



## SURGICAL REMOVAL OF COMPLEX FIBROADENOMAS AND THE INCIDENCE OF UPGRADE, RETROSPECTIVE ANALYSIS IN A CANCER CENTRE.

### Surgery

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### ABSTRACT

Breast cancer (BC) is the foremost cause of mortality associated to female cancer among the world. Fibroadenomas are one of the most common benign breast diseases, Radiologically, fibroadenomas appear as a slightly homogenous, lobulated, isoechoic or hypoechoic solid mass. The objective of the study is to present the fibroadenoma characteristics observed at Mediclinic city hospital, Dubai, UAE. Therefore, we conducted a retrospective observational cross-sectional study to identify the characteristics of fibroadenoma with total of 116 patients from 2014 to 2019. All 116 cases were females, and diagnosed with fibroadenoma between the ages of 15 to 60 with a Bi-RADS score of 3 to 5. Patients were followed up till 6 months. 28 (20.74 %) of the fibroadenomas were stable sized, size growth observed in 2 (1.48 %), size growth stabilised after 6 months in 2 (1.48 %), 74 (54.81 %) fibroadenomas were surgically excised. Our study reported Complex fibroadenoma and Complex fibroadenoma patients with complex features like atypical hyperplasia, Atypical lobular hyperplasia enhances the risk of causing breast cancer. Additionally, study has demonstrated that, surgical removal of complex fibroadenomas and fibroadenomas with complex features is the best way to reduce the risk of carcinoma.

### KEYWORDS

Breast cancer (BC), Fibroadenoma, Complex fibroadenomas, Lobular carcinoma in situ (LCIS), Phyllodes tumours (PT), Human papillomavirus (HPV), Bi-RADS, Bi-RADS 3, Bi-RADS 4, Bi-RADS 5.

#### INTRODUCTION:

Breast cancer is the foremost cause of mortality associated to female cancer among the world. Fibroadenomas are the most common type of breast disease that occurs in women usually below the age of 35 years old.[1] A fibroadenoma is a painless, unilateral, benign breast tumour that is a solid, not fluid-filled, lump. It may shrink after menopause and therefore, are less common in post-menopausal women.[2]

Histologically, fibroadenomas consist of an epithelial and stromal component. Fibroadenomas are classified into simple and complex. Cysts >3 mm in size, sclerosing adenosis, epithelial calcifications or papillary apocrine changes can be considered as Complex fibroadenomas.

Radiologically, fibroadenomas appear as a slightly homogenous, lobulated, isoechoic or hypoechoic solid mass. Typically considered a benign tumour, reports exist of both invasive and *in situ* neoplasms being found within the fibroadenoma.[3] Invasive ductal carcinoma is the most common pathological type 1. Lobular carcinoma *in situ* (LCIS) is a neoplastic proliferation of the epithelial cells of the breast lobule.

Originally, this was considered a pre-cancer to invasive lobular carcinoma, similar to the relationship between ductal carcinoma *in situ* and invasive ductal carcinoma. However, LCIS is now considered a general marker for breast cancer risk, rather than a true pre-cancer.[3]

Phyllodes tumours (PT) and Fibroadenomas (FA) are part of the spectrum of breast fibroepithelial lesions. Whilst FAs are benign tumours of frequent occurrence, which are usually managed conservatively, PTs are rare and may recur locally or even metastasize to distant sites.[4]

In the year 2018, breast cancer (BC) is the most common cancer among the women registering a total of 2.08 million new cases (11.6% of all new cases among females) across the World. Accounting for 15% of the total cancer-related deaths, it is the first most common cause of cancer deaths among women, worldwide.

In Indian context, BC remains the most frequent (27.7%) cancer among women with the urban and metropolitan regions reporting high rates of incidence than rural region. Going by the numbers, in 2018 about 87,090 women died due to BC in India (11.1% of total women cancer).

Recently, different studies suggested association of human papillomavirus (HPV) with BC. But, frequency of HPV infection in

BC varied widely (1.6–86%) among different studies. Inconsistent HPV infection was also reported in different molecular subtypes of BC.[5]

Fibroadenomas are common benign lesions of the breast that usually present as a single breast mass in young women. They are assumed to be aberrations of normal breast development or the product of hyperplastic processes, rather than true neoplasms. The clinician often faces the dilemma whether to remove the mass or to monitor it by means of periodic follow-up examinations.

A balanced and rational approach to the management of a fibroadenoma of the breast needs to address the crucial questions about its association with breast cancer, especially whether or not it is a marker of increased risk of breast malignancy. Another consideration to be weighed is that a substantial percentage of these lesions undergo spontaneous regression.[6] The management of fibroadenomas is solely dependent on patient age and clinical findings.[7] Breast Imaging-Reporting and Data System (BI-RADS) is a risk assessment tool.

BI-RADS 1 and 2 for normal and benign masses, BI-RADS 3 is used for both palpable and non-palpable masses, BI-RADS 4 and 5 for suspicious or highly suspicious masses.

Therefore, we conducted a retrospective observational cross-sectional study in Mediclinic city hospital, Dubai, UAE, to identify the characteristics of fibroadenoma.

#### Methodology

##### Patients

This is a retrospective observational cross-sectional study. The study included 116 fibroadenoma patients from 2014 to 2019. The data was collected retrospectively from the electronic patient database of Mediclinic city hospital, Dubai, UAE. The inclusion criteria was female population who were diagnosed with fibroadenoma between the ages of 15 to 60 with a Bi-RADS score of 3 to 5 and the exclusion criteria was pregnant women and male breast cancer patients.

##### Follow up and outcome

Follow up done by the electronic medical record system included patient demographics, preoperative examination, surgical records, and postoperative detailed pathological description and diagnosis reports. The follow up by phone or mail included important information on the medical history that was not acquired from the electronic medical record system, detailed process of visits to other hospital(s), especially the initial operation records and postoperative pathologic examination results, the frequency of postoperative re-examination and date and

result of the last breast examination, tumour recurrence or metastasis or not, and tumour related death or not. Cases were lost to follow up if a large amount of clinical data was missing, or if the patient rejected follow up due to personal reasons, or if the contact failed.

**Statistical analysis**

Statistical analysis was done by estimating the demographic parameters and parameters of incidence in women with fibroadenoma. All the statistical analysis was performed using the STATA software. All characteristics were summarized descriptively. For continuous variables, data were represented using means ± SD. For categorical data, descriptive statistics like percentages and frequencies were used in the data summaries and the data represented was in the form of tables.

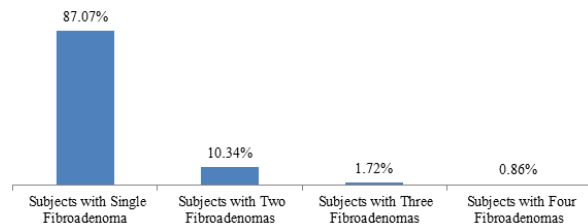
**RESULTS:**

**Patient Demographics**

Study includes 116 female patients presented with fibroadenoma. The average age at presentation was 37.51±7.21 years while the minimum and maximum age of presentation was 17 and 63 respectively. 20.69% of the patients were lost to follow-up during the study. 33.62% of the patients had fibroadenoma which was greater than 20 mm. 87.07% of the patients had single fibroadenoma, remaining had multiple fibroadenomas. The results can be observed in Table 1. Figure 1 represents distribution of number of fibroadenoma's observed in the patients.

**Table 1: Summary of patient demographics**

PARAMETER	RESULT (N=116)
Age (Years; Mean±SD)	37.51±7.21
Number of patients who were Lost to Follow up n (%)	24 (20.69%)
Number of patients with Fibroadenoma Size greater than 2cm (20mm) n (%)	39 (33.62 %)
Number of patients with Single Fibroadenoma n (%)	101 (87.07 %)
Number of patients with Two Fibroadenomas n (%)	12 (10.34 %)
Number of patients with Three Fibroadenomas n (%)	2 (1.72 %)
Number of patients with Four Fibroadenomas n (%)	1 (0.86 %)



**Figure 1: Number of Patients with Fibroadenoma Characteristics**

The mean size of fibroadenoma at presentation was 17.31±9.69 mm, where the maximum size was 70 mm and minimum size was 4.40 mm. Characteristics of fibroadenoma such as shape, margin and echogenicity were recorded during the study. 56.30 % of the fibroadenomas had ovoid shaped followed by irregular (26.67 %), round (10.37 %), bilobed (2.22 %), irregular lobulated, mildly irregular, non-parallel and triangular shaped fibroadenomas. 2 fibroadenomas were of unknown shape. 65.19% of fibroadenomas had a lobulated margin followed by circumscribed (24.44 %), ill-defined (5.93 %), irregular (1.48 %), spiculate (0.74 %) and stellate (0.74 %) margins respectively.

Most of fibroadenomas were identified as Hypo (90.37%), followed by mixed (8.15 %) and iso (0.74 %) on echogenic examination. 39.26 % of fibroadenomas had vascularity and 8.89 % of the fibroadenomas were calcified. The results can be observed in Table 2.

**Table 2: Summary statistics of Fibroadenoma Size in mm**

PARAMETER	RESULT (n=135)
Fibroadenoma Size (mm; Mean±SD)	17.31±9.69
Fibroadenoma Shape n (%)	
Bilobed	3 (2.22 %)

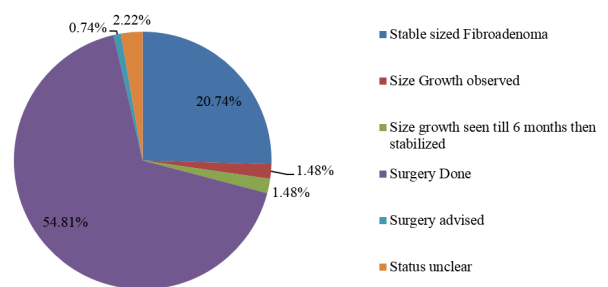
Irregular	36 (26.67 %)
Irregular lobulated	1 (0.74 %)
Mildly irregular	1 (0.74 %)
Non-parallel	1 (0.74 %)
Ovoid	76 (56.30 %)
Round	14 (10.37 %)
Triangular	1 (0.74 %)
Unknown	2 (1.48 %)
Fibroadenoma Margin n (%)	
Circumscribed	33 (24.44 %)
Ill-defined	8 (5.93 %)
Irregular	2 (1.48 %)
Lobulated	88 (65.19 %)
Spiculate	1 (0.74 %)
Stellate	1 (0.74 %)
Fibroadenoma Echogenicity n (%)	
Hypo	122 (90.37 %)
Iso	1 (0.74 %)
Mixed	11 (8.15 %)
Vascularity n (%)	
Yes	53 (39.26 %)
No	81 (60.00 %)
Min	1 (0.74 %)
Calcification n (%)	
Yes	12 (8.89 %)
No	122 (90.37 %)
Min	1 (0.74 %)

**6 Months Follow up**

At follow-up 54.81% of the fibroadenomas were excised through surgery and 20.74% of the fibroadenomas were stable. 2 fibroadenomas showed growth in size and in 2 fibroadenomas the growth was stabilized after 6 months. Data on 25 fibroadenomas was not available as the patients were lost to follow up. The results can be observed in Table 3. Figure 2 represents the fibroadenoma status distribution at 6 months follow up.

**Table 3: Summary statistics of Fibroadenoma in Patients at 6 Months Follow up**

PARAMETER	RESULT (n=135) n (%)
Stable sized fibroadenoma	28 (20.74 %)
Size growth observed	2 (1.48 %)
Size growth seen till 6 months then stabilized	2 (1.48 %)
Surgery done	74 (54.81 %)
Surgery advised	1 (0.74 %)
Status unclear	3 (2.22 %)



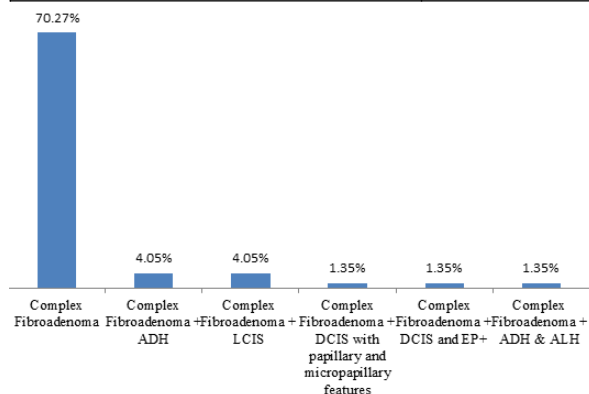
**Figure 2: Status of Fibroadenoma in Patients at 6 Months Follow up**

**Histopathology of Fibroadenoma in Surgery Patients**

From Table 4 we can observe the histopathological status of the fibroadenomas excised through surgery. 70.27 % of the excised fibroadenomas were complex fibroadenomas. However, other fibroadenomas had complications in combination with complex fibroadenoma such as Atypical Ductal Hyperplasia, Atypical Lobular Hyperplasia, Ductal Carcinoma in situ, Lobular Carcinoma in situ etc., the variations in the histopathology can be observed in Table 4. Figure 3 represents the histopathology of fibroadenoma observed post-surgery.

**Table 4 : Summary statistics of Histopathology of Fibroadenoma in Surgery Patients**

PARAMETER	RESULT (n=74) n (%)
Complex Fibroadenoma	52 (70.27 %)
Complex Fibroadenoma with Atypical Ductal Hyperplasia (ADH)	3 (4.05 %)
Complex Fibroadenoma plus Lobular Carcinoma in situ (LCIS)	3 (4.05 %)
Fibroadenoma	2 (2.70 %)
Tubular adenoma	2 (2.70 %)
Complex Fibroadenoma with Atypical Ductal Hyperplasia and Atypical Lobular Hyperplasia (ALH)	1 (1.35 %)
Complex Fibroadenoma plus Ductal Carcinoma in situ (DCIS) with papillary and Micropapillary features	1 (1.35 %)
Complex Fibroadenoma plus Ductal Carcinoma in situ low grade, EP+	1 (1.35 %)
Complex Fibroadenoma plus Lobular Carcinoma in situ confined to Fibroadenoma	1 (1.35 %)
Not Available	1 (1.35 %)
Others	7 (9.46 %)



**Figure 3: Histopathology of Fibroadenoma in Surgery Patients**

**DISCUSSION:**

Fibroadenoma is a biphasic tumour consisting of epithelial and stromal components. Recent studies identified frequent mutations in the stromal component suggesting that this tumour was primarily stromal neoplasm. Breast carcinoma may arise within a benign tumour or the tumours may coexist independently. The incidence of a carcinoma evolving within a fibroadenoma was 0.002% to 0.0125%. Only 10% of these tumours were infiltrating ductal carcinoma. The clinical and imaging findings are frequently those of benign fibroadenomas. Fibroadenomas are not typically considered as a risk factor of carcinoma. However, fibroadenoma shows in about half of the cases proliferative changes like sclerosing adenosis, epithelial calcifications and papillary apocrine metaplasia that classify it as complex fibroadenoma and a long-term risk factor for breast cancer. Breast cancer was less important in the absence of proliferation and family history of breast cancer. In cases of proliferation, the presence of atypia was critical and family history was an independent risk factor for breast cancer.[1]

Two different studies were conducted to know, the differentiation between fibroadenoma & invasive ductal carcinoma and growing fibroadenoma. The mean age of the patients with fibroadenoma was found to be 39 years (range, 18-81years) 36.7 years (range, 15-75 years) respectively,[8,9] which is in agreement with our study results where the mean age observed was 37.39 years.

Also the mean age varied extensively in few cases which are as follows, median age for fibroadenoma was 23.0 years in a study conducted to differentiate triple-negative breast cancer and fibroadenoma.[10] In another study intended to analyse the various breast masses the mean age at diagnosis was found to be 46.9 years (range, 27 to 80years).[11] While another study was conducted to assess the similarities between phyllodes tumour and fibroadenoma the mean age was observed to be 27.0 years (range 15 to 49 years).[12]

In our study we observed that the shapes of fibroadenomas were mostly oval 76 (56.30 %) followed by irregular 36 (26.67 %) and round masses 14 (10.37 %).

Most of the cancers found inside the breast fibroadenoma were *in situ* carcinoma or early breast cancer with minimal or small tumour size.[11] Hence tumour size plays a significant role in diagnosis of various benign and malignant breast tumours. In present study the mean size of tumour is found to be 17.31 mm which is similar to few other researches where mean and median size of palpable fibroadenomas was 18.6 mm and 16.5 mm, respectively (size range, 6-57 mm). The mean tumour size of the fibroadenoma in few studies observed was 2.46 cm (range, 0.8 to 5.1 cm)[13] which is similar to our study. In another study, mean size of tumour at the time of surgery was reported as 2.46 cm (range 0.8 to 5.1 cm)[12] which is similar to our study.

A study was conducted in 1430 subjects to assess the growth of fibroadenoma through regular follow up, 83 patients were identified who had enlarging lesions with an incidence of 5.8%. As many of the patients were lost to follow up true incidence cannot be calculated. In contrast to this, the present study reveals most of the fibroadenomas were stable during follow-up with lower incidence of size growth.[14,15] In our study number of hypo echoic lesions were more (90.37 %) which is in agreement with other studies which reported similar results.

**CONCLUSION:**

Fibroadenomas are one of the most common benign breast masses encountered in the adolescents. Even though the malignancy arising with fibroadenoma is rare, regular follow-up to assess the growth and characteristic features of fibroadenoma is necessary to manage the patient. Management of Fibroadenomas may present challenges if the mass is not resolving, is increasing in size, or is symptomatic. Studying features of breast masses like size, margins and echogenicity helps in differentiating fibroadenomas with other malignancies of breast.

Atypical Ductal Hyperplasia and Atypical Lobular Hyperplasia is not a form of breast cancer. It is an indication for women who may have a risk factor for developing breast cancer in the future.

Complex fibroadenoma and Complex fibroadenoma patients with complex features like atypical hyperplasia, Atypical lobular hyperplasia enhances the risk of causing breast cancer.

In summary, in our study, 70.27% of fibroadenomas were complex and 17.55% of complex fibroadenomas with complex features. They were larger and, although most presented with benign imaging features, they also had some characteristics that could help in differentiating them from their simple counterparts, namely, an Ovoid shape, Lobulated margin, Hypo echo structure and the presence of microcalcifications,

In our 6 months follow-up study 20.74 % of Fibroadenomas were Stable in size, 54.81 % of patients underwent surgery and only 2% of Growth observed initially after that stabilized.

Our study has suggested that, Surgical excision of complex fibroadenomas and fibroadenomas with complex features is the best way to reduce the risk of carcinoma and to improve quality of life.

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