



## Original Article

# A Study on different histological variants of Phyllodes tumour of Breast and Fibroadenoma with special emphasis to differentiate Fibroadenoma from Benign Phyllodes tumour – A Retrospective 2 years study in a Tertiary care centre

Authors

**Dr Gopinath Barui<sup>1</sup>, Dr Tripti Das<sup>2</sup>, Dr Santanu Nandy<sup>3</sup>**

<sup>1</sup>Associate Professor, <sup>2,3</sup>Post Graduate Trainee

Department of Pathology, R.G. Kar Medical College and Hospital, Kolkata-700004

Corresponding Author

**Dr Tripti Das**

Post Graduate Trainee, Department of Pathology

Address: AB Ladies Hostel, R.G. Kar Medical College and Hospital, 1, Khudiram Bose Sarani, Kolkata-700004, West Bengal, India

Mobile no. 9635781818, Email: [triptidasrgk@gmail.com](mailto:triptidasrgk@gmail.com)

## Abstract

**Background:** Fibroadenoma is the most common benign breast tumour in adolescent and young women of child bearing age group arising from the Terminal Duct Lobular Unit (TDLU) and featuring a proliferation of both epithelial and stromal elements. Phyllodes tumours are rare fibro epithelial tumours of the breast tumours account for 0.3–1% of all primary tumours of the breast predominantly in middle-aged women. Intra canalicular fibroadenoma with increased stromal cellularity closely mimics benign phyllodes tumour but it has to be differentiated properly as clinical management and prognosis are different in both the cases.

**Materials and Methods:** A retrospective observational study was done in Department of Pathology, R.G. Kar Medical College and Hospital, Kolkata; over a period of 2 years from January 2016 to December 2017. Total 127 cases of fibroadenoma and 19 cases of phyllodes tumour cases were analyzed.

**Results:** Out of total 146 cases, 127 cases (87%) were Fibroadenoma and rest 19 cases (13%) were Phyllodes tumours. Out of 19 cases of phyllodes tumours 11 (57.8%) were Benign Phyllodes, 7 (36.8%) were Borderline Phyllodes and 1 (5.4%) was Malignant phyllodes. Fibroadenomas were most common in the 11-20 yrs (45.67%) age group, followed by 21-30 yrs (36.22%), while phyllodes were more common in 41-50 yrs (36.84%) age group. Fibrocystic changes were present in 13.39% cases of fibroadenoma. Fibroadenoma and Benign Phyllodes tumour of breast were differentiated on the basis of 3 histological feature i.e. stromal cellularity, cellular pleomorphism and mitotic activity.

**Conclusion:** There is various histomorphological variants of fibroadenoma and 3 types of phyllodes tumour; which were studied and this knowledge is very helpful where there is overlapping features of both the tumours and chance of confusion is present. Special emphasis was given to differentiate fibroadenoma from benign phyllodes.

**Keywords:** Phyllodes tumour, fibroadenoma, breast.

## Introduction

Fibroepithelial tumours are a heterogenous group of biphasic neoplasms consisting of a proliferation of both epithelial and stromal components. Fibroadenoma and Phyllodes tumours constitute the major entities<sup>[1]</sup>.

Fibroadenoma is the most common benign breast tumour, usually occur in young women (specially less than 30 years of age).It consists of a circumscribed breast neoplasm arising from the Terminal Duct Lobular Unit (TDLU) and featuring a proliferation of both epithelial and stromal elements<sup>[1]</sup>.

Grossly, fibroadenomas are ovoid and well-circumscribed. The cut surface is grey or white, solid, rubbery, bulging, with a slightly lobulated pattern and slit-like spaces. Variations depend on the amount of hyalinization and myxoid change in the stromal component. Histologically, it is an admixture of stromal and epithelial proliferation, giving rise to two distinct growth pattern-pericanalicular and intracanalicular. The epithelial component of Fibroadenoma can show varying degree of usual ductal hyperplasia, metaplastic changes, sclerosing adenosis can also occur. Most fibroadenomas do not recur after complete surgical excision<sup>[1]</sup>.

Intracanalicular fibroadenoma with increased stromal cellularity closely mimics benign phyllodes tumour, with the distinction based on the finding of well developed fronds resulting from a markedly exaggerated intra canalicular growth pattern accompanied by stromal cellularity usually diffuse, but sometimes accentuated around epithelial clefts, in the phyllodes tumour<sup>[1]</sup>.

Juvenile fibroadenoma reveals hyperplasia of both the stromal and epithelial components,with stroma manifesting increased cellularity and the epithelium shows hyperplasia, often with the tufted pattern characteristic of Gynaecomastia or virginal hypertrophy<sup>[2]</sup>.

Complex fibroadenoma contains cysts more than 3mm in size, sclerosing adenosis, epithelial calcifications or papillary apocrine hyperplasia, reported to be associated with slightly increased

relative risk of subsequent development of breast cancer. Cellular fibroadenomas, as defined by prominent cellular stroma, may show histological features that overlap with those of benign phyllodes tumour<sup>[1]</sup>.

Phyllodes tumours account for 0.3–1% of all primary tumours of the breast and for 2.5% of all fibro epithelial tumours of the breast. They occur predominantly in middle-aged women (average age at presentation, 40–50 years) about 15–20 years later than for fibroadenomas.

It is characterized by a double-layered epithelial component arranged in clefts surrounded by a hypercellular stromal/ mesenchymal component which in combination elaborate leaf-like structures<sup>[1]</sup>. The term *cystosarcoma phyllodes* (phyllo =Greek for leaf) was used to emphasize the leaf-like pattern, fleshy and cystic gross appearance of the lesion<sup>[3]</sup>. Phyllodes tumours are classified into benign, borderline and malignant categorieson the basis of a combination of histological features, including the degree of stromal hyper cellularity, mitoses and cytological atypia, stromal overgrowth and nature of the tumour borders/margins<sup>[1]</sup>.

Several grading systems have been proposed, but the use of a three-tiered system, to include benign, borderline, and malignant PT is preferred, because this approach leads to greater certainty at the ends of the spectrum of these fibro epithelial lesions. Grading is based on semi-quantitative assessment of stromal cellularity, cellular pleomorphism, mitotic activity, tumour margin/border appearance and stromal distribution/over growth<sup>[1]</sup>.

**Histological features of Fibroadenoma, Benign, Borderline and Malignant Phyllodes tumours (WHO)**

Histological features	Fibroadenoma	Benign Phyllodes	Borderline Phyllodes	Malignant Phyllodes
Tumour border	Well defined	Well defined	Well defined, may be focally permeative	Permeative
Stromal cellularity	Variable, usually uniform	Cellular, usually mild, may be non-uniform or diffuse	Cellular, usually moderate, may be non-uniform or diffuse	Cellular, usually marked and diffuse
Stromal atypia	None	Mild or none	Mild or moderate	Marked
Mitotic activity	Usually none	Usually few (<5/10HPF)	Usually frequent (5-9/10HPF)	Usually abundant ( $\geq 10/10$ HPF)
Stromal overgrowth	Absent	Absent	Absent, or very focal	Often present
Malignant heterologous elements	Absent	Absent	Absent	May be present

The histological features used to distinguish benign, borderline, and malignant PT should be considered together, because emphasizing an individual feature may result in over-diagnosis, especially in the case of mitotic activity PTs should be graded according to the areas of highest stromal cellular activity and most florid architectural pattern<sup>[1]</sup>.

Most PTs behave in a benign fashion, with local recurrences occurring in a small proportion of cases. Very rarely (about 2% or less overall), the tumour may metastasize, mainly in the cases of tumours of malignant grade<sup>[1]</sup>.

A margin of at least 1cm of normal breast tissue surrounding all aspects of the tumour is preferred. Most of the tumours can safely be treated by wide local excision, but simple mastectomy should be considered for patients who have a lesion with microscopic features suggesting a particularly aggressive behaviour or very large lesion<sup>[2]</sup>.

**Place of Study:** Department of Pathology, R.G. Kar Medical College and Hospital, Kolkata, West Bengal, India

**Duration of Study:** 2 years (January 2016 to December 2017)

**Study Design:** Retrospective observational study

**Study Material:** Past records of Histopathology Data register, available at the Department of Pathology, R.G. Kar Medical College and Hospital

**Materials and Methods**

This study was conducted in the Department of Pathology, R.G. Kar Medical College and Hospital. It was a retrospective observational review of the histopathology register, available in the department; done over a period of 2 years (January 2016 to December 2017). Total no. of biopsy samples received in the department during this 2 years period was 33,027. Total no. of breast specimens which were histopathologically confirmed either as Fibroadenoma or Phyllodes tumours were 146, were included in this study. Only the excision biopsy samples and mastectomy specimens were included in the study. No incisional biopsy cases or core biopsy samples were considered. The data regarding the age of the female patients, size of the tissue, gross appearance, and most importantly the histopathological diagnosis were collected. The blocks and slides were collected from the department, slides were reviewed, and also fresh sectioning done in cases where needed and stained with haematoxylin and eosin and checked under microscope. Histopathological diagnosis were done in each cases again.

**Results**

A total of 146 cases were studied. Out of total 146 cases, 127 cases (87%) were Fibroadenoma and rest 19 cases (13%) were Phyllodes tumours [Table 1]. Out of 19 cases of phyllodes tumours 11 (57.8%) were Benign Phyllodes, 7 (36.8%)

were Borderline Phyllodes and 1(5.4%) was Malignant phyllodes [Table 2]. Fibroadenoma were most common in the 11-20 yrs(45.67%) age group, followed by 21-30 yrs(36.22%),while phyllodes were more common in 41-50 yrs (36.84%) age group [table3].Among the total 11 benign phyllodes tumour, 7 cases were seen in the age group 41-50 yrs (45.46%), while in cases of borderline phyllodes 4 cases out of 7 cases, seen in the age group 31-40 yrs (57.14%)&only 1 malignant phyllode case were in the study, seen in a 22 yrs old women [Table4].

There were 1 case of complex fibroadenoma, 1 case of juvenile fibroadenoma, 1 case of giant fibroadenoma found in the study [Table 6]. Secondary changes like fibrocystic changes ( in 17 cases), apocrine metaplasia (in 7 cases) and areas of focal epithelial hyperplasia (in 1 case) were also seen [Table 6]. Fibroadenoma and Benign Phyllodes tumour of breast were differentiated on the basis of 3 histological feature i.e. stromal cellularity, cellular pleomorphism and mitotic activity [Table 5].

**Table no. 1:** Distribution of cases

Total no. of cases	Fibroadenoma	Phyllodes tumour
146	127(87%)	19(13%)

**Table no. 2:** Incidence of different types of Phyllodes Tumours

Total no. of cases	Benign Phyllodes	Borderline Phyllodes	Malignant phyllodes
19	11 (57.8%)	7 (36.8%)	1 (5.4%)

**Table no. 3:** Incidence of cases of Fibroadenoma and Phyllodes tumours on the basis of age

Diagnosis	11-20 years	21-30 years	31-40 years	41-50 years	51-60 years	>60 years
Fibroadenoma(n=127)	58(45.67%)	46(36.22%)	18(14.17%)	4(3.15%)	1(0.79%)	x
Phyllodes Tumours(n=19)	x	3 (15.79%)	6 (31.58%)	7(36.84%)	2(10.52%)	1(5.27%)

**Table no. 4:** Incidence of Different types of Phyllodes tumours on the basis of age

Age range	Benign Phyllodes (total cases 11)	Borderline Phyllodes (total cases 7)	Malignant phyllodes (only 1 case)
21-30	2 (18.18%)	0	1
31-40	2 (18.18%)	4 (57.14%)	0
41-50	5 (45.46%)	2 (28.57%)	0
51-60	2 (18.18%)	0	0
>60	0	1 (14.29%)	0

**Table no.5:** Differentiation between Fibroadenoma and Benign Phyllodes tumour on the basis of Histological features

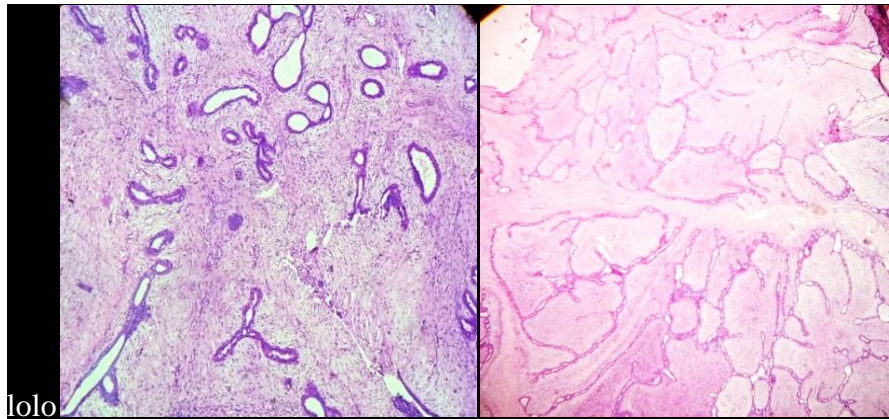
Histological Type	Stromal Cellularity	Cellular Pleomorphism	Mitotic Activity
Fibroadenoma	Variably cellular, usually uniform cellularity	Nil	Nil
Phyllodes tumour	Mildly cellular, diffuse cellularity	Mild	<5/10 HPF

**Table no. 6:** Secondary changes/histomorphological variations observed in Fibroadenoma cases (28 cases out of 127 cases)

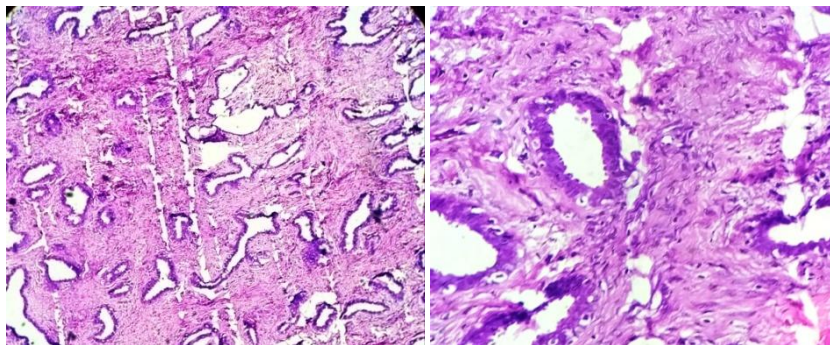
Secondary changes/ morphological variations	Total no. of cases (n=28)	Total percentage of cases(n=22.05%)
Apocrine metaplasia	7	5.51%
Fibrocystic changes	17	13.39%
Focal areas of epithelial hyperplasia	1	0.79%
Giant fibroadenoma	1	0.79%
Juvenile fibroadenoma	1	0.79%
Complex fibroadenoma	1	0.79%



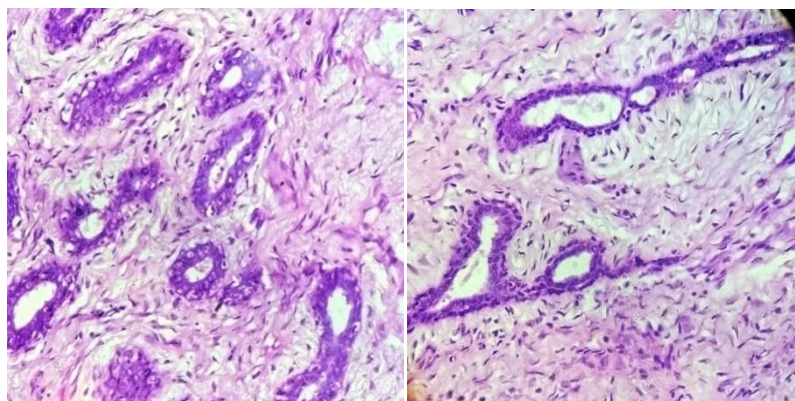
- Note: i) 17 cases of Fibrocystic changes seen in the age group between 15-45 years  
 ii) 7 cases of apocrine metaplasia seen in the age group between 19 -52 years.  
 iii) the only case of Giant fibroadenoma was seen in a 52 years old women.  
 iv) the only case of juvenile fibroadenoma was seen in a 35 years old women.  
 v) the single case of complex fibroadenoma was seen in a 57 years old women.



**Figure no. 1:** Low power view of Fibroadenoma of Breast (pericanalicular pattern-left & intracanalicular pattern-right) (H& E,100X)

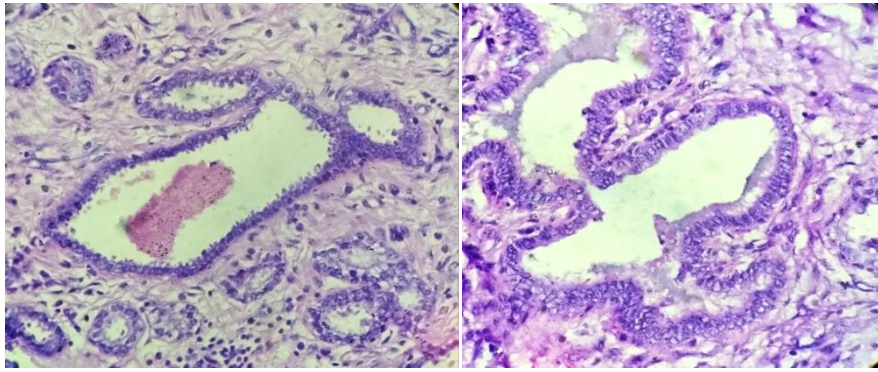


**Figure no. 2 :** Low power (left) and high power view (right) of Fibroadenoma with fibrocystic disease (H& E,100X & 400X)

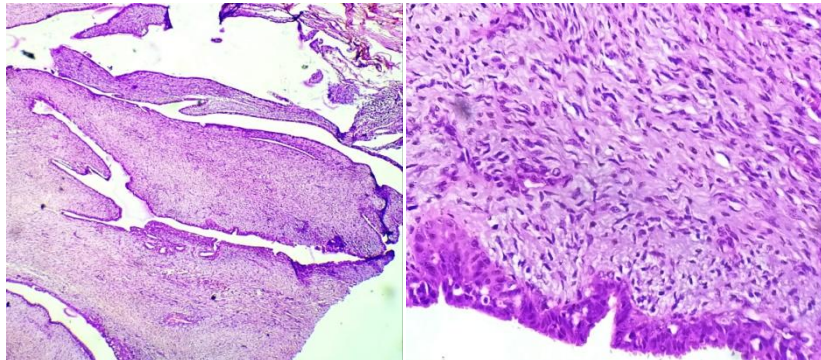


**Figure no. 3 :** High power view of Juvenile Fibroadenoma showing increased stromal cellularity with a fascicular stromal arrangement, a pericanalicular epithelial growth pattern(right)(H& E,400X), & High power view of Cellular fibroadenoma shows a pericanalicular growth pattern with a mild and diffuse increase in stromal cellularity (left)

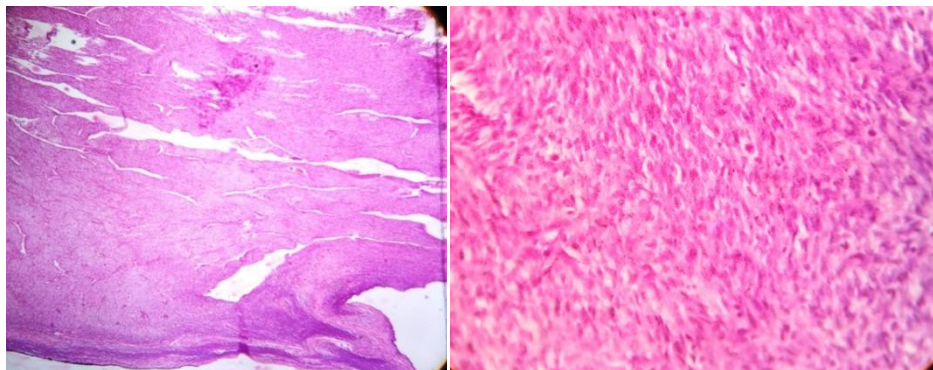




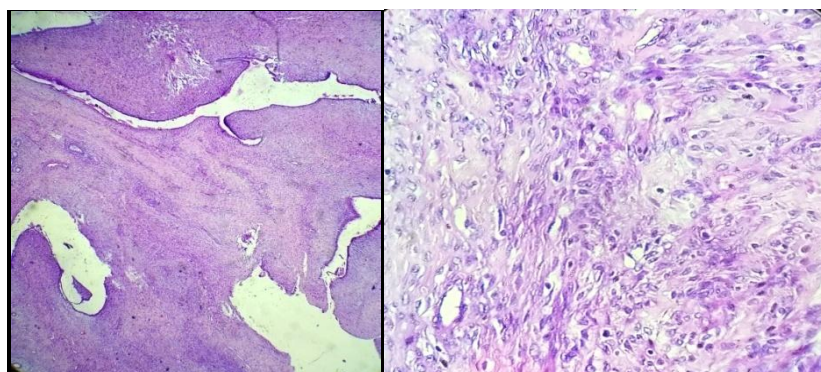
**Figure no. 4 :** High power view of Complex Fibroadenoma



**Figure no. 5 :** Low power (left) and high power(right) view of Benign Phyllodes ,compared to a Fibroadenoma;there is increased stromal cellularity and overgrowth- giving rise to the typical eaf like architecture(left) along with subepithelial accentuation of stromal cellularity (right).



**Figure no.6 :** Low power (left) and high power(right) view of Malignant Phyllodes. The stromal cells show nuclear hyperchromasia,pleomorphism and numerous mitotic figures (right)



**Figure no. 7 :** Low power (left) and high power(right) view of Borderline Phyllodes. Features are intermediate between Benign and Malignant Phyllodes

## Discussion

Fibroadenoma is the most common benign breast tumour in adolescent and young women of child bearing age group<sup>[1]</sup>. In our present study a total of 146 cases were studied, out of which 127 cases (87%) were Fibroadenoma and rest 19 cases (13%) were Phyllodes tumour.

Fibroadenoma were most common in the 11-20 yrs (45.67%) age group, followed by 21-30 yrs (36.22%), and after 40 yrs the incidence (4%) is very low. Some studies show rising rate in second decade<sup>[4,5]</sup>.

Secondary changes like fibrocystic changes seen in 13.39% cases of fibroadenomas and apocrine metaplasia in 5.51% cases and areas of focal epithelial hyperplasia seen in 1% of fibroadenomas. Fibrocystic changes were seen in the age group ranges from 15-45 years, with mean age of 25.05 years and median value of 21 yrs. Contrary to this, fibrocystic changes within fibroadenomas showed preponderance towards elder age group in an study<sup>[6]</sup>. Apocrine metaplasia was seen in the age group ranges from 19-52 years with mean age of 30.71 years and median value of 28.

Several studies have described progression of fibroadenoma to phyllodes tumour<sup>[7,8]</sup>.

Kuijper et al., have documented that fibroadenoma not only progresses in a stromal direction to phyllodes tumour, but also progresses in an epithelial direction towards carcinoma in situ<sup>[7]</sup>.

It has been reported that malignant changes in fibroadenoma are found in only 0.1% of cases, usually involving the epithelial components, and the large majority are in situ lesions<sup>[9,10]</sup>; while sarcomatous transformation of the stroma of fibroadenoma is believed to be an even rare phenomenon. Approximately 20% of the fibroadenomas have been found to have chromosomal aberration<sup>[11]</sup>.

In the present study phyllodes tumours were most common in 41-50 yrs (36.84%) age group, followed by 31-40 years age group (31.58%). The single case of Malignant phyllodes was seen in a 22 years old young women. In the present study,

most of the phyllodes tumour (57.8%) were benign phyllodes, 36.8 % cases were borderline phyllodes and 5.4% cases were malignant phyllodes.

Phyllodes tumour are characterized by expansion and increased cellularity of the stromal component. In some Phyllodes tumour stromal cellularity is denser in the periductal stroma near the epithelial components. Mitotic activity also tends to be accentuated in this distribution.

Stromal over growth has been defined as absence of an epithelial component in at least one microscopic field at 40x total magnification (10x ocular objective and 4x microscopic lens objective). It is more common in high-grade malignant PTs, but can also occur in low-grade (borderline) PTs. The tumors arise from periductal rather than intralobular stroma and usually contain only sparse lobular elements. Most PTs have a heterogeneous histologic appearance<sup>[3]</sup>.

Lee et al defined the stromal cellularity as mild increase in atleast 50% of the stroma in phyllodes tumour compared to typical fibroadenoma, stromal overgrowth with no epithelium. Subepithelial condensation of stromal cells is best predictors of phyllodes tumour<sup>[12]</sup>.

PTs have been a subject of intense investigation by IHC to identify markers that could be predictive of local, regional recurrence, the likelihood that the recurrent lesion will be higher grade and the propensity to develop distant metastases. The expression of some antigens has been found to correlate with grade and/or recurrence. or with neither, and different studies have sometimes reported different findings<sup>[3]</sup>.

Chia et al evaluated the expression of a panel of CKs (CK7, CK14, AE1:3, and CAM5.2) in the stromal component of PTs. CK7 showed focal patchy positivity in 1% to 5% of stromal cells. The CK positive cells appeared to be equally distributed in subepithelial and peripheral areas<sup>[13]</sup>.

## Conclusion

The commonest fibroepithelial tumour in a female breast is fibroadenoma, in the present study with



the most common age group affected is 11-20 years. young women usually present with a palpable mass and older women with a mammographic density. Excision done in most of the cases. Phyllodes tumours are rare tumours of breast, majority are detected as palpable mass, but a few found by mammography. Most PTs behave in a benign fashion, with local recurrences. Very rarely (about 2% or less overall), the tumour may metastasize, mainly in the cases of tumours of malignant grade.

Histological grading of phyllodes tumours helps to achieve a correct diagnosis. Intracanalicular type of fibroadenoma and juvenile fibroadenoma should be differentiated properly from benign phyllodes for proper management of the patient and to prevent recurrence. Cellular fibroadenoma is very difficult to differentiate from benign phyllodes, sharing same histological features, with both possessing a low potential for local recurrences.

#### Limitations

- 1) Since this study was done in a tertiary care centre and the study period is only last 2 years; a better conclusive opinion is possible from a study of a larger sample of long duration.
- 2) Only excision biopsy sample and mastectomy specimens were included in the diagnosis.
- 3) Immunohistochemical marker study to differentiate grading of phyllodes tumours could not be done due to financial constraints.

**Conflict of interest:** Nil

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