Fibrocystic Breast Changes: Imaging and Pathological Correlational Study of a Sample in The Kurdistan Region of Iraq

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Abstract

Background and objectives: Fibrocystic changes of the breast are the most common breast changes observed globally. The study aimed to assess these changes using ultrasound and correlate the imaging findings with histopathological changes to determine accuracy.

Methods: A prospective cross-sectional study included 240 women who were diagnosed with fibrocystic breasts between January 2022 and July 2023 at a specialized medical center in Duhok city. Ultrasound was performed to evaluate changes in the breast. Imaging results were classified according to the guidelines of the American College of Radiology's Breast Imaging Reporting and Data System. Women with moderate imaging findings underwent ultrasound guided needle aspiration. The samples obtained were sent for cytological and histopathological evaluation. A correlation was conducted between the results of both of these modalities.

Results: The age group most affected was 29-49 years. Bilateral breast involvement was the most prevalent, accounting for 78% of the cases. 74% of the affected women complained of cyclical mastalgia. Ultrasound findings mainly show simple cysts, clustered cysts, and duct ectasia, accounting for 29%, 30%, and 15% respectively. BI-RAD 2, followed by 3, and then 4A were the most common imaging categories. Simple cyst (36%), ducts with apocrine metaplasia (23%), and epithelial hyperplasia without atypia (18%) were the most commonly observed histopathological findings. Statistically significant accuracy was observed regarding the imaging and cytological correlations in BI-RAD 3and 4A.

Conclusion: A strong correlation was observed between the ultrasound findings of breast fibrocystic changes and the histopathological evaluation.

Keywords: Breast Imaging Reporting and Data System, Fibrocystic, Fine needle aspiration, Ultrasound.

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Introduction

Fibrocystic changes of the breast (FCC) are considered the most common breast pathological condition observed among women in the reproductive age group, particularly those between the ages of 20 and 50. The incidence of FCCs peaks in perimenopausal women. Multiparous women with fewer than four children are also at a higher risk.[1] An alteration in the terminal duct lobular unit (TDLU) is the key to its subsequent pathological sequences.[1, 2] Its development is linked to hormonal status. Studies have shown a positive correlation between high estrogen levels and the occurrence of fibrocystic disease. Terminal duct lobular changes lead to subsequent apocrine metaplasia, clear cell changes, eosinophilic change, and microcystic involution resulting in epithelial hyperplasia and accumulation of secretions, resulting in duct dilation and subsequent cysts formation.[3] Up to 30% of women who experience benign breast diseases (BBDs) require treatment at some point in their lives.[4] The triple assessment, which includes clinical examination, radiological imaging, and pathological analysis, has become the standard approach for evaluating breast diseases.[5,6] Clinical presentations usually include mastalgia, which is commonly reported to be cyclical (related to the menstrual cycle). Other symptoms may include breast lump or nipple discharge. Bilateral involvement is more common than unilateral involvement.[2,4,7] Interstitial assessment of the pattern of breast lesions (whether diffuse or focal), localization, categorization of FCC as well as the role of Doppler study and elastography in investigating these lesions, should be considered.[1,2,4] Nashville histopathological(HPE)classification, proposed by Love, S.*et al.*, is a more comprehensive system that categorizes FCC changes into non-proliferative lesions, proliferative lesions without atypia, and proliferative lesions with atypia.[5,6] Breast Imaging Reporting and Data System (BI-RADS) is a risk assessment and quality assurance tool developed by the American College of Radiology provides a widely accepted lexicon and reporting schema for breast imaging. Its latest classification, the 5th edition, was introduced in 2013 included specific tools for classifying and categorizing diffuse and focal breast lesions into BI-RADS 0, 1, and 2: considered negative for cancer and may appear as normal or simple cysts, or as clustered simple microcysts.[8] BI-RADS 3: characterized by the appearance of partially circumscribed or complicated cysts or as breast abscesses.BI-RADS 4A and 4B: observed as complex cystic and solid masses or intraductal lesions. BI-RADS 4 C: characterized by either solid, irregular mass or multiple intraductal lesions with poorly defined margins and clustered microcalcifications and are suspicious of malignancy BI-RADS 5 and 6 categories, arranged as having high likelihood of malignancy, were excluded from this study.[7,8,9] The aim of this study was finding out the main clinical and imaging criteria of breast FCC using ultrasound (US), correlating them with the cytological and HPE results.

Patients and methods

A prospective cross-sectional study conducted on two hundred and forty women over a period of 18 months, from January 2022 to July 2023, at a specialized medical center in Duhok City. Valid written consent was obtained from the patients after explaining the study. A pre-tested questionnaire was prepared for data collection. It included a detailed history covering various aspects such as family history of breast diseases, menstrual and obstetric history, as well as a history of taking contraceptive pills, duration, type, and distribution of pain

and any other associated clinical features. Females who referred for breast imaging and appeared as having breast FCC changes were included in the study. Females with a history of breast carcinoma, lactating women, those who had undergone previous breast surgeries or breast augmentation, and those with indeterminate HPE and cytological results were excluded from the study. Clinical diagnosis was made by the specialists. Included cases were referred to routine hematological and hormonal investigations, with particular emphasis on estrogen levels. Information about their medical history, pain patterns, and hormonal disturbances was collected. US of the breast and guidance for interventions were performed using Samsung HS40 ultrasound machine. A linear high-frequency probe (8-13 MHz) was used, with Doppler, S harmonic and shear wave elastoscan added as necessary, the researchers had at least 19 years Us, Doppler and guided biopsy experience in different major hospitals. Supplies for US-guided fine needle aspiration (FNA) included a sterile syringe, 1½-inch 22- and 25-gauge hypodermic needles, sample collection tubes, slides, culturette, and a spinal needle, in cases of indeterminate FNA results, core biopsy estimated by a specialized histopathologists.US-guided intervention was performed in all the lesions categorized under BRADS 3, BIRADS 4a/b/c. After collecting and analyzing the cytological and histopathological data, it was presented in the form of tables. The study approved by the ethical committee of the Ministry of Higher Education and the College of Medicine at the University of Duhok. All women's data were entered using the computerized statistical software, statistical Package for the Social Sciences (SPSS Version 26). Descriptive statistics were presented as frequencies and percentages. The accuracy of US in detecting findings was measured in regard to cytology as accuracy percentage of the confirmed results by cytology.

Results

Multiparous women were more affected than nulliparous women in the present study, accounting for 61.7% of the total number, mastalgia was the most common clinical presentation observed in the present study, accounting for 74% of cases. Cyclical-related pain was more prevalent than non-cyclical pain, accounting for 73.7% of the total cases. Table (1).

Table (1): Distribution of the patients according to the selected factors

Characteristics		No. Of Patients (N=240)	Percentage (%)
Age	17-27y	42	17.5
	28-38y	99	41.25
	39-49y	81	33.75
	50-60y	18	7.5
Parity	Multiullipara	148	61.7
	Nulliltipara	92	38.3
Symptomatic		188	78.33
Asymptomatic		52	21. 73
Clinical presentation:			
Mastalgia		178	74.22
Nipple discharge		44	18.33
Feeling of lump		18	7.53
Unilateral breast changes		53	22.11
Bilateral breast changes		187	77.91
Related to Menstrual cycle		177	73.75
Not-Related to Menstrual cycle		63	26.25
Related to Estrogen Increment		182	75.83
Not-Related to Estrogen Increment		58	24.21

According to the BIRADS classification, BI-RAD 2 was observed more frequently followed by BI-RAD 3, BI-RADS 4A, BI-RAD 4B and finally BI-RAD 4C, Table (2).

Table (2): Distribution of patients according to BIRADS classification

BI-RAD Classification	N (240)	Percentage (%)
2	93	38.75
3	81	33.75
4A	39	16.25
4B	22	9.23
4C	5	2.08

From the total number of 240 cases, 147 of them (suspicious cases starting from BI-RADS 3 till BI-RADS 5) underwent biopsy, Table (3).

Table (3): Distribution of patients underwent biopsy

BI-RAD Classification	N (147)	Percentage (%)
3	81	55.10
4A	41	27.89
4B	19	12.92
4C	6	4.08

According to US criteria, the most common finding was clustered cysts formation, seen in 29.58% of the cases. This was followed by simple cysts at 28.75% and duct ectasia at 16.25%. Intraductal lesions, complex solid cystic, and solid lesions were infrequent, forming 6.6%, 5%, and 1.6% respectively, Table (4).

Table (4): Distribution of patients according to US criteria

Findings	No (240)	Percentage%
Simple cysts	69	28.75
Clustered cysts	71	29.58
Complicated cysts	29	12.08
Complex solid cystic	12	5
Duct ectasia	39	16.25
Intraductal lesions	16	6.66
Solid lesions	4	1.66

According to cytological and HPE findings, simple cyst formation was the most common form seen in 36% of the total number followed by duct with apocrine metaplasia 23%, epithelial hyperplasia without atypia 18.3%, Table (5).

Table (5): Distribution of the patients according to cytological and HPE results

Findings	N (147)	Percentage (%)
Simple cyst formation	53	36.05
Ducts with apocrine Metaplasia	34	23.13
Epithelial hyperplasia without atypia	27	18.36
Sclerosing adenosis	12	8.16
Intraductal papilloma	10	6.80
Ductal hyperplasia	11	7.48

When US compared to cytology in the diagnosis it was found that the accuracy of US was 95% in detecting both BI-RADS 3 and BI-RADS 4A, 68% for detecting BI-RADS 4B and 66% for BI-RADS 4C, Table (6).

Table (6): The final correlation results between the US classification starting from BI-RADS 3 to BI-RADS 4C and the and cytological results

BI-RAD	No. of patients diagnosed by US	No of patients confirmed by Cytology	Accuracy of US
3	81	77	95.1%
4A	41	39	95.1%
4B	19	13	68.4%
4C	6	4	66.6%

Discussion

Fibrocystic breast changes are a term commonly used by radiologists to describe a group of benign histopathological findings in the breast. In pathological considerations, the use of the term is becoming less popular because pathologists are encouraged to list each specific diagnostic entity encountered in breast specimen.[10] They are more commonly found in women who are nulliparous or have low parity, experience late-onset menopause, have a thin body build, or use exogenous estrogen replacement therapy.[10,11] Clinical symptoms often attributed to FCC include breast pain, nipple discharge, and the presence of solitary or multiple breast lumps (often caused by cysts that wax and wane). Benign entities associated with FCC include proliferative lesions, such as usual ductal hyperplasia and sclerosing adenosis, as well as non-proliferative lesions, including cysts, apocrine metaplasia, and stromal fibrosis. Fibrocystic change can be either diffuse or focal.[10] In this study, the most common age range of the affected women was 29-49 years. Similar results were found in studies conducted in the Iraqi Kurdistan region.[7, 9] ,as well as in six other comparable studies conducted by Deva, Sangma, Samal S,Choe A , Mohammed A and Singh.[1,2, 5, 10-12] Overall, 82.14% of females in Iraqi Kurdistan are below the age of 60. This indicates that the Kurdish society has a higher proportion of young women compared to elderly women, as well as early menarche among them.[11] This phenomenon increases the likelihood of more pathological changes in premenopausal women. Multiparous women were more affected than nulliparous women in the present study, accounting for 61.6% of the total number. Similar findings were also observed in three studies conducted in the Kurdistan Region.[7,11,12], and two other similar studies conducted in India.[1,5] Mastalgia was the most common clinical presentation observed in the present study, accounting for 74% of cases. Cyclical-related pain was more prevalent than non-cyclical pain, accounting for 73% of the total cases. These findings are consistent with other comparable studies conducted by Akreyi H, Hamawandi N, Ghalib et al and Mohammed A.[7, 9, 11, 12] They also observed that mastalgia was the most prevalent clinical presentation followed by feeling of breast lump and nipple discharge. However, a study conducted by Singh in 2022 reported that the most common clinical presentation was the sensation of a lump in the breast, this could be due to their small sample size.[13] The main factors associated with FCC have been found to be related to hormonal disturbances, particularly elevated estrogen levels. This finding is supported by another study which showed that the risk of developing breast FCC is elevated by approximately 2.5 times in women with high estrogen levels compared to those with normal levels.[3] Similar findings were also observed in a study conducted by Ghalib et al who observed that hormonal imbalance especially estrogen is highly associated with the disease process.[11] Our results are consistent with the well-established understanding that prolonged exposure of breast tissues to endogenous estrogen can have adverse effects on breast ducts.[10] In a study conducted by Kumar a significant correlation was observed between the occurrence of FCC and the use of contraceptive pills.[14] In the present study, which was based on findings from the US, simple cysts and clustered cystic formations were the most frequently observed breast changes among the patients. These two types of cysts accounted for more than half of the cases included in the study, followed by duct ectasia, while complicated cysts were found in 12% of the cases. The least were Intraductal and solid lesions 6.6%, 1.6% respectively. Similar findings were reported

in a study conducted by Mohammed A in 2022 who observed that simple breast cysts, clustered cysts, and duct ectasia were the most common benign breast changes in their sample study in correlation with the HPE results.[12] They also observed that the FCC accounted for a significant portion of benign breast changes among the participants. Similar findings were also observed in a study conducted by Khalaf.[16] Fibrocystic disease was the 2nd most common finding in their study, ranged from single simple cyst to multiple cysts in another study conducted by Deva in 2022, similar ultrasonic findings were also discovered, mirroring our own study. The simple cyst was the most prevalent followed by clustered and complicated cysts.[1] According to the present study, the most common BIRADS ultrasonic classification of FCC was found to be BIRADS 2 followed by BIRADS 3, BIRADS 4A, BIRADS 4B and then BIRADS 4C. Similar findings were observed in other comparable studies. They also found that BIRADS 2 was the most common, followed by BIRADS 3, and then BIRADS 4A.[1,16,17] This observation was explained by them as most of the FCCs are regarded as benign ductal hyperplastic and proliferative processes. According to the HPE results, the most common pathological finding observed in the present study was simple cyst formation (36%), followed by apocrine metaplasia (23%). Epithelial hyperplasia without atypia (18.3%), sclerosing adenosis (8%), and intraductal papilloma. Ductal hyperplasia was found in a small percentage, leading to the observation that when FNA US biopsy undergone and proven to be benign on histopathological examination, patients do not require any further imaging follow up or surgery. Those showing features of sclerosing adenosis or epithelial hyperplasia (proliferative lesions without atypia) and epithelial hyperplasia with atypia should be

followed up or surgically excised due to their association with breast malignancies. The above findings were consistent with another similar study; duct ectasia recorded 12% in their study followed by cyst formation.[12] In a recent comparable study conducted in 2022, researchers found that simple cyst formation was the most common occurrence (65%), followed by ducts with apocrine metaplasia (14%), epithelial hyperplasia without atypia, sclerosing adenosis and a combination of intraductal papillomas and ductal hyperplasia.[1] When US compared to cytology in the diagnosis during the present study it was found that the accuracy of US was 95% in detecting both BI-RADS 3 and BI-RADS 4A. It was 68% for detecting BI-RADS 4B and 66% for BI-RADS 4C. Similar findings were also observed in a study conducted by Khalaf. A correlation of ultrasound BIRADS categories and their pathological diagnosis revealed that the number of malignant cytological categorization increased with higher BIRADS categories, strong correlation found in their study regarding BIRADS 3 followed by BIRADS 4A and then BIRADS 4B.[16] In another similar recent study conducted by Deva, US findings of BI-RADS 3 categorization performed 100% accuracy with the histopathological results. 75% regarding BIRADS 4A, B.[1] Similarly, in another study conducted by Khalaf.[16], their sample consisted of 155 women. The study found that the characteristic imaging findings from the US imaging regarding the breast FCC were the most commonly and strongly correlated with the pathological results, with an accuracy of 79%.[16] In a study conducted by Kaur in 2019, they found that the ultrasonic findings of benign breast changes performed high diagnostic accuracy correlated with HPE results, achieving 100% accuracy. Another study found that the US had a high accuracy in diagnosing FCC, with a sensitivity of 85.7%, specificity of 91%, and positive predictive value of

75%.[18] In a recent study conducted on benign breast lesions, it was found that the US performed with a sensitivity of up to 97% and specificity, positive and negative predictive values of 94%, 79%, and 98% respectively when combined with the clinical and imaging findings.[19]

Conclusions:

The correlation between ultrasound findings and histopathological examination in the US BI-RADS 3, 4B, and then 4C and D categories is of considerable importance. Both the US and HPE can contribute to an early and definitive diagnosis of fibrocystic changes, making them valuable tools in monitoring previously diagnosed cases and assisting in their management. When FNA US biopsy undergone and proven to be benign on histopathological examination, patients do not require any further imaging follow up or surgery. Those showing features of sclerosing adenosis or epithelial hyperplasia (proliferative lesions without atypia) and epithelial hyperplasia with atypia should be followed up or surgically excised due to their association with breast malignancies.

Conflict of interest:

No conflict of interest

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References:

1- Deva B, Vakamudia U, Thambiduraia L, Joseph L, Sirinivasan J. Imaging and Pathological Correlation in Spectrum of Fibrocystic Breast Disease and its Mimics – our Experience. Arch Breast Cancer. 2022; 9(4): 465-73.

2- Sangma MB, Panda K, Dasiah S. A clinico-pathological study on benign breast diseases. J Clin Diagn Res. 2013;7(3):503-6.

3- Kohnepoushi P, Dehghanbanadaki H, Mohammadzedeh P, Nikouei M, Moradi Y. The effect of the polycystic ovary syndrome and hypothyroidism on the risk of fibrocystic breast changes: a meta-analysis. Cancer Cell Int. 2022; 19;(1):125-33.

4- Selvakumaran S, Sangma MB.Study of various benign breast diseases.Int Surg J2017;4(1):339-43.

5- Samal S, Swain PK, Pattnayak S. Clinical, pathological and radiological correlative study of benign breast diseases in a tertiary care hospital. Int Surg J 2019;6(7):2428-32.

6- Szep M, Chiorean A, Roman R, RogojanL, DumaM,Cluj N. et al. Imaging spectrum of breast focal fibrocystic changes: mammography, conventional ultrasound, Eur Radiol. https://dx.doi.org/10.1594/ecr2014/C -1237/

7- Akreyi, H. The role of breast ultrasound in assessing patients with mastalgia in Erbil, Iraq. Zanco J Med Sci.2013, 17(1), 331-36.

8- Spaka DA, Plaxco JS, Santiago L, Dryden MJ, Dogan BE. BI-RADS® fifth edition: A summary of changes. Diagn Interv Imaging. 2017;98(3):179-90.

9- Hamawandi N. A prospective Study On Mastalgia in Sulaimania,Iraq. Bas S Surg 2010; 16(2): 46-54.

10- Choe A, Kasales C, Mack J, Al-Nuaimi M, Karamchandani D. Fibrocystic Changes of the Breast: Radiologic–Pathologic Correlation of MRI, J. Breast Imaging. 2022; 4, (1): 48–55.

11- Ghalib H, Ali D, Molah Karim S, Gubari M, Mohammed S, Marif D et al. Risk factors assessment of breast cancer among Iraqi Kurdish women: Case-control study J Family Med Prim Care. 2019; 8(12): 3990–7.

12- Mohammed.A. Benign breast disorders in female. Revista de Senología y Patología Mamaria 2022; 35(1) :42-8.

13- Singh B, Chakrabarti N. A Clinicopathological Study of Benign Breast Diseases in Females. Med. J. Dr. D.Y. Patil Vidyapeeth.2022; 15(3): 346-51. DOI: 10.4103/mjdrdypu.mjdrdypu_171_20/

14- Kumar N, Prasad J. Epidemiology of benign breast lumps, is it changing: a prospective study. Int Surg J 2019;6(2):465-9.

15- Yousif Z, Yacoub S. Patterns of Breast Diseases Among Women Attending Breast Diseases Diagnosing Center in Erbil City/Iraq. Glob.J Health Sci. 2018; 10 (4):114-26.

16- Khalaf M, Abd Allah I. The Value of Using Grey Scale Ultrasound in the Estimation of Palpable Breast Lumps in a Specialist Breast Clinic in Mosul City of Iraq. (Ann Coll Med Mosul 2021; 43 (1):29- 4.

17- Khan.S, Hussain A. Diagnosis Of Fibrocystic Disease Of Breast on Ultrasound. Int. J. Adv. Res. 2019; 7(2): 557-60.

18- Kaur D, Garg T, Sachdeva P, Niranjan R. Triple assessment in Diagnosis of Benign Breast Diseases: An Institutional Study. J.med.sci.clin.res.2019 ;7 (10): 588-97.

19- Bangaru H, Chandra AS, Gaiki VV.Clinical radiological and pathological assessment of benign breast lumps: our institutional experience. Int Surg J2017; 4(11):3627-32.