epithelial components. This bi-plasia can be arranged in two growth patterns: peri-canalicular (stromal proliferation around epithelial structures) and intracanalicular (stromal proliferation compressing the epithelial structures into clefts).

These tumors characteristically display hypo-vascular stroma compared to malignant neoplasms. Furthermore, the epithelial proliferation appears in a single terminal ductal unit and describes duct-like spaces surrounded by a fibroblastic stroma. The basement membrane is intact according to the DECEMBER 2007 EDITION OF "FIBROADENOMA OF THE BREAST".

Further molecular investigations revealed that up to 66% of the fibroadenoma cases harbored mutations in the exon (exon 2) of the mediator complex subunit 12 (MED12) gene. These mutations were restricted to the stromal component. These findings were speculated to agree with the conditions associated with fibroadenoma discovered by which are:

- Beckwith-Wiedemann syndrome
- Maffucci syndrome
- Cowden syndrome

Out of 82% of histology specimen received for the period of five years, 13% were excised breast masses and 5% was confirmed positive for fibroadenoma. Out of this 5% of positive cases from 2016 to 2020, there was a slight and irregular interval of 1-4% increase each year. The prevalence of fibroadenoma was mostly seen in youths of ages 18-39 years having 75%, followed by adolescence of ages <18 years with 22% and lastly older adults of ages 40-59 years with 3%. The cause of this prevalence is unknown but with the current view of fibroadenoma cases in this study it can be predicted that there might be subsequent increase of cases in of this specific age group in the future.

The prevalence of fibroadenoma in ages 18-39 years, indicated an instability in the reproductive hormones of the female due to estrogen and progesterone receptors. According to GREENBERG R, these hormones stimulated the fibroadenomas via hormone-receptor mechanism leading to excessive proliferation of epithelial and stromal cells but undergo atrophy during menopause. The constant and alarming increase in fibroadenoma cases in ages 18-39 years from the chart above suggests a progressive and harbored mutations in the exon (exon 2) of the mediator complex subunit 12 (MED12) gene of the stromal cells of the breast which

leads to the excessive proliferation. These findings agree with the discoveries made by on the "CONDITIONS ASSOCIATED WITH FIBROADENOMA".

Furthermore, according to the NOVEMBER 2018 edition of "FIBROADENOMAS OF THE BREAST", complex/multiple fibroadenoma cases in the pre-menopausal years of a female, could result in phyllodes tumor at the age of 45-59 (menopausal years) which increases the risk of breast cancer. The data collected in this research showed evidence of these cases between ages 40-59 years. Which indicates a growing risk of phyllodes tumor which is an indicator of breast cancer after several recurrences.

Conclusively, since the data presented showed high prevalence of fibroadenoma cases in ages 18-39 annually it indicates that these individuals in this age group experienced sporadic instability of the reproductive hormones either due to childbearing, abortion, or genetic hormonal abnormalities. This suggests that there might be increased rates of abortion occurring among this age group in Nigeria or lack of proper postnatal care in Nigeria tertiary hospitals [1-12].

Declaration

Ethical Approval and Consent to Participate

This analytical study and the consent to participate was granted and Approved by the Hospital Management Board, Federal Capital Territory, Nigeria. The data collected and used in this research was approved by the department of Clinical Pathology in a Nigerian tertiary hospital for the awareness of clinical scientists on the prevalence of fibroadenoma cases among teenagers and young adults in Nigeria.

Ethical Statement

We ensured that all research was conducted in accordance with ethical principles and confidentiality. We also ensured that all research conducted was in accordance with the approval of the Hospital Management Board of Nigeria (FCT chapter). The use of patients-clinical records and patients' confidentiality was duly observed with an ethics of respect for cultures, communities, the individuals/person, and independent knowledge.

Consent for Publication

The research was independently carried out by the author and co-supervised by another clinical scientists. The authorization of publication is based on the rights of the author who conducted this research.

Availability of Data and Material

The availability of data used in this research study was easily obtained during and after the research. The materials used in this research study was easily accessible within the clinical pathology department of the tertiary hospital.

Competing Interest

There was no competing interest involved in this research study.

Funding

No external funding

Author's Contribution

The author contributed to the documentation, compiling, and interpretation of the data obtained from this research.

Acknowledgement

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