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Ultrasound Lexicon in diagnosis and management of breast fibroadenoma: when to follow up and when to biopsy

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Abstract

Background: To detect the accuracy of breast ultrasound in diagnosis of fibroadenoma and differentiate between typical and atypical ones. The impact of ultrasound criteria on patient management. (Biopsy versus follow up). A prospective study were done to 71 patients. Diagnosis was reached either by performing follow up study or after revision of core biopsy/surgical specimens.

Results: In our study, we had 35 ultrasound detected atypical fibroadenoma, seven out of the 35 (20 %) proven to be complex fibroadenoma by pathology while in another 20 patients, 36 fibroadenomas with typical criteria were detected by both ultrasound and regular follow up. The most ultrasound features which showed statistical significance were the posterior shadowing feature (100% atypical versus 25% typical with significant p value < 0.01), and vessel arrangement (85.7% versus 0% have central arrangement with significant p value < 0.01) helped to differentiate between simple and complex ones. We calculate the sensitivity, specificity, PPV, and NPV to be 100%, 74%, 46%, and 100%.

Conclusion: Arrangement of vessels and posterior features are the most important criteria to differentiate simple and complex FAD.

Keywords: Ultrasound, Fibroadenoma, Typical, Atypical, Biopsy

Background

Fibroadenomas (FAD) are mostly benign tumors consisted of both epithelial and stroma contents. They are usually noticed in young-aged women [1].

Those who are obese or gained weight (20–3 kg) within 18 years showed high risk of appearance of fibroadenoma. As well as severe stress may increase the risk as endogenous level of estrogen increased also. Fibroadenomata have an inverse relationship with increasing age [2].

It is the most seen benign tumor in the breast in young women. Women usually presented with a mass which is firm and mobile. Fibroadenomata are known to be hormonally sensitive as they usually enlarged with pregnancy and lactation due to rising of hormones. Fibroadenomata may undergo infarction during pregnancy as it outgrew its blood supply presenting with painful mass in women [3].

Ultrasound detects fibroadenomata and often presents as oval-shaped lesion with their width is larger than their anteroposterior diameter, associate with gentle lobulations which are fewer than four, their margins are circumscribed with homogenous echogenicity ranging from isoechoic to hypoechoic tissue pattern associated with thin echogenic capsule indicating benign lesion, while the surrounding vague echogenicity indicates malignancy [4].

So the occurrence of any non-classical appearance places the lesion in Breast Imaging-Reporting and Data System (BI-RADS) category 4a or higher and that may require a biopsy to rule out malignancy:

1. The presence of angular or irregular margins.
2. Three or more lobulations or microlobulations.
3. Acoustic shadowing resulted from calcifications [5].

Old patients with median age of 47 years often present with complex fibroadenomata while the simple fibroadenoma usually occurred in patients with median age of 28.5 years and

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often smaller in size. Breast cancer risk increases in patients with complex fibroadenomas than the classical ones [6].

The American Society of Breast Surgeons guideline indicates that the best diagnostic procedure choice for US-visible lesions is ultrasound-guided core needle biopsy and those which are superficial in location can be easily excised by minimally invasive ablation techniques which are divided into:

These techniques can be divided into:

High-intensity focused ultrasound (HIFU)
Laser ablation
Cryoablation
Vacuum assisted biopsy [4]

Aim of work
The objective of this study is to detect the accuracy of breast ultrasound in diagnosis of fibroadenoma and differentiate between typical and atypical ones.

Methods
The study was a cross-sectional comparative study which included 52 patients referred to the Radiology Department, in the period between July 2016 and March 2017. The study was approved by the Editorial Review Board of the Radiology Department.

Inclusion criteria
Inclusion criteria includes female patients complaining of breast mass or pain.

Exclusion criteria
All other breast masses with typical criteria for being simple cysts, lipomas, carcinomas, postoperative cases, and recurrent lesions.

Methodology in details
Female patients' candidate for breast ultrasound.

Ultrasound examination
Ultrasound examination was performed for all cases by 8–12 MHz linear array transducer (General Electric (GE), Logic 7 machine).

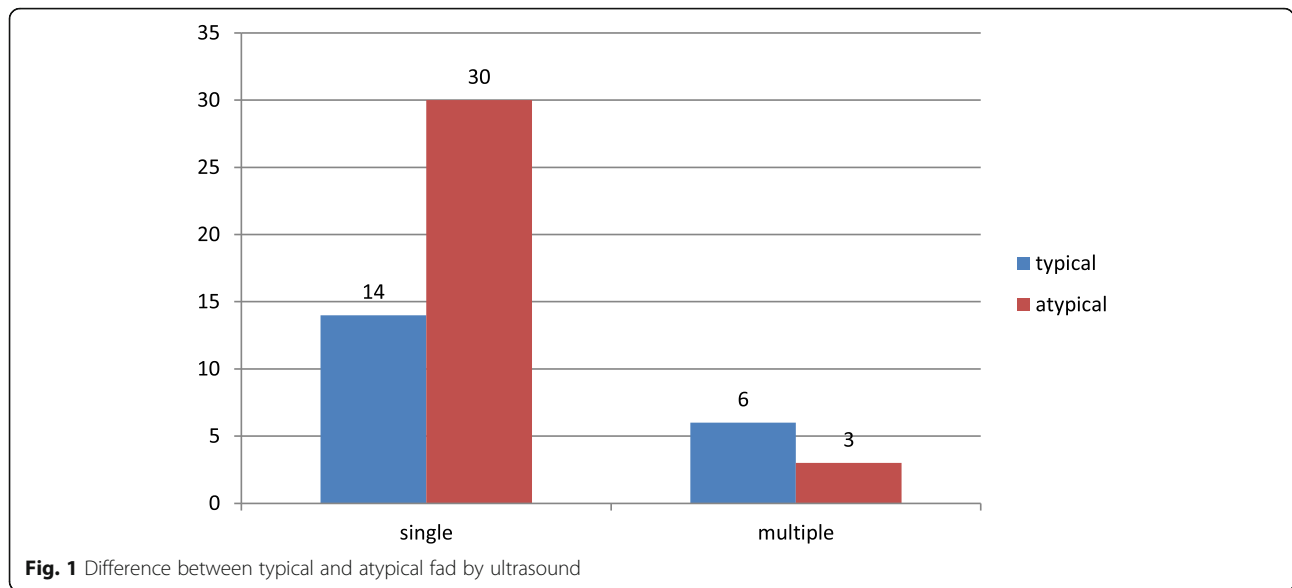We used sector probe 3–5 MHz in large masses.

Survey systematic scanning in radial, sagittal, and transverse planes and in other planes whenever necessary. The mass was scanned in both longitudinal and transverse planes to obtain three diameters.

The US lexicon includes morphologic features of solid breast masses according to ACR 2013 (Table 1).

The size of the tumor was determined on US to be its maximum diameter measured in any imaging plane. Color Doppler US was used; the color box had been determined to

Table 1 Ultrasound breast imaging Lexicon

Ultrasound Lexicon		
Breast composition	a. homogeneous - fat b. homogeneous - fibroglandular c. heterogeneous	
Mass	shape	oval - round - irregular
	margin	Circumscribed **or** Not-circumscribed: indistinct, angular, microlobulated, spiculated
	orientation	parallel - not parallel
	echo pattern	anechoic - hyperechoic - complex cystic/solid hypoechoic - isoechoic - heterogeneous
	posterior features	no features - enhancement - shadowing - combined pattern
Calcifications	in mass - outside mass - intraductal	
Associated features	architectural distortion - duct changes - skin thickening - skin retraction - edema - vascularity (absent, internal, rim) - elasticity	
Special cases *(cases with a unique diagnosis)*	simple cyst - clustered microcysts - complicated cyst - mass in or on skin - foreign body (including implants) - intramammary lymph node - AVM - Mondor disease - postsurgical fluid collection - fat necrosis	

Zonderland and Smithuis 2014 [7]

Fig. 1 Difference between typical and atypical fad by ultrasound

include the target lesion and minimal normal surrounding breast tissue. The color gain had been adjusted to a level that could detect low-velocity vascular flow in target lesion with minimal background noise. Color Doppler images had been obtained to reveal the maximum amount of vascular flow at the target lesion. We depend on number of vessels and their arrangement rather than indices.

Ultrasound guided core

Biopsies of the breast were performed in indicated cases using 14-gauge needle. Multiple core biopsies from 4 to 6 were taken from different part of lesions.

Patients were categorized into two groups according to ultrasound criteria:

Group I Twenty patients had 36 fibroadenomas with typical benign criteria on ultrasound; six of them underwent excisional biopsy and proved to be typical, the other 14 patients were followed up for 3, 6, and 12 months either prospective or retrospective according to time of presentation and showed stationary course. The mean age of this group was (22 ± 5.3) and range (18–35) years.

Group II Thirty two patients had 35 atypical fibroadenomas age range (19–41) years and their mean age 28.8 with atypical ultrasound criteria.

Statistical analysis

For statistical analysis, comparison between categorical data was performed using Chi-square test.

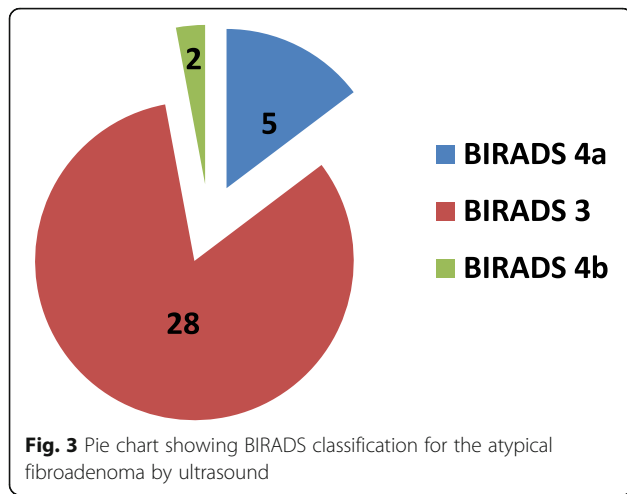**Fig. 2** Pie chart representing distribution of fibroadenomas in breast quadrants
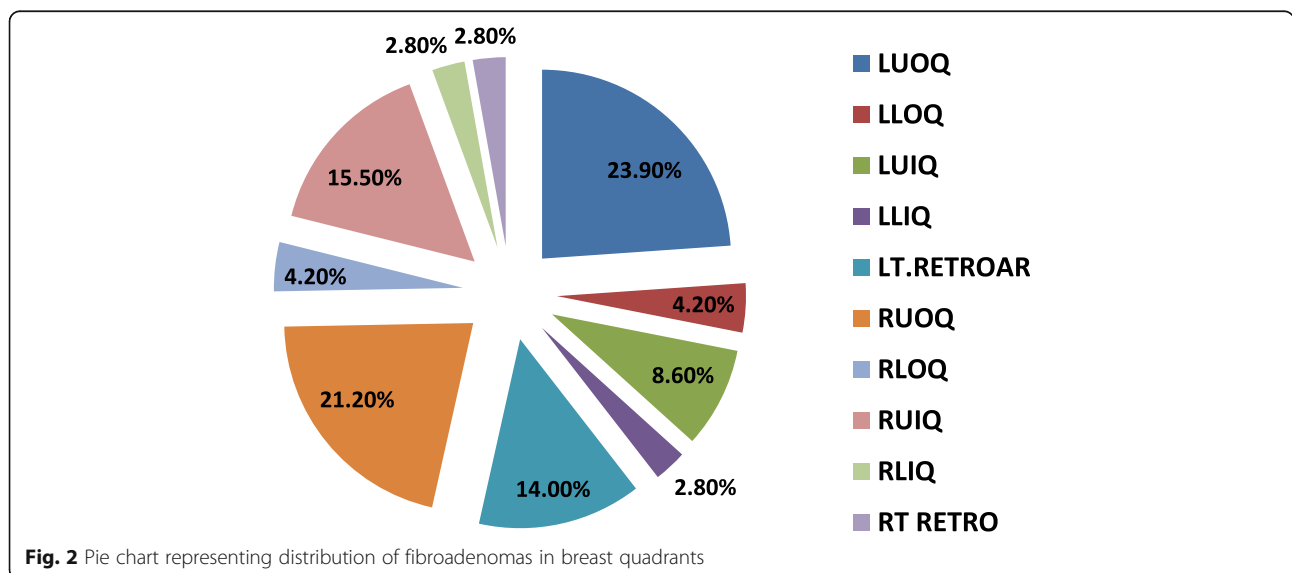
Fig. 3 Pie chart showing BIRADS classification for the atypical fibroadenoma by ultrasound

Imaging findings identified on ultrasound were reported and their frequencies were calculated. The diagnoses (whether benign or suspicious criteria) were postulated according to ultrasound findings were then correlated with the pathological diagnosis versus follow up. In reference to this accuracy, measures were then calculated for ultrasound, namely sensitivity, specificity, positive, and negative predictive values.

Diagnostic indices

$$*Sensitivity = \frac{Number\ of\ true\ positive\ results\ (TP)}{(Number\ of\ true\ positive\ results\ (TP) + Number\ of\ false\ negative\ results(FN)} \times 100$$

$$*Specificity = \frac{Number\ of\ true\ negative\ results\ (TN)}{(Number\ of\ true\ negative\ results\ (TN) + Number\ of\ false\ positive\ results\ (FP)} \times 100$$

$$*Positive\ predictive\ value = TP/(TP + FP)\ x100$$

$$*Negative\ predictive\ value = TN/(TN + FN)\ x100$$

Descriptive and comparative analysis

- Cases which are diagnosed as typical fibroadenoma by ultrasound and proved to be typical fibroadenoma in final diagnosis either by histopathology or follow up were considered as true negative cases ($N = 20$).

- Cases which are diagnosed as atypical fibroadenoma by ultrasound and proved to be atypical fibroadenoma in final diagnosis by histopathology were considered as true positive cases ($N = 6$).

- Cases which are diagnosed as typical fibroadenoma by ultrasound and proved to be atypical fibroadenoma in final diagnosis by histopathology were considered as false negative cases ($N = 0$).
- Cases which are diagnosed as atypical fibroadenoma by ultrasound and proved to be typical fibroadenoma in final diagnosis either by aspiration cytology, histopathology were considered as false positive cases ($N = 7$)

Results
Demographic data
The study included 52 patients (71 Fibroadenomas); their age ranged from 18 to 41 years. The patients were complaining of breast masses, breast pain, or cases with breast masses coming for follow up (Figs. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, and 14).

- The age range for those showing atypical criteria of fibroadenoma on US is (19–41) years and mean is 28.8 ± 7.4.

- The age range for those with typical criteria of fibroadenoma on US is (18–35) years and mean is 22.5 ± 5.3 (Table 2).

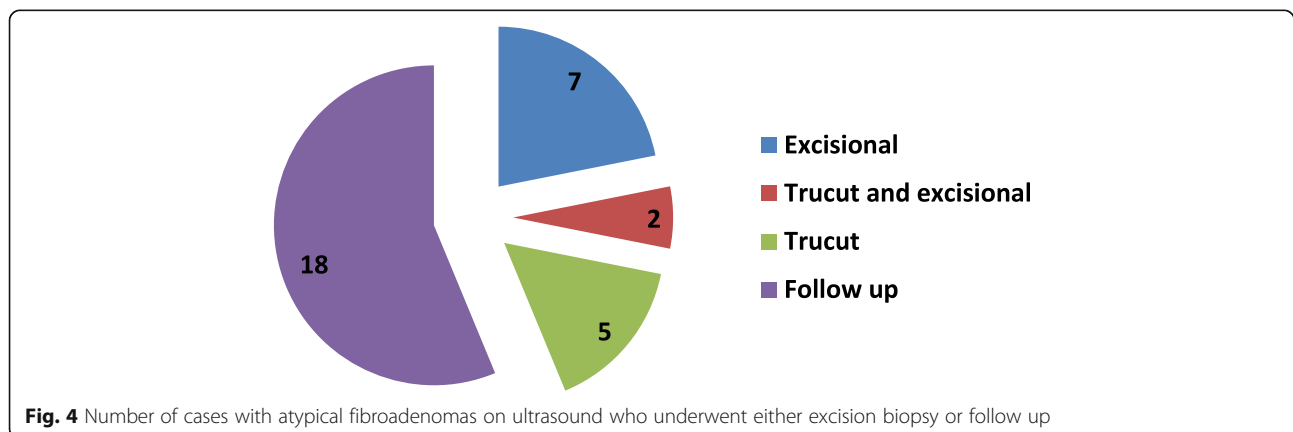- There were six pregnant patients (11.3%) in our study, and their age range is (24–27).

Fig. 4 Number of cases with atypical fibroadenomas on ultrasound who underwent either excision biopsy or follow up
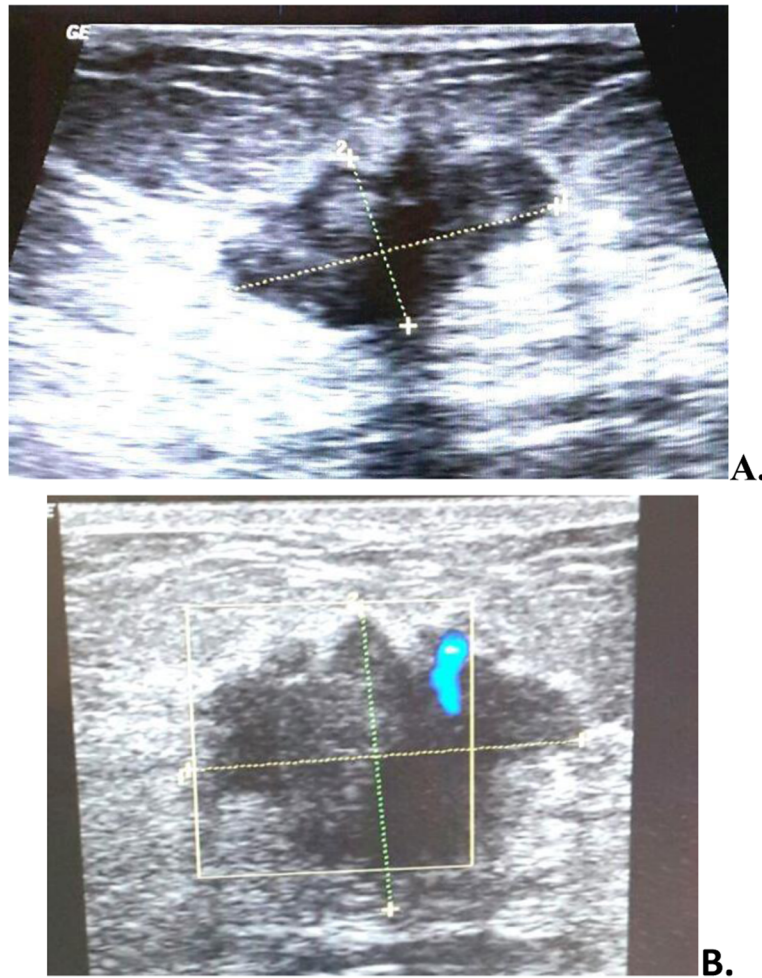
Fig. 5 Female patient 36 years old presented with mass in right upper breast quadrant. **a** Ultrasound shows an oval hypoechoic mass, measuring 2.7 × 2 cm with angulated border and lobulation, parallel to skin surface showing posterior shadowing and no vascularity by colour Doppler. It was proven to be complex fibroadenoma by core biopsy. She came for follow up after 6 months. **b** The mass increased in size than the previous exam, it was irregular in shape, heterogeneous echogenicity, with speculated border showing vascularity by colour Doppler and not parallel to skin surface. By biopsy, it was proven to be malignant.

Patients were categorized into two groups according to ultrasound criteria:

Group I

Twenty patients had 36 fibroadenomas with typical benign criteria on ultrasound; six of them underwent excisional biopsy and proved to be typical, the other 14 patients were followed up for 3, 6, and 12 months either prospective or retrospective according to time of presentation and showed stationary course. The mean age of this group is (22 ± 5.3) and range is (18–35) years.

Group II

Thirty-two patients had 35 atypical fibroadenomas with age range of (19–41) years and their mean age is 28.8 with atypical ultrasound criteria including, e.g.,

- Orientation: (one case not parallel).

- Margins: angular margin (five cases), irregular (three cases), lobulations > 3(two cases), and one case with microlobulations.

- Posterior features: shadowing due to calcification or hyperechoic masses with posterior shadowing (five cases) and posterior enhancement (100% atypical versus 25% typical).

- Vascularity: increased vascularity (four cases).

- Vessel arrangement: central (eight cases) and both central and peripheral (ten cases) (Table 3).

- Nine patients had multiple fibroadenomas and 43 patients had single one. Multiplicity was more with typical fibroadenoma.
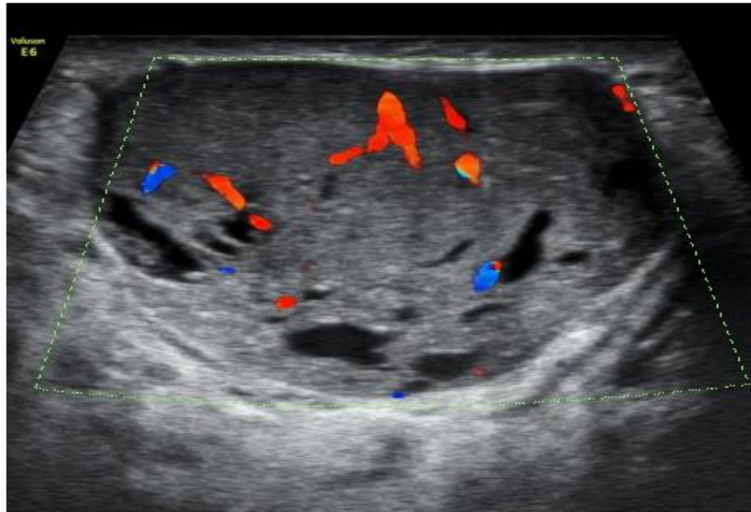
Fig. 6 Pregnant female 26 years old presented with mass in the left breast. Ultrasound shows an oval mass with mixed echogenicity smooth border, measuring 4.5 × 2.7 cm at upper quadrant parallel to skin surface showing cystic degeneration and high vascularity by colour Doppler But maintaining normal arborization (Benign pattern normal with pregnancy (BIRADS 3). On follow up, it remains stationary course

- We had 38 FAD at left breast and 33 FAD at right breast. Fibroadenoma was more at LUOQ.

We had 38 FAD at left breast as follows:

UOQ : N = 17/71

LOQ : N = 3/71

UIQ : N = 6/71

LIQ : N = 2/71

Retroareolar : N = 10/71

Thirty-three FAD at right breast as follows:

UOQ : N = 15/71

UIQ : N = 11/71

LOQ : N = 3/71

LIQ : N = 2/71

Retroareolar : N = 2/71

Diagnosis was reached either by performing follow up study prospective or retrospective in 32 cases or after re-vision of core biopsy/surgical specimens 20 cases.

Thirty-two cases with atypical criteria by ultrasound were categorized according to ultrasound BIRADS. (Five patients were categorized as BIRADS 4a, two patients BIRADS 4b, and 28 patients BIRADS 3).

- Complex fibroadenomas (five of the seven complex FADs (71.4%) show higher *BIRADS* (4a or 4b) than simple ones (2 0R 3)).

- Seven of them underwent excisional biopsy, five trucut biopsy, two trucut followed by excisional biopsy, and 18 were followed up 3, 6, and 12 months showing no changes.

- From the 32 patients having atypical criteria by US, six patients (seven fibroadenomas) proved to be complex fibroadenoma by pathology; their mean age was (35.66 ± 6.37) and range (23–41). The mean size of the mass (2.3 ± 1.29), while the other 26 patients who proved to be typical fibroadenoma their age was (26.5 ± 5.3), range (19–39), and mean size of the masses (1.8 cm), so complex FAD appears to be larger in size than typical FAD and also it occurs in older age. However, there was no significant difference regarding the mean age between the groups as well as size ($p > 0.05$) (Table 4).

- Shape: Rounded or irregular border is insignificant in differentiation complex from typical fibroadenoma (Table 5).

- Most simple and complex fibroadenomas presented with a parallel orientation to the skin surface (71.4% versus 92.9% with significant *p* value < 0.01) (Table 6).

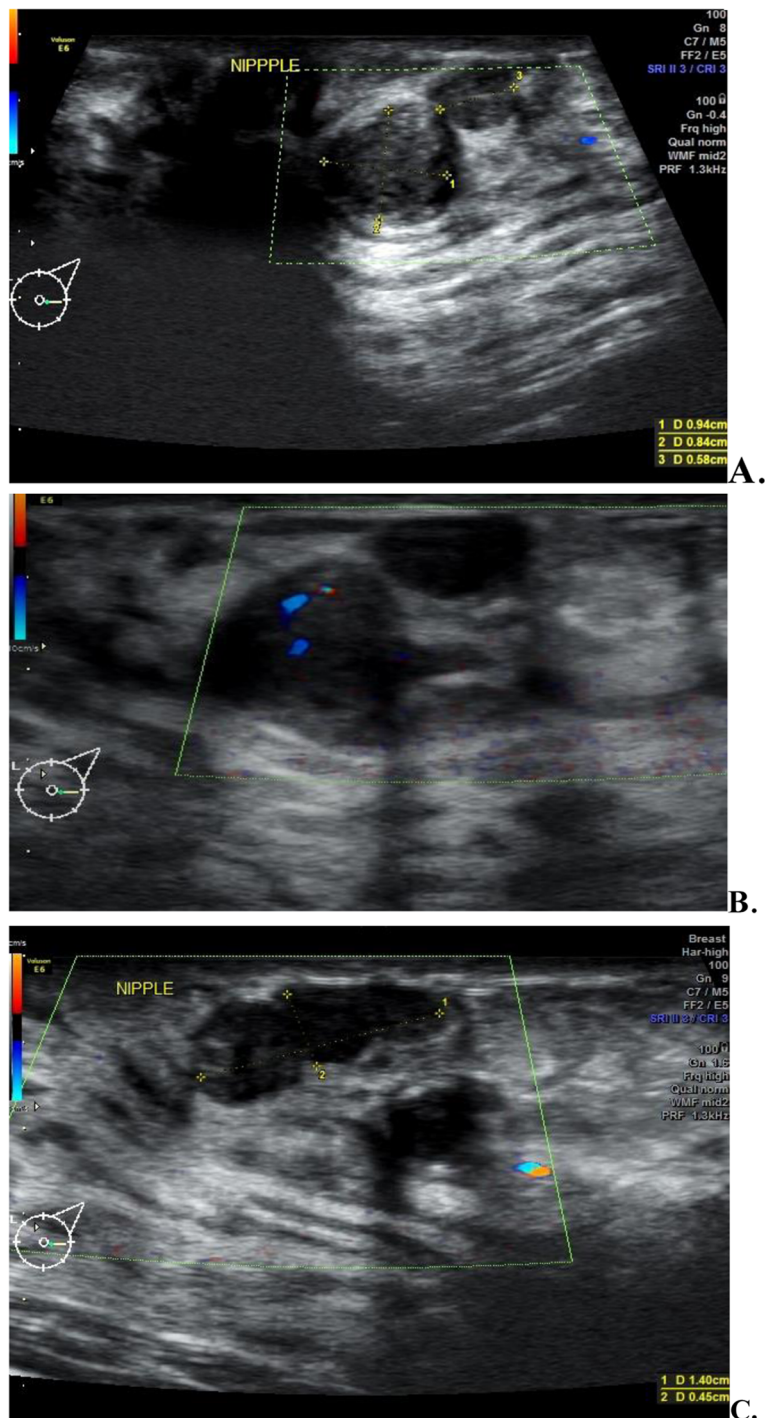- Complex fibroadenomas presented more frequently with uncircumscribed borders than typical ones

Fig. 7 Female patient 23 years old presented with two left breast masses. **a** Ultrasound shows two isoechoic lobulated masses retro areolar at 3 o'clock Lesion measures 10 × 9 mm, globular in shape, and likely ductal in extension. **b** Colour Doppler showing vascularity, no architectural distortion, or calcifications. **c** The other shows lobulated out line, measuring 1.4 × 0.5 cm, showing no vascularity on colour Doppler. (BIRADS 4A) .Excisional biopsy revealed fibroadenoma with fibrocystic changes and focal floroidepitheliosis
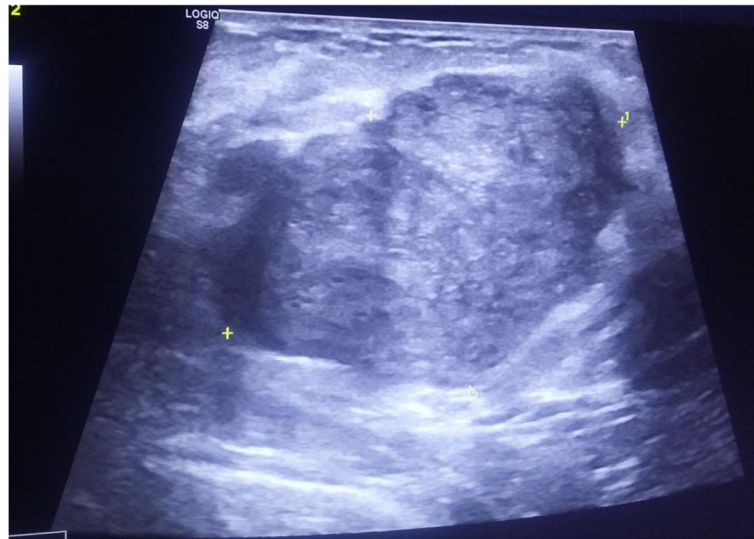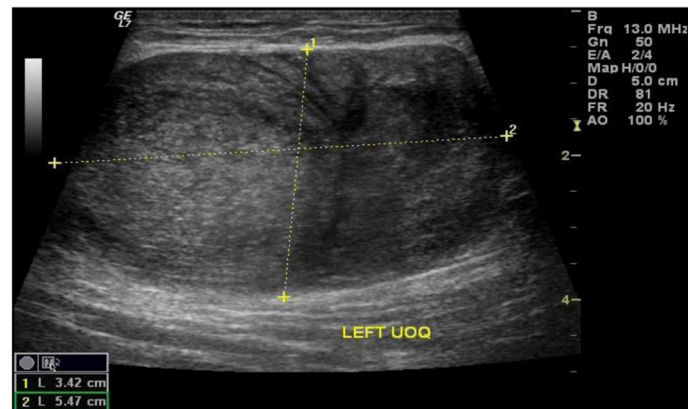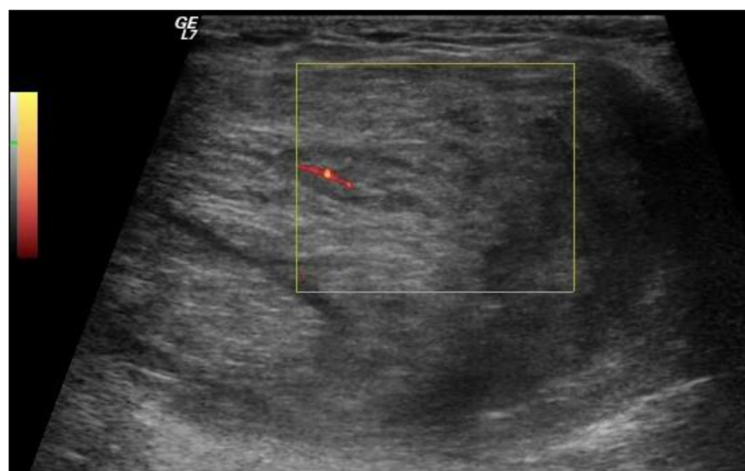
Fig. 8 Twenty-year-old female complained of left breast mass. Ultrasound shows oval mass measuring 5.5 × 4 cm with angulated border, heterogeneous echogenicity, showing calcifications inside at LUOQ. Excisional biopsy was done and proved to be typical fibroadenoma
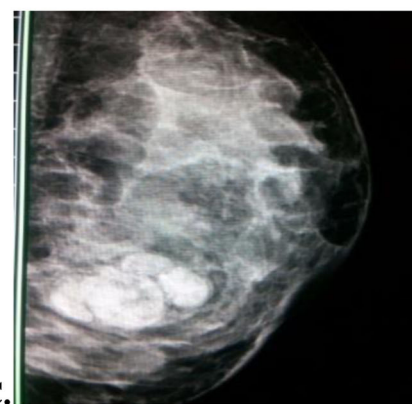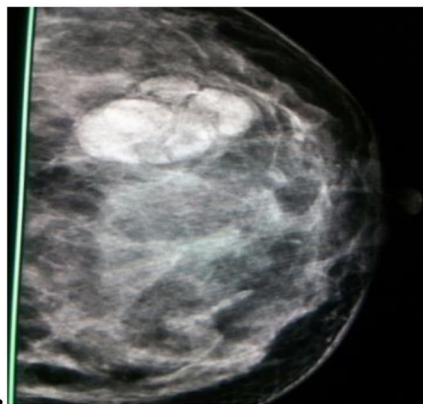

Fig. 9 Female 27 years old presented with palpable lump on left breast. **a** Gray scale ultrasound shows An oval-shaped mass, isoechoic with lobulated border at LUOQ measuring 5.5 × 3.4 cm, parallel to skin surface (BIRADS 3). **b** Colour Doppler shows mild vascularity. It is proven to be typical fibroadenoma

Fig. 10 Female 35 years old presented with left breast lump. Ultrasound shows **a** rather well-defined oval mass of mixed echogenecity at 4 o' clock measuring 3.6 × 2.1 cm casting posterior shadowing, showing no vascularity by colour Doppler. **b** Craniocaudal (CC). **c** Mediolateral (ML). It shows rounded macrolobulated high-density lesion in lower outer quadrant. It is proven to be typical fibroadenoma
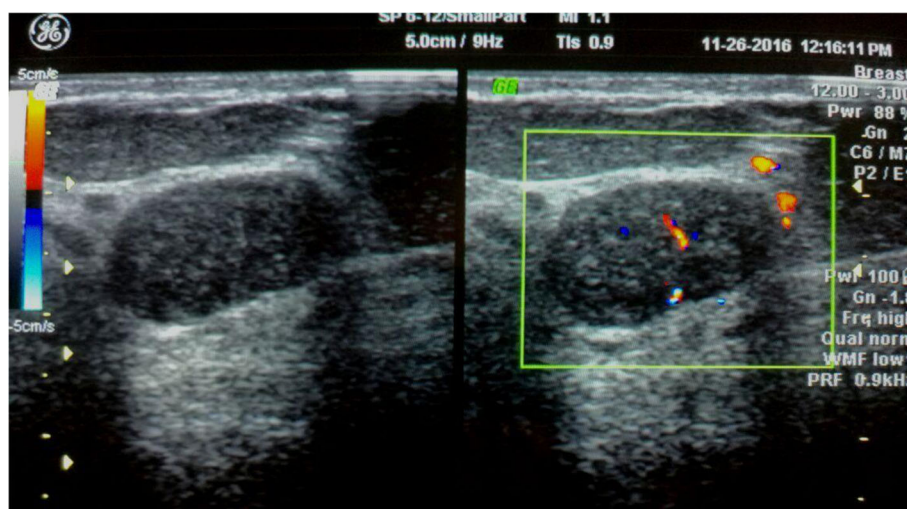

Fig. 11 Female 35 years old presented with right breast lump. US shows a well-defined oval mass measuring 1.6 × 1 cm, isoechoic with central vascularity showing cystic degeneration and posterior enhancement with edge shadowing. By biopsy, it was proved to be complex fibroadenoma
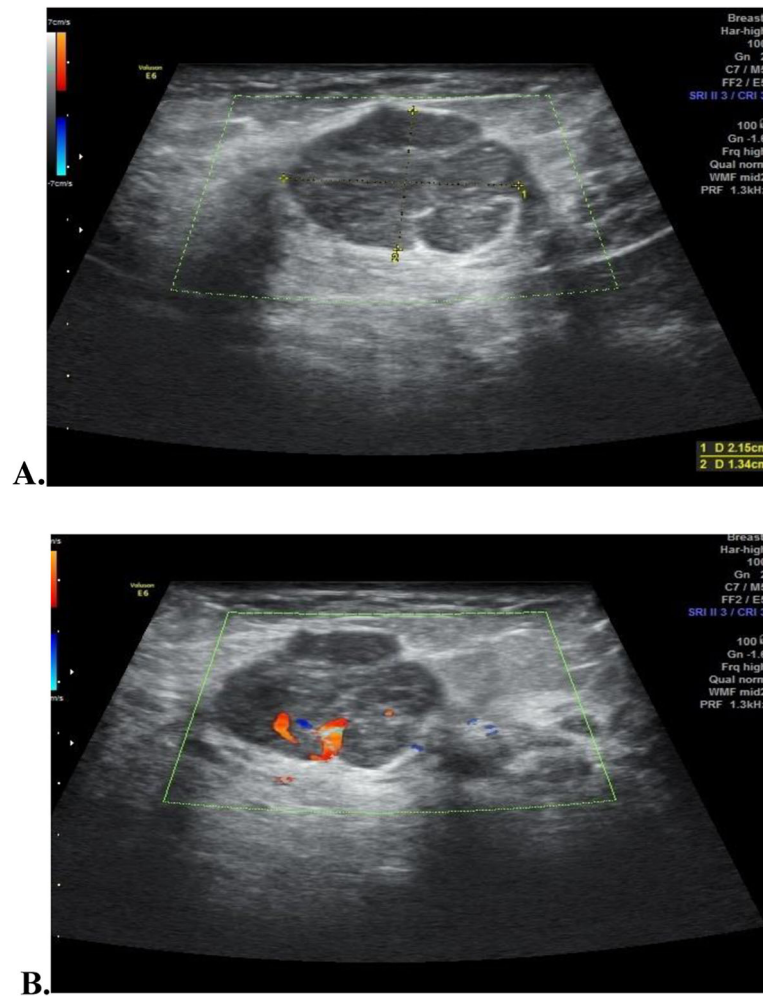
Fig. 12 Twenty-five-year-old female presented with right breast lump. **a** Ultrasound shows oval isoechoic, macrolobulated mass at right breast at 8 o'clock measuring 2.1 × 1.3 cm showing posterior enhancement with edge shadowing. **b** Colour Doppler shows vascularity (mild peripheral and few central). The lesion was proved to be typical fibroadenoma by biopsy

(57.2% versus 28.6%, with no significant *p* value) (Table 7).

- Also complex fibroadenomas showed more posterior enhancement than typical ones (100% versus 25% with significant *p* value < 0.01) (Table 8).

- Complex fibroadenomas present more isoechoic 57.2% than simple one (57.2% versus 35.7%, with no significant *p* value), also typical FAD present more with mixed echogenecity (42.9% versus 42.8%) (Table 9).

- Regarding colour Doppler, complex fibroadenomas showed more frequently central vessels arrangement (85.7% versus 0 %, *p* < 0.01) but with fewer vascularity (Table 10).

- Complex fibroadenoma presents more with cystic degeneration than typical one (43% versus 10.7% with no significant *p* value) (Table 11).

- Also complex fibroadenomas show associated findings as fibrocystic changes more than simple ones (57.1% versus 7.1% with no significant *p* values). Five patients with atypical FAD by ultrasound have associated fibrocystic changes (three of which proved to be complex FAD and two proved to be typical ones), and one has ductal extension (proved to be complex) (Table 12).

- Patients with (BI-RADS category 4) underwent exicisonal biopsy or trucut needle biopsy (seven
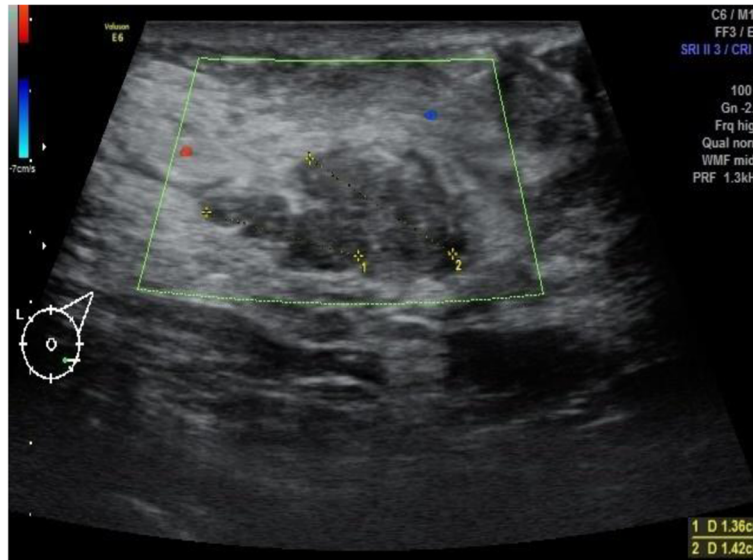
Fig. 13 Twenty-five-year-old female presented with left breast mass. Ultrasound shows an oval isoechoic mass at 4 o'clock measuring 1.4 × 1.4 cm, its border shows angulation, no vascularity on colour Doppler .On follow up, the mass remains stationary course

cases); however, some patients with (BI-RADS category 3) underwent exicisonal biopsy or trucut needle biopsy (seven cases); others preferred to follow up (21 cases).

- One case was pathologically proved complex FAD (1/7) by core biopsy and on follow up after 6 months, it showed malignant criteria and excision was done (invasive ductal carcinoma).
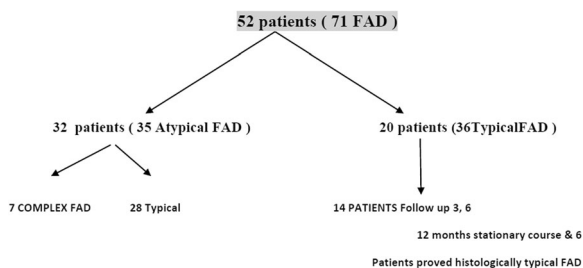
- Six pregnant females with age range (24–27), mean (21 ± 1), and mean size (2.6 ± 1.9) cm showed atypical criteria as follows:

Echogenecity: Two isoechoic with cystic changes, three mixed echogenecity, and one hyperechoic with cystic changes.

Border: One of them shows micro lobulation, one macrolobulated, and other four are well defined borders.

Vascularity: Much vascularity (one case), other five cases show few vascularity.

Vessel arrangement: Central and peripheral vascularity (five cases).

- Four of them followed up after giving birth and the fibroadenomas remain stationary in size, while two underwent trucut biopsy and it was proven to be typical FAD.

Discussion

The presence of a breast lump is often a reason of great concern. With the recent advances in the technology of ultrasound in the last 20 years, ultrasound could easily differentiate between malignant and benign breast lesions [8].

Radiologists should be aware with different breast benign lesions to be able to distinguish them from the malignant ones. Fibroadenomata are known to be benign tumors composed of stromal as well epithelial components [1].

US is considered to be the best imaging modality in patients younger than 30 years old and pregnant women, as it carried no risk of exposure to radiation, providing imaging-guided biopsy if needed and allowing safe follow up method [4].

Fibroadenomata are known to be the most seen benign tumor in adolescent girls and young-aged patients usually raised from both stroma and epithelium of terminal
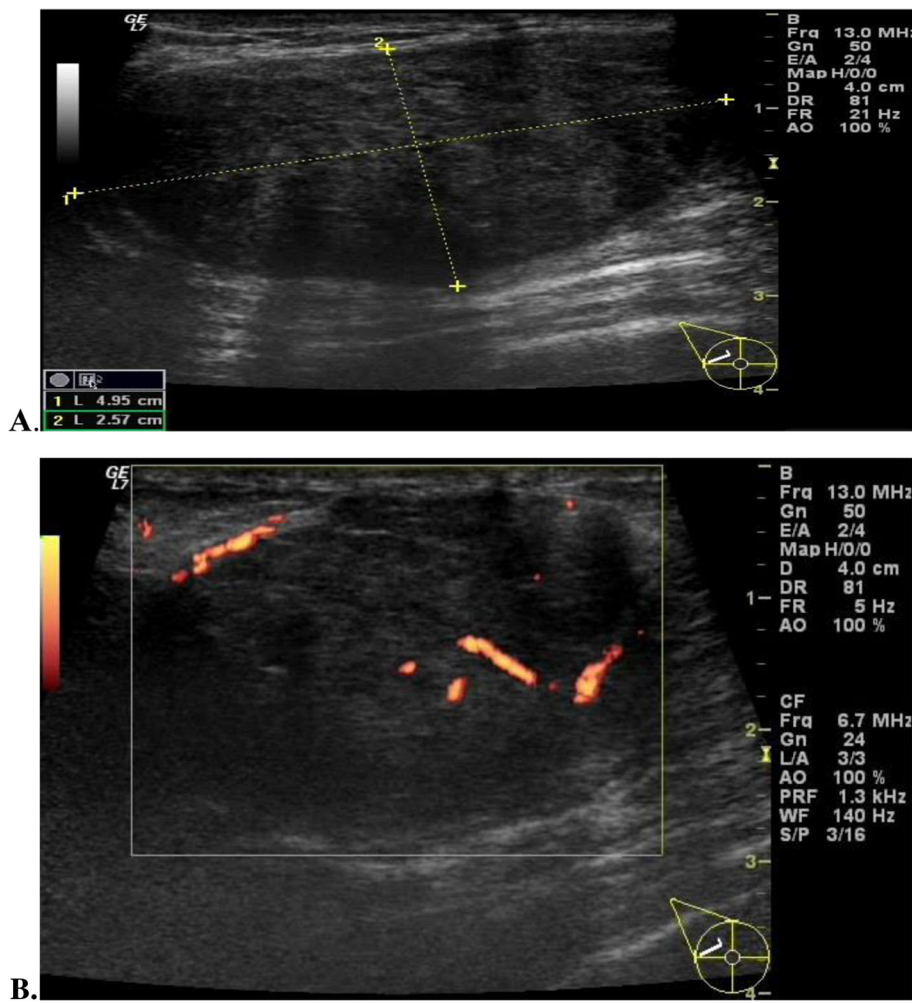
Fig. 14 Twenty-nine-year-old female presented with right breast mass. **a** Gray scale ultrasound shows an oval well-defined isoechoic mass measuring 5 × 2.6 cm. **b** Color Doppler shows central and peripheral vascularity. On follow up, the mass remains stationary in course

duct-lobular unit which are of two types both intracanalicular and pericanalicular [7].

The term of complex fibroadenoma referred to the presence of cystic changes with the cysts were more than 3 mm as well as sclerosing adenosis, epithelial apocrine changes, and epithelial calcifications [6].

So the BI-RADS US descriptors of solid breast lesions included margin, shape, lesion boundary, orientation, posterior acoustic features, and internal echo pattern [9].

As the varied management of complex fibroadenomata depended upon differentiation between complex and simple ones, so imaging characteristic of both is worthwhile [9].

Table 2 Patient age correlated with ultrasound findings

	Range	Mean ± SD
Typical	18–35	22.5 ± 5.3
Atypical	19–41	28.8 ± 7.4

In this study, we discussed the accuracy of breast ultrasound in diagnosis of fibroadenoma and differentiate between typical and atypical ones and assess the impact of imaging by ultrasound on patient management (biopsy versus follow up). The diagnoses (whether benign or suspicious criteria) were postulated according to ultrasound. Findings were then correlated with the pathological diagnosis versus follow up.

We had two groups of patients:

Group I is composed of 20 patients with 36 typical fibroadenomas showing typical criteria by ultrasound and by follow up showing stationary course.

Peek et al 2015 (10) stated that up to 59% of FAD showed regression or complete resolution within 5 years. Also, Lee and Soltanian in 2015 stated that 10–40% of fibroadenomas spontaneously regress. But in our study, the 36 typical fibroadenomata showed stationary course throughout their follow up [7].

Table 3 Difference between typical and atypical FAD by ultrasound

Sonographic features	Typical FAD	Atypical FAD
Grey scale imaging	N = 36	N = 35
A. Shape		
Oval	33 (91.7%)	32 (91.4%)
Round to irregular	3 (8.3%)	3 (8.6%)
B. Border		
Well circumscribed/(lobulated < 3)	36 (100%)	24 (68.6%)
Lobulated (> 3)	0	2 (5.7%)
Angular	0	5 (14.3%)
Irregular	0	3 (8.6%)
Microlobulations	0	1 (2.8%)
C. Echogenecity		
Iso	26 (72.2%)	14 (40%)
Mixed	9 (25%)	16 (45.7%)
Hypo	1 (2.8%)	3 (8.6%)
Hyper	0	2 (5.7%)
D. Orientation		
Wider than taller	36 (100%)	31 (88.6%)
Deeper more than wider	0	4 (11.4%)
E. Posterior acoustic features		
None	26 (72.2%)	16 (45.7%)
Enhancement	8 (22.2%)	14 (40%)
Shadowing	2 (5.6%)	5 (14.3%)
F. Arrangement of vessels		
Central	0	7 (20%)
Peripheral	7 (19.4%)	9 (25.7%)
Both	0	10 (28.6%)
No	29 (80.6%)	9 (25.7%)
G. Vascularity		
Few	7 (19.4%)	23 (65.7%)
Much		3 (8.6%)
No	29 (80.6%)	9 (25.7%)
H. Associated findings		
Yes	1 (2.8%)	6 (17.1%)
No	35 (97.2%)	29 (82.9%)

Table 4 Mean size and age of typical and complex FAD

	Typical FAD	Complex FAD	p value
Mean size	1.8 cm	2.3 cm	> 0.05
Mean age	26.5 ± 5.3	35.66 ± 6.37	> 0.05

Table 5 Comparison between typical and complex FAD regarding shape

Shape	Complex FAD proven by biopsy	Typical FAD proven by biopsy/follow up	p value
Oval	5 (71.4%)	26 (92.9%)	< 0.01
Round to irregular	2 (28.6%)	2 (7.1%)	> 0.05

Ultrasound features of typical fibroadenomas as reported by Kovatcheva et el. 2015 were isoechoic or hypoechoic to fat, oval, or rounded well-defined masses, macrolobulated outline homogenous or heterogeneous internal echotexture, thin echogenic capsule and finely color Doppler showed avascular or low vascular mass [4].

In our study, typical fibroadenomas features were coinciding with the previously forementioned features. Further, 91.6% of the typical FAD were oval in shape, 86.1% showed well-defined borders, 91.6% showed large width than their antero posterior diameter, with homogenous internal echogenicity in about 72.2%, and those with heterogeneous echogenicity were due to either the presence of calcification or cystic degenerations.

Peek et al. 2015 stated that up to 59% of FAD showed complete regression within 5 years [10]. Gordon et al. in 2003 reported that fibroadenomata volume might increase up to 16% in a month in younger women than 50 years, and up to 13% per month in women above 50 years and finally up to 20% in the maximal dimension over 6 months for women of all ages [11]. In our study, the followed up typical fibroadenomas cases show a stationary course throughout the 6-months follow up times.

Group II in our study, 35 fibroadenomata, had atypical criteria by ultrasound; seven were proven to be complex fibroadenomas by pathology. Their ages range from 23 to 41 and mean size (2.3 ± 1.29), while the age of the other patients with typical fibroadenomas (28 typical FAD) ranges from 19 to 39, mean size (1.8 cm).

Lee et al. 2015 reported that the mean age of the 64 patients with complex FA was 40 years (range, 22–66 years) and mean size 1.44 cm, range (0.5–7 cm) were larger than the simple FAs (mean, 1.21 cm; range, 0.6–8 cm), but the difference was not statistically significant [12].

According to Pinto et al. 2014, the mean age of complex fibroadenoma group was 42 years (range, 22–70 years) and mean size 1.9 cm, which were larger than simple fibroadenomas mean size (1.9 versus 1.3 cm) coinciding with our study [9].

Table 6 Comparison between typical and complex FAD regarding orientation

Orientation	Complex FAD proven by biopsy	Typical FAD proven by biopsy/follow up	p value
Wider than deeper	5 (71.4%)	26 (92.9%)	< 0.01
Deeper than wider	2 (28.6%)	2 (7.1%)	> 0.05

Table 7 Comparison between typical and complex FAD regarding borders

Borders	Complex FAD proven by biopsy	Typical FAD proven by biopsy/follow up	p value
Well circumscribed	3 (42.8%)	20 (71.4%)	< 0.01
Lobulated (> 3)	2 (28.6%)	_	> 0.05
Angular	2 (28.6%)	3 (10.7%)	> 0.05
Irregular	–	3 (10.7%)	> 0.05
Microlobulations	–	2 (7.2%)	> 0.05

Table 9 Comparison between typical and complex FAD regarding echogenecity

Echogenecity	Complex FAD proven by biopsy	Typical FAD proven by biopsy/follow up	p value
Iso	4 (57.2%)	10 (35.7%)	> 0.05
Mixed	3 (42.8%)	12 (42.9%)	0.02
Hypo	–	4 (14.2%)	0.04
Hyper	–	2 (7.2%)	> 0.05

Gogoi and Borgohain in 2015 stated that complex fibroadenoma occurred in older patients (median age 47 years) compared to simple fibroadenoma (median age 28.5 years) and often it was smaller in size (1.3 cm average diameter) [6].

Also, Kuijper A et al. in 2001 reported that CF were smaller than simple fibroadenomas and measures on average 1.3 cm as compared to simple fibroadenoma, the average size of which 2.5 cm [13].

Ultrasound features of complex fibroadenomata as reported in Selvi 2015 were heterogeneous echotexture, internal cysts, and sclerosing adenosis particularly in the periphery can cause angular margins [5].

Some ultrasound features might place the lesion in the BIRADS category 4a or higher and that might require a biopsy to rule out malignancy like angular margin, more than three lobulations or microlobulations and also calcification casting acoustic shadowing.

Dupont et al. [14] found out that 22% of the reported fibroadenomata were pathologically proven complex as well as Sklair–levy et al. 2008 also declared that 15.7% of biopsy-roven fibroadenoma were complex [15].

In addition, Pinto et al. 2014 also detected that 16% of biopsy-proven adenomas were complex ones. All of them were nearly matching our study which stated that 20% of pathologically proven were complex [9].

Dupont et al. in 1994 noted that the cumulative risk of invasive breast carcinomas in women with complex FAs was 3.1 times greater than the risk in the normal population and 1.89 times greater than that in women with simple FAs. They recommended that patients with complex FAs should undergo screening mammographic

surveillance, beginning at age 35 or 40 years. In contrast, other investigators in a multicenter study have suggested that complex FA without atypia on histology confers no significant increase in risk of subsequent breast cancer [12].

Sklair–Levy et al. 2008 reported a low incidence of malignancy (1.6%) in complex FA during a mean follow-up period of 2 years; as a result, they suggested conservative management for women with complex FA [16]. Peek et al. 2015 reported that malignant transformation within FAD is considered exceptionally rare (0.002–0.0125%) and there is a 1.3–2.1 increased risk of breast cancer in women with FAD compared to the general population [10]. Gogoi and Borgohain in 2015 stated that the incidence of carcinoma developing in a fibroadenoma is only 0.1 to 0.3%. Sanders et al. in 2015 A retrospective analysis of the pathologic findings of core biopsy of 2062 fibroadenomas (FA) and their long-term outcome revealed malignancy or atypia in 12 (0.58%) [17]. In our study, one out of the seven pathologically proven complex fibroadenoma changed to carcinoma in follow up after 6 months.

Regarding value of color Doppler, Lee et al. in 2015 concluded that the degree of vascular flow in complex FAs was significantly higher than it was in simple FAs and that complex fibroadenomata tended to have more aggressive features and high BIRADS category on gray scale

Table 8 Comparison between typical and complex FAD regarding acoustic features

Posterior acoustic features	Complex FAD proven by biopsy	Typical FAD proven by biopsy/follow up	p value
None	0	19 (67.9%)	> 0.05
Enhancement	7 (100%)	7 (25%)	< 0.01
Shadowing	0	2 (7.1%)	> 0.05

Table 10 Comparison between typical and complex FAD regarding vascularity

Arrangement of vessels	Complex FAD proven by biopsy	Typical FAD proven by biopsy/follow up	p value
Central	6 (85.7%)	0 (%)	< 0.01
Peripheral	0	10 (35.8%)	< 0.01
Both	0	9 (32.1%)	< 0.01
No	1 (14.3%)	9 (32.1%)	0.01
Vascularity			
Few	6 (85.7%)	16 (57.1%)	0.03
Much	0	3 (10.8%)	(> 0.05)
No	1 (14.3%)	9 (32.1%)	< 0.01

Table 11 Comparison between typical and complex FAD regarding calcification and cystic degeneration

Calcification and cystic deg	Complex FAD proven by biopsy N = 7	Typical FAD proven by biopsy/follow up N = 28	p value
Ca	0	3	
Cystic	3 (43%)	3 (10.7%)	> 0.05
Both	2 (28.5%)	6 (21.4%)	> 0.05
No	2(28.5%)	16 (67.9%)	

ultrasound [12] According to Hooley in 2013, the irregular branching central or penetrating vascularity within a solid mass raised suspicion of malignant neovascularity [15].

In our study, complex FAD demonstrated more frequent central arrangement of mild vascular flow than simple fibroadenoma (85.7% versus 0 %, $p < 0.01$) and that 71.4% of complex fibroadenomata showed high BIRADS (4a or 4b) than simple ones (2 or 3).

Pinto et al. in 2014 reported that complex fibroadenomas presented more frequently with an oval shape, circumscribed contours, a parallel orientation to the skin surface, no posterior acoustic features, and no calcifications [9].

While Lee et al. in 2015 stated that complex fibroadenomata represented more with round to irregular shape and uncircumscribed margin and the other features like echogenicity, posterior acoustic pattern, boundary, and orientation of masses did not differ significantly between the two groups ($p > 0.05$) [12].

In our study, complex FAD showed more frequently oval shape in about 71.4%, isoechoic texture in 57.2%, uncircumscribed contour in 57.2% lesions, parallel orientation to the skin surface in 71.4% lesions, and finely posterior enhancement 100% in all lesions.

As a result, the ultrasound features including vessel arrangement and posterior features show significant difference between typical and complex FAD with p value of < 0.01.

Small descriptive study done by You et al. in 2010 demonstrated that complex fibroadenomas frequently presented with cystic changes and a complex echo texture [18]. In our study, 57.2% of complex fibroadenomas presented with isoechoic texture. Further, 28.5% present with calcification and cystic degeneration, 42.8% present with cystic degeneration only with no significant difference. Also complex fibroadenomas showed associated

Table 12 Comparison between typical and complex FAD regarding associated findings

Associated findings	Complex FAD proven by biopsy	Typical FAD proven by biopsy/follow up	p value
Yes	4 (57.1%)	2 (7.1%)	> 0.05
No	3 (42.9%)	26 (92.9%)	

findings as fibrocystic changes more than simple ones (57.1% versus 7.1% with no significant p values).

Substantial physiological changes during pregnancy and lactation made it challenging to evaluate patients presenting with a breast problem. Most findings in pregnant and lactating patients were benign. Ultrasound was the first-line recommended imaging modality for all pregnant women and for lactating patients less than 30 years of age [3].

Joshi et al. in 2013 stated that during pregnancy, fibroadenomata sometimes showed atypical features like cystic changes, increased vascularity, and/or prominent ducts. The presence of atypical features such as microlobulations, irregular outline, heterogeneous echogenicity, posterior acoustic shadowing, and extensive hypoechogenicity should lead to percutaneous core biopsy to confirm the diagnosis [3].

In our study, six pregnant cases with FAD showed atypical criteria, one of them showed microlobulated outline, one showed increase vascularity, while the remaining five showed vascular arrangement of central and peripheral position.

Two out of six were proven to be typical FAD by biopsy, and the other four showed stationary course during their follow up after delivery.

So in our study, ultrasound showed high sensitivity (100%), specificity was 74%, PPV was 46%, while NPV was 100% in the initial diagnosis and characterization of fibroadenomata.

In our study, we verified the role of ultrasound and color Doppler in the diagnosis of fibroadenomata as well as the differentiation between simple and complex fibroadenomas for optimal management (biopsy versus follow up).

Conclusion

Breast ultrasound and color Doppler played a specific role in diagnosis of fibroadenoma, differentiation between typical and atypical ones, and assess the impact of imaging by ultrasound on patient management (biopsy versus follow up).

Certain sonographic features are associated with complex fibroadenomata and can help the radiologist to decide which ones require biopsy, like vessel arrangement and posterior features ($p < 0.01$). Complex fibroadenomata should be managed carefully.

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