

Lactation Effect on Findings of Contrast-Enhanced and Diffusion-Weighted Magnetic Resonance Imaging in Patients with Idiopathic Granulomatous Mastitis

Ayşegül Altunkeser¹
Fatma Zeynep Arslan^{1*}
Mehmet Ali Eryılmaz²
M Kazım Körez³

¹Department of Radiology, University of Health Science, Konya Training and Research Hospital, Konya, Turkey

²Department of General Surgery, University of Health Science, Konya Training and Research Hospital, Konya, Turkey

³Department of Statistics, Faculty of Science, Selçuk University, Konya, Turkey

Abstract

Introduction: Idiopathic granulomatous mastitis is a benign chronic inflammatory disease of the breast. Lactation is considered as one of the most important risk factors. We investigated the effect of lactation on the findings of contrast-enhanced and diffusion-weighted magnetic resonance imaging (DW-MRI) in IGM and aimed to identify the most observed findings.

Methods: Contrast-enhanced and DW-MRI of 40 patients with lactation history in the last 5 years and 35 patients reporting no lactation history had been reevaluated retrospectively. Morphological features, enhancement pattern and kinetics of lesions were assessed based on BI-RADS. The presence of diffusion restriction was evaluated and apparent diffusion coefficient (ADC) values were obtained. MRI findings with lactation status were compared.

Results: Non-mass contrast enhancement ($p < 0.02$), cluster pattern ($p < 0.008$) and fistula formation ($p < 0.035$) were more frequently seen in patients with a lactation history than in patients reporting no lactation history. On MRI most common observed findings were concomitantly mass and non-mass contrast enhancement and abscess formation. Diffusion restriction was present in all of the lesions and the mean ADC values were $0.93 \pm 0.25 \times 10^{-3} \text{ mm}^2/\text{s}$.

Conclusion: Lactation status increases the incidence of non-mass contrast enhancement, cluster pattern and fistula formation on MRI.

Keywords

Idiopathic granulomatous mastitis; Contrast-enhanced magnetic resonance imaging; Diffusion-weighted imaging; Lactation

Introduction

Granulomatous diseases of the breast are a rare clinical condition in which the pathogenesis is still not fully understood; tuberculosis, sarcoidosis, foreign body reaction, mycotic and parasitic infections, autoimmune diseases, infection, trauma and oral contraceptive pill use, ethnicity, breast feeding, and prolactinemia are one of the describing risk factors [1,2]. Idiopathic granulomatous mastitis (IGM) categorized as granulomatous disease of breast is relatively rare, benign, chronic inflammatory breast lesion which clinically and radiographically could misdiagnose as a inflammatory breast carcinoma [3]. However cause of IGM is not clear, its frequency is increasing with lactation, pregnancy and hyperprolactinemia [4].

The sonography and mammography (MG) findings of IGM are widely described, and magnetic resonance imaging (MRI) findings have been reported in a limited number of patients. There are only few reports about diffusion-weighted magnetic resonance imaging (DW-MRI) findings, the apparent diffusion coefficient (ADC) values of the IGM and MRI findings [5].

To the best of our knowledge; the relationship between MRI findings and lactation which is an important risk factor has not been investigated. To evaluate the association between lactation status and MRI findings, we compared MRI findings of IGM patients with and without lactation history. We also aimed to describe contrast-enhanced MRI, DW-MRI findings of IGM, ADC values of IGM by revealing the radiological features of IGM in a large patient series.

Materials and Methods

In this study, we retrospectively evaluated the MRI findings of 75 IGM patients diagnosed between 2010-2018. Ethical approval obtained from local committee of our hospital. Patients were divided into two groups based on whether breast feeding in the recent five

Article Information

DOI: 10.31021/jcro.20192120
Type: Research Article
Journal Type: Open Access
Volume: 2 Issue: 1
Manuscript ID: JCRO-2-120
Publisher: Boffin Access Limited

Received Date: 30 November 2018

Accepted Date: 06 March 2019

Published Date: 08 March 2019

*Corresponding author:

Fatma Zeynep Arslan
Department of Radiology
University of Health Science
Konya Training and Research Hospital
Hacı Şaban Mah, Meram Yeni Yol Caddesi
PC: 42090, Meram, Konya, Turkey
Tel: 0506 438 24 30
E-mail: Zeynep_a1002@hotmail.com

Citation: Altunkeser A, Arslan FZ, Eryılmaz MA, Körez MK. Lactation effect on findings of contrast-enhanced and diffusion-weighted magnetic resonance imaging in patients with idiopathic granulomatous mastitis. J Cancer Res Oncobiol. 2019 Mar;2(1):120

Copyright: © 2019 Altunkeser A, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 international License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

years or not.

Group 1 consisted of 40 patients with lactation history; group 2 consisted of 35 patients without lactation history. Patients with specific granulomatous diseases such as sarcoidosis, tuberculosis, cat strach disease, breasts with implants, trauma and bacterial mastitis were excluded from the study. All of the patients had undergone tru-cut biopsy or segmental mastectomy and pathologically proven as IGM. The clinical and pathological findings obtained from local database of our hospital. Of the 75 patients with IGM; 26 of had undergone mammographic examination. MG examinations were performed using a Full Field Digital Mammography System (mammomat inspiration, Siemens, Erlangen, Germany). All of our patients had MRIs.

MR Protocol

All examinations were performed using dedicated 16-channel double breast coil with 1.5 Tesla MRI (Magnetom Aera; Siemens Healthcare, Erlangen, Germany) equipped with 45-mT/m gradients and the patient is placed in the prone position on the table. The image protocol was bilateral, coronal flashed-grappa (TR/TE: 417/11 ms, matrix: 352 × 384, slice thickness: 3 mm, FOV: 180-500 mm) 352 × 384, slice thickness: 3 mm, FOV: 280-300 mm) T1W started with sequences. Then T2W TIRM (TR/TE: 2770/66 ms, matrix: 352 × 384, inversion time: 150 ms, flip angle: 150 degrees, spatial resolution: 0.7x0.7x2 mm, acquisition time: 3 minutes 26 seconds) DWI (TR/TE: 6200/88, long distance resolution: 2.7x2.7x4 mm, slice thickness: 3 mm, FOV: 258-300 mm, B values 0 and 800 s/mm², spectral fat saturation and acquisition time: Minute 47 seconds). Dynamic study was obtained with FLASH (TR/ TE: 4.79/1.70 ms, spatial resolution: 0.8x0.8x1.3 mm, cross-sectional thickness: 1.6 mm, FOV: 318-500 mm). Gadopentetate dimeglumine was intravenously administered at a dose of 0.1 mmol/kg of body weight.

The all assessments were performed by a experienced radiologists (AA) in the field of breast imaging. The MRI and MG findings of the lesions were classified on the basis of the breast imaging reporting and data system (BI-RADS) lexicon established by the American college of radiology [6]. We defined type A and B breast pattern as dominantly lipomatous type 1, dominantly fibroglandular type 2 was also included type C and D breast pattern. Mammographically, lesions were defined as asymmetric density, structural distortion, and mass lesion according to their appearance. Those without pathological findings were evaluated as normal. On MRI, enhancement patterns of lesions were categorized as mass and non mass enhancement (NME). Subsequently; morphological features, internal enhancement and kinetic curves were evaluated, presence of diffusion restriction was investigated and ADC values were obtained. Morphological features of masses were assessed according to their shapes (round, oval or irregular), margins (circumscribed or not). Internal enhancement features were classified as homogeneous, heterogeneous, or rim enhancement. The NME features were also described depending on their distribution as focal, linear, segmental, regional, multi regional or diffuse and internal enhancement patterns defined as homogeneous, heterogeneous, clumped, or clustered ring. The time-signal intensity curve patterns determined as persistent (type 1), plateau (type 2) or washout (type 3). Diffusion restriction features of lesions were classified as single and multiple and ADC values were obtained via region of interest (ROI). After describing lesions features on MRI, the MRI and DWI findings of Groups 1 and 2 were compared and the effect of lactation on MRI findings were investigated. We also determined frequently encountered features of IGM by assessing MRI findings of all patients.

Statistical analysis

Frequency of MRI findings and presence of diffusion restriction and mean ADC values of all patients were demonstrated. The statistical analysis was performed with the SPSS 22 software (Copyright IBM Corporation and its licensors 1989, 2012). The results of the descriptive statistics were given as mean ± standard deviation (SD) and min-max. MRI findings based on lactation status were compared with Chi-square test. The association between ADC

values and lactation status were investigated by using Kruskal Wallis and Mann Whitney-u test. *p* value less than 0.05 was considered as statistically significant.

Results

A total of 75 patients were reevaluated, retrospectively. Median age was 35 (ranging from 23 to 65). While 60% of our patients suffered from mastodynia, rest of them presented with palpable mass. 12% of our patients were breastfeeding, there was a lactation history within recent five years in 41% of them. The rest of them had no recent lactation history. The rate of right and left breast involvement was almost equal. While one third of our patients had breast pattern as dominantly lipomatous type 1, fibroglandular dominantly type 2 pattern was noted in rest of them. Abnormal mammographic finding were not noted in 17% of our patients, asymmetrical density, distortion and mass lesion were seen in of 47.8%; 30.4 and 4.3; respectively (Table 1). Microcalcifications were not detected in any of our patients. When the MRI findings were compared between group 1 and group 2 according to the lactation status, NME and mass association, clustered-ring type enhancement as a non-mass internal contrast enhancement pattern and fistula formation co-occurrence were statistically significant (Table 2) (Figures 1-3). There was no significant difference between the morphological features and enhancement patterns. On DWI, there was no significant difference between groups 1 and 2 in terms of diffusion restriction and mean ADC values.

When general describing features of lesions on MRI are summarized; mass lesion detected in 84% of all patients, NME also noted in 97% of all patients. The most frequently observed features were masses with a round shape (50.6%), a well circumscribed (58.6%), and rim enhancement pattern (69.3%). Of the NMEs,

	Mean ± SS	Min-Max
Age	35.08 ± 8.25	23-65
BMI	27.77 ± 4.95	15-46
	Frequency (n)	Percentage (%)
Complaint		
Mastodynia	45	60.0
Stiffness in thebreast	30	40.0
Lactation Status		
Positive	35	46.67
Negative	9	12.0
Positive with in recent 5 years	31	41.33
Side		
Right	37	49.33
Left	38	50.67
Patern		
Type 1	19	25.33
Type 2	56	74.67
Appearance on MG		
Normal	4	17.39
Asymmetric density	11	47.83
Structural distortion	7	30.43
Mass	1	4.35

N: Number; MG: Mammography

Table 1: Descriptive characteristics of IGM patients

	Lactation			
	Yes (%)	No (%)	Total	p-value
MRI findings				
NME+Mass**	22 (62.86)	33 (82.50)	55	0.025*
NME	8 (22.86)	7 (17.50)	15	
Mass**	5 (14.29)	0 (0)	5	
Internal enhancement pattern (NME)				
Absent**	5 (14.29)	0 (0)	5	0.008*
Homogeneous	5 (14.29)	10 (25.0)	15	
Heterogeneous	22 (62.86)	18 (45.0)	40	
Clumped	1 (2.86)	2 (5.0)	3	
Clustered ring**	2 (5.71)	10 (25.0)	12	
Other MRI findings				
Fistula+edema**	8 (22.86)	20 (50.0)	28	0.035*
Nipple retraction+edema	9 (25.71)	6 (15.0)	15	
Fistula+nipple retraction+edema	3 (8.57)	6 (15.0)	9	
Edema**	15 (42.86)	8 (20.0)	23	

*p value less than 0.05 was considered statistically significant

Table 2: Relationship between lactation status and MRI findings

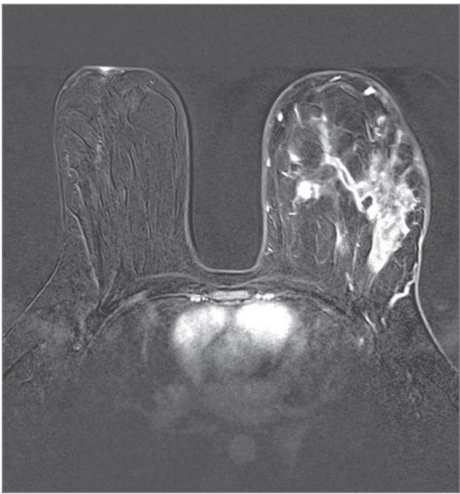


Figure 1: A 24-year-old IGM patient with regional, non-mass asymmetric enhancement and amorphous mass enhancements in the left breast on subtraction T1W image

the mostly seen features were regional distribution (53.3%) and heterogeneous enhancement patterns (53.3%). The time-intensity curves of the dynamic studies showed benign type 2 kinetic curves (plateau enhancement pattern) in the majority of lesions (60 out of 75, 80%). Washout pattern was seen in only 4 lesions which was accounted for 5%. As for the other MRI findings; parenchymal edema was detected in all of the patients. Fistula formation and nipple retraction was present in 49%, 32% of all patients, respectively. On DWI examination; ADC values obtained in 79% of all patients. 54% of these patients had multiple, rounded diffusion restricted areas; of 45% had a single areas. Mean ADC value was 0.93 (ranged from 0.40 to 1.50) (Table 3)(Figure 4 a,b,c).

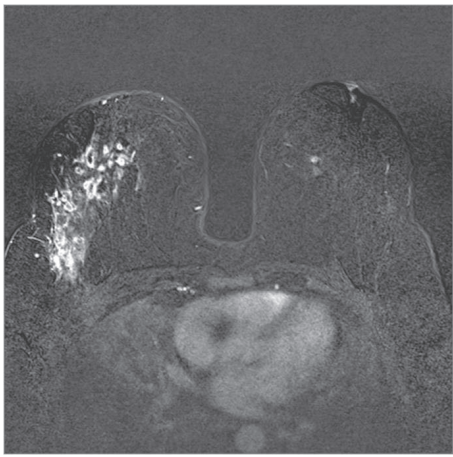


Figure 2: Clustered ring pattern enhancement areas is seen in the right breast of 34 year old patient with IGM on subtraction T1W image

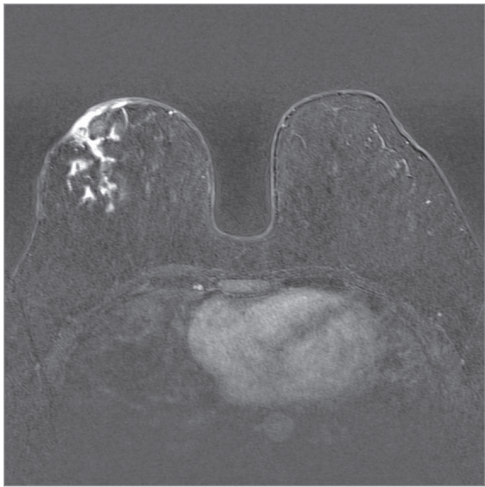


Figure 3: Fistula tract extending to the periareolar site is seen in the right breast of patient with IGM on T1W subtraction images

	Frequency (n)	Percentage (%)
Diffusion Restriction Area		
Single	26	45.61
Multiple	31	54.39
ADC	Mean ± SS	Min-Max
	0.93 ± 0.25	0.40-1.50

Table 3: Diffusion restriction status and mean ADC values of patients with IGM

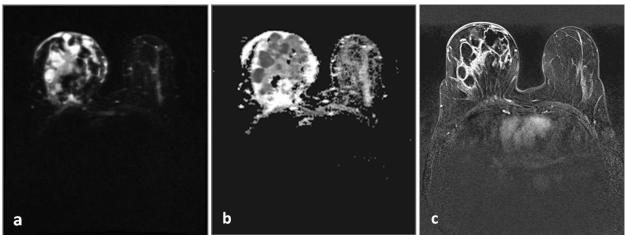


Figure 4: A 46-year-old patient is diagnosed with IGM. In the right breast (a) numerous round shaped diffusion restriction areas on DWI, (b) numerous round hypointense areas with lower ADC values on ADC mapping, (c) hypointense areas with peripheral rim-like contrast enhancement and non-enhancing central area is demonstrated on DWI and T1A dynamic subtraction images

Discussion

IGM is a rarely encountered benign disease generally affecting women with childbearing age [7]. Patients may complain of a hard lump causing nipple retraction and fistulas on the skin [8]. The vast majority of patients have at least one live birth, history of lactation within last five years [9]. The association between IGM and lactation is explained by various hypotheses. It is hypothesized that protein-rich secretion accumulates in the ducts, especially due to hormonal changes in pregnancy and lactation, leading to dilatation of the ducts and leakage into the periductal area. Leakage into the periductal area may have an important role in development of IGM which is characterized with multiple abscess formation and accompanying suppurative necrosis by leading chemical mastitis [10,11]. Taylor et al. [2] assumed that leakage of the protein-rich secretion initiated a granulomatous response. In our research evaluated the effect of lactation on MRI findings; we found that the co-occurrence of clustered-ring enhancement pattern and fistula formation was more frequent. Clustered ring type enhancement is the pattern of contrast enhancement that defines the enhancement around the duct. The increase in enhancement of the periductal stroma may be seen secondary to infectious processes and malignancies [6]. Regarding the fact that this type of clustered ring pattern enhancement pattern is more frequent in our patients with lactation history has supported the hypothesis of chemical inflammation. Leakage of milk into the periductal area and leading chemical inflammation may be one of the most important factors in the development of IGM. Moreover; co-occurrence of fistula formation was more frequent in our lactating patients, this may be related to the fact that the inflammatory reaction is being provoked by lactation. In other words lactation might be the factor triggering the event, then contributing to the acceleration. Being aware of the increased possibility fistula development in IGM patients with lactation history could be guiding in follow ups and treatment choice; which does not yet have a established treatment algorithm.

Imaging features of IGM is atypical and characteristic features of IGM has not been radiologically described. A core needle biopsy is always necessary to obtain definitive diagnosis [12]. Mammographic appearance can be vary from asymmetrical density increasement to small, multiple, nodularities [13]. IGM also can be observed on MG as illdefined masses with spiculated contours; however microcalcifications generally do not accompany IGM different from the malignancy. Asymmetrical density increasement and parenchymal distortion without accompanying microcalcifications was observed in most of our patients as mammographic appearances corresponding to literature data [13,14].

Since IGM is rarely seen, there are very few studies in the literature that describe MRI findings. Our study has included one of the largest patient series, detailing the breast MRI findings of IGM. We investigated MRI findings of our patients as contrast-enhanced and diffusion-weighted imaging. Most important finding observed in most our patients was multiple numerous abscess formation. Most of them were well-circumscribed round lesions with rim-shaped enhancement pattern, besides in 1 to 3 patients expressed irregular margins and shaped nonspecific lesions. Abscess formation was reported as very suggestive finding of IGM in literature data [14,15]. Shelfout et al. [16] found that nonspecific ill-defined masses lesions with multiple ring-like abscess formations is one of the most common appearance on dynamic MRI.

Regional asymmetrical enhancement, which was heterogeneously, was also one of the common findings in almost all of our patients on contrast-enhanced sequences. While Van ongeval et al. [17] described as one of most frequent MRI pattern of IGM as segmental heterogenous contrast enhancement, segmental enhancement pattern was rare in our series. In the research investigating enhancement patterns of IGM, reported as time-intensity curves may varied from patient to patient and from lesion to lesion [14]. Erozgen et al. [18] found that benign curves are more frequent. We mostly observed plato pattern, which is suitable for both benign and malign lesions. On diffusion weighted imaging (DWI); diffusion

restriction can be frequently seen, since the inflammatory response in IGM leads to reduce in diffusion of water. The recent literature data has revealed that diffusion restriction is seen and ADC values is lower than normal breast parenchyma in patients with IGM [7,19]. A point to be emphasized; multiple, round-shaped hypointense areas were seen in more than half of our patients; which was characteristic appearance on ADC mapping. All patients had diffusion restriction and lower ADC values.

Conclusion

In conclusion, lactation status affects MRI findings, increases, clustered ring enhancement, fistula formation, co-occurrence of mass and NME. The most important contrast-enhanced and DWI MRI finding was parenchymal oedema, multiple abscesses and round-shaped hypointense areas on ADC mapping.

References

1. Tavassoli FA. Pathology of the Breast, 2nd edition. NewYork: McGraw-Hill; 1999.
2. Taylor GB, Paviour SD, Musaad S, Jones WO, Holland DJ. A clinicopathological review of 34 cases of inflammatory breast disease showing an association between corynebacteria infection and granulomatous mastitis. *Pathology*. 2003 Apr;35(2):109-119.
3. Kessler E, Wolloch Y. Granulomatous mastitis: a lesion clinically simulating carcinoma. *Am J Clin Pathol*. 1972 Dec;58(6):642-646.
4. Illman JE, Terra SB, Clapp AJ, Hunt KN, Fazzio RT, et al. Granulomatous diseases of the breast and axilla: radiological findings with pathological correlation. *Insights Imaging*. 2018 Feb;9(1):59-71.
5. Yilmaz R, Demir AA, Kaplan A, Sahin D, Ozkurt E, et al. Magnetic resonance imaging features of idiopathic granulomatous mastitis: is there any contribution of diffusion-weighted imaging in the differential diagnosis? *Radiol Med*. 2016 Nov;121(11):857-866.
6. American College of Radiology. Breast imaging reporting and data system (BI-RADS). 5th Edition. Reston, Va: American College of Radiology. 2013.
7. Fazzio RT, Shah SS, Sandhu NP, Glazebrook KN. Idiopathic granulomatous mastitis: imaging update and review. *Insights Imaging*. 2016 Aug;7(4):531-539.
8. Sakurai T, Oura S, Tanino H, Yoshimasu T, Kokawa Y, et al. A case of granulomatous mastitis mimicking breast carcinoma. *Breast Cancer*. 2002;9(2):265-268.
9. Azlina AF, Ariza Z, Arni T, Hisham AN. Chronic granulomatous mastitis: diagnostic and therapeutic considerations. *World J Surg*. 2003 May;27(5):515-518.
10. Tuli R, O'Hara BJ, Hines J, Rosenberg AL. Idiopathic granulomatous mastitis masquerading as carcinoma of the breast: a case report and review of the literature. *Int Semin Surg Oncol*. 2007 Jul;4:21.
11. Pereira FA, Mudgil AV, Macias ES, Karsif K. Idiopathic granulomatous lobular mastitis. *Int J Dermatol*. 2012 Feb;51(2):142-151.
12. Erhan Y, Veral A, Kara E, Özdemir N, Kapkac M. A clinicopathologic study of a rare clinical entity mimicking breast carcinoma: idiopathic granulomatous mastitis. *Breast*. 2000 Feb;9(1):52-56.
13. Memis A, Bilgen I, Ustun EE, Ozdemir N, Erhan Y. Granulomatous mastitis: imaging findings with histopathologic correlation. *Clin Radiol*. 2002 Nov;57(11):1001-1006.
14. Ozturk M, Mavili E, Kahriman G, Akcan AC, Ozturk F. Granulomatous mastitis: radiological findings. *Acta Radiol*. 2007 Mar;48(2):150-155.
15. Heer R, Shrimankar J, Griffith CDM. Granulomatous mastitis can mimic breast cancer on clinical, radiological or cytological

- examination: a cautionary tale. *Breast*. 2003 Aug;12(4):283-286.
16. Schelfout K, Tjalma WA, Cooremans ID, Coeman DC, Colpaert CG. Observations of an idiopathic granulomatous mastitis. *Eur J Obstet Gynecol Reprod Biol*. 2001 Aug;97(2):260-262.
 17. Van Ongeval C, Schraepen T, Van Steen A, Baert AL, Moerman P. Idiopathic granulomatous mastitis. *Eur Radiol* 1997;7(7):1010-1012.
 18. Eroozen F, Ersoy YE, Akaydin M, Memmi N, Celik AS, et al. Corticosteroid treatment and timing of surgery in idiopathic granulomatous mastitis confusing with breast carcinoma. *Breast Cancer Res Treat*. 2010 Sep;123(2):447-452.
 19. Rieber A, Tomczak RJ, Mergo PJ, Wenzel V, Zeitler H, et al. MRI of the breast in the differential diagnosis of mastitis versus inflammatory carcinoma and follow-up. *J Comput Assist Tomogr*. 1997 Jan-Feb;21(1):128-132.

Supplementary Tables

	Lactation			
	No (%)	Yes (%)	Total	p
Mass				
Shape				
Absent	8 (22.86)	7 (17.50)	15	0.149
Oval	3 (8.57)	0 (0)	3	
Round	14 (40.0)	24 (60.0)	38	
Irregular	10 (28.57)	9 (22.50)	19	
Margin				
Absent	8 (22.86)	7 (17.50)	15	0.638
Regular	18 (51.43)	26 (65.0)	44	
Irregular	7 (20.0)	6 (15.0)	13	
Spiculated	2 (5.71)	1 (2.50)	3	
Internal Enhancement Pattern				
Absent	8 (22.86)	7 (17.50)	15	0.675
Homogeneous	1 (2.86)	1 (2.50)	2	
Heterogeneous	4 (11.43)	2 (5.0)	6	
Rim	22 (62.86)	30 (75.0)	52	
NME				
Absent	5 (14.29)	0 (0)	5	0.168
Focal	2 (5.71)	4 (10.0)	6	
Lineer	1 (2.86)	1 (2.50)	2	
Segmental	1 (2.86)	0 (0)	1	
Regional	17 (48.57)	23 (27.50)	40	
Multiple Regional	8 (22.86)	9 (22.50)	17	
Diffuse	1 (2.86)	3 (7.50)	4	
Contrast Kinetics				
Persistent	7 (20.0)	4 (10.0)	11	0.231
Plateau	25 (71.43)	35 (87.50)	60	
Washout	3 (8.57)	1 (2.50)	4	
Diffusion Restriction				
Single	15 (55.56)	11 (36.67)	26	0.188
Multiple	12 (44.44)	19 (63.33)	31	
ADC	Mean ± SS (n)	Mean ± SS (n)		
	0.91 ± 0.23 (30)	0.96 ± 0.27 (27)		0.399

Table 4: The Association between Lactation and Features of Enhanced and DW-MRI

	Frequency (n)	Percentage (%)
MRI findings		
NME+Mass	55	77.33
NME	15	20.0
Mass	5	6.67
Shape		
Absent	15	20.0
Oval	3	4.0
Round	38	50.67
Irregular	19	25.33
Margin		
Absent	15	20.0
Regular	44	58.67
Irregular	13	17.33
Spiculated	3	4.0
Internal Enhancement Pattern		
Absent	15	20.0
Homogenous	2	2.67
Heterogenous	6	8.0
Rim	52	69.33
	Frequency (n)	Percentage (%)
NME		
Absent	5	6.67
Focal	6	8.0
Lineer	2	2.67
Segmental	1	1.33
Regional	40	53.33
Multiple Regional	17	22.67
Diffuse	4	5.33
NME Internal Enhancement		
Absent	5	6.67
Homojen	15	20.0
Heterojen	40	53.33
Clumped	3	4.0
Clustered ring	12	16.0
Contrast Kinetics		
Persistent	11	14.67
Plateau	60	80.0
Washout	4	5.33

NME: Nonmass internal enhancement

Table 5: General MRI findings