Original Article

Dynamic Contrast Enhanced Magnetic Resonance Imaging in Evaluation of Various Breast Pathologies with Histopathological Correlation

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ABSTRACT

Introduction: MRI Breast came as a promising modality for evaluation of breast pathologies. Dynamic Contrast-Enhanced (DCE) MRI of the breast has recently emerged as the most sensitive (95-100%) instrument for the detection of breast cancer which makes it an excellent tool in specific clinical situations, such as the screening of patients at high risk for breast cancer, evaluation of the extent of disease in patients with a new diagnosis, axillary carcinoma of unknown primary, assessing neoadjuvant chemotherapy treatment response and detection of local recurrence in patients who have received breast-conservation therapy.

Aim: To study the characterization of various breast masses and differentiating breast lesions into benign and malignant based on their contrast enhancement curves and correlating them with histopathological diagnosis.

Materials and Methods: An observational Study was performed on 52 patients for duration of two years. For MRI imaging; a

Philips Achieva 1.5 Tesla MRI Machine was used. All the patients underwent FNAC and/or HPE following MRI. Patients with lump/pain in breast, nipple discharge/nipple retraction were included in the study.

Results: Most of the patients were females and in 41-50 years age group. Most common type enhancement curve in the malignant tumours was the type 3 curve. Majority of the malignant tumours showed diffusion restriction on DWI. On correlation with histopathology, the sensitivity of MRI was found to be 96.29%, specificity 89.47 %, positive predictive value 92.85% and negative predictive value 94.44% and accuracy 93.47%.

Conclusions: Dynamic contrast enhanced MRI is useful in accurate diagnosis of breast lesions, its detection and also in monitoring the breast lesions. MRI has the advantage of being non-invasive, three dimensional and the extension of the lesions are better visualised on MRI.

INTRODUCTION

The incidence of breast cancer is rising in many of the countries and it is a major health problem [1-4]. The increased incidence of breast cancer is mainly attributed to the increase in number of women with major risk factors such as early age of menarche, late age of first pregnancy, few number of pregnancies, reduced breast feeding, late menopause, obesity, alcohol consumption, inactivity and hormone replacement therapy [4].

Various modalities are available for the evaluation of the breast pathologies and screening of breast cancer like Conventional and Digital X ray Mammography (Screening and diagnostic), Tomo-mammography, Sono-mammography and MR mammography. Mammography is easily available, acceptable and cheap investigation, hence a good screening test for examination of breast cancer [5,6].

In 1993, American College of Radiology (ACR) proposed a standardized mammographic reporting system known as Breast Imaging Reporting and Data System (BI-RADS) so that the reporting will be easy and uniform everywhere. This will reduce the chances of confusion and help in monitoring of patients. The combination of a normal mammogram and a normal sonogram has a negative predictive value greater than 98%. The use of sonography as an adjuvant to mammography may increase accuracy by up to 7.4% [7].

MRI breast came as a promising modality for evaluation of breast pathologies. However, initially there was no standardized reporting system. But now the radiologist can refer to the ACR BIRADS 5th

edition which provides us with the reporting guidelines in terms of imaging terminologies and how to describe the abnormality in mammography, ultrasound and MRI. It actually helps in standardisation of reporting system and helps in follow up of patient.

Dynamic Contrast-Enhanced (DCE) MRI of the breast has recently emerged as the most sensitive (95-100%) instrument for the detection of breast cancer. The sensitivity of MRI makes it an excellent tool in specific clinical situations, such as the screening of patients at high risk for breast cancer, evaluation of the extent of disease in patients with a new diagnosis, axillary carcinoma of unknown primary, assessing treatment response during neoadjuvant chemotherapy and detection of local recurrence in patients who have received breast-conservation therapy [8].

There are many studies carried out on MRI breast, however we wanted to study the characteristics of different breast pathologies on MRI and role of enhancement kinetic curves in differentiation into benign and malignant lesion in a tertiary care government hospital. So, this study was carried out to evaluate the role of DCE-MRI in various breast pathologies and its correlation with the histopathological diagnosis.

MATERIALS AND METHODS

It was a prospective observational study conducted in a tertiary care hospital in central India, Government Medical College, Nagpur. A total of 52 patients referred from Surgery, Oncology (radiotherapy) departments were included in the study. The study was approved by ethics committee of the institution and written informed consent

was taken from all participating patients. We studied the various types of contrast enhancement curve which were helpful to characterise the lesions as benign and malignant. We correlated them with the histopathological findings and calculated sensitivity, specificity, predictive values and accuracy of MRI in evaluating breast pathologies. The study was carried out from July 2013 to Nov 2015.

Inclusion Criteria
Patients with lump/pain in breast, females with nipple discharge/ nipple retraction and high risk patients for screening (those with history of first degree relatives with breast cancer).

Exclusion Criteria
Patients with MRI incompatible device like pacemaker, aneurysmal clips, orthopaedic implants etc., claustrophobic patients.

Materials
Study was performed on Magnetic resonance imaging Machine Philips Achieva 1.5 Tesla.

Technique
Patients were asked to come nil per oral for 4-6 hours prior to the examination. Medical and relevant clinical history was taken. Previous Mammograms, Ultrasonography (USG) reports, if available, were reviewed.

DCE-MRI was performed on all 52 Patients on a Philips Achieva 1.5 Tesla MR System. Scan was done using pelvis coil and positioning stand with apertures due to non-availability of the dedicated breast coil. The examination was performed in the prone position with the breast hanging freely into the aperture of the coil.

Topogram position: Centre of coil, middle of breast.

T1W_TSE, T2W_TSE, SPIR T1W_TSE and dynamic contrast SPIR T1W_TSE sequences were done with slice thickness: 3 mm and field of view 30 cm. In some patients with large breast, size the field of view was enlarged to 36 cm.

IV contrast Gadopentetate Dimeglumine (469 mg/mL) was used. The dose administered was 0.1 mmol/kg body weight. No contrast reactions were encountered. The average scan time was 30 minutes. Multiple acquisitions were obtained after the intravenous contrast bolus. Five post-contrast acquisitions were obtained with each acquisition less than 2 minute. High temporal resolution was used.

Kinetic curve enhancement curves were generated by the basic T1 perfusion software analysis of dynamic contrast enhanced images. Region of interest was chosen in the area of maximum enhancement in the initial phase of enhancement. The morphology of the lesion, its T1, T2 characteristics, diffusion restriction and type of enhancement and kinetic enhancement curves were assessed.

All the patients underwent FNAC and/or HPE following MRI. They were followed up with the cytological and histopathological reports which were correlated with the MRI diagnosis.

RESULTS
Most of the patients (46.15%) were in age group of 41-50 years. Out of 52 patients, 51 patients (98.1 %) were female; 41(78.84%) patients presented with chief complaint of lump in the breast and eight (15.38%) patients presented with nipple discharge. Malignant tumours were the most common (65.38%) breast pathology. In present study, Left breast was the most common (58.82%) site for malignant breast cancer with upper outer quadrant being the most common (38.23%) location of the malignant breast tumours [Table/Fig-1].

FNAC was performed on 49 out of 52 cases, FNAC was not performed in two cases of lymphangioma and one case of haemangioma in which excision biopsy was performed on the basis of MRI diagnosis [Table/Fig-2].

Pathology	No of patients
Benign lesion	9 (17.30%)
Malignant lesion	34 (65.38%)
Abscess	2 (3.84%)
Fat necrosis	2 (3.84%)
Lymphangioma	2 (3.84%)
Granulomatous lesion	1 (1.92%)
Hemangioma lesion	1 (1.92%)
Lipoma	1 (1.92%)
Total	52 (100%)

[Table/Fig-1]: Various pathologies among the studied population.

Pathology	FNAC positive	FNAC negative/ indeterminate	Histopathology (excision/ core biopsy)
Abscess	2	0	-
Lymphangioma	0	0	2
Haemangioma	-	-	1
Fibroadenoma	4	1	5
Phyllodes Tumour	1	1	2
Malignant	30	4	34
Fat necrosis	1	1	2
Lipoma	-	1	1
Granulomatous lesion	1	-	-
Fibrocystic Disease	2	-	0
Total	49		47

[Table/Fig-2]: Findings on FNAC and histopathology.

Out of 34 patients with malignant tumours, FNAC was positive for malignant cells in 30 (88.23%) patients and was indeterminate in four (11.76%) patients.

Following FNAC, Histopathology was performed in 47 patients out of 52, Biopsy was not done in two cases of abscesses, two cases of fibrocystic disease and one case of granulomatous lesion. Histopathology was diagnostic in all 34 (100%) patients with malignancy and all benign tumours and fat necrosis. Mass like enhancement was the most common pattern of enhancement (86.53%) [Table/Fig-3].

Type	No. of cases
No Enhancement	4 (7.69%)
Mass Like	45 (86.53%)
Non Mass Like	3 (5.76%)
Total	52 (100%)

[Table/Fig-3]: MRI enhancement type.

Out of 34 malignant lesions, 23 (67.64%) showed heterogeneous enhancement and nine (26.47%) showed homogeneous enhancement and two (5.88%) lesions showed rim enhancement. Rim enhancement was also seen in cases of lymphangioma and abscesses. In present study, heterogeneous enhancement was the most common (67.64%) type of enhancement pattern in malignant tumours. Heterogeneous enhancement was also seen in 20 % cases of Fibroadenoma and both cases of Phyllodes tumour.

Out of 45 lesions which showed mass like enhancement, kinetic enhancement curves were generated in 40 patients. Enhancement kinetic curves were not generated in five patients who showed rim like enhancement.

In present study, 26 (76.47%) out of 34 patients with malignant tumours showed type 3 enhancement curve and eight (23.52 %) patients showed type 2 curve. In the present study, majority of the Malignant lesions (76.47%) showed type 3 curves.

Fibroadenoma showed type 1 curve in 75% of cases and type 2 enhancement curves in 25 % of cases. In the present study, Type 1 curve was the most common type of enhancement curve in the fibro adenoma [Table/Fig-4].

Type of enhancement curve	Type 1	Type 2	Type 3	Total
Malignant lesion (xx)	-	8 (23.52%)	26 (76.47%)	34 (100%)
Fibroadenoma	3 (75%)	1 (25%)	-	4 (100%)
Phyllodes tumour	-	1 (100%)	-	1 (100%)
Fat necrosis	-	1 (100%)	-	1 (100%)
Total	3 (7.5%)	11 (25%)	27 (67.5%)	40 (100%)

[Table/Fig-4]: Type of enhancement curve in breast lesions.

A total of 29 (85.29%) out of 34 malignant tumours showed diffusion restriction, five (14.70 %) did not show diffusion restriction. Fibro adenoma, lymphangioma, fat necrosis and lipoma did not show diffusion restriction. Diffusion restriction was seen in abscesses and one out of two cases of Phyllodes tumour [Table/Fig-5].

	Diffusion restriction present	Diffusion restriction absent	Total
Malignant tumours	29 (85.29%)	5 (14.70%)	34 (100%)
Fibroadenoma	-	5 (100%)	5 (100%)
Phyllodes Tumour	1 (50%)	1 (50%)	2 (100%)
Haemangioma	1 (100%)	-	1 (100%)
Lymphangioma	-	2 (100%)	2 (100%)
Abscess	2 (100%)	-	2 (100%)
Fat necrosis	-	2 (100%)	2 (100%)
Lipoma	-	1 (100%)	1 (100%)

[Table/Fig-5]: Diffusion restriction in various breast lesions.

Infiltrating ductal carcinoma was the commonest type of malignancy in 26(76.47%) patients in present study followed by lobular carcinoma four (11.76%) and Ductal carcinoma in situ four (11.76%).

In present study, majority of the invasive tumours showed diffusion restriction, 25 (96.15%) out of 26 cases of infiltrating ductal cancers and three (75%) out of four cases of invasive lobular carcinomas. Ductal carcinoma in situ showed diffusion restriction in one (25%) out of four cases [Table/Fig-6].

Histologic type of malignancy	Diffusion restriction present	Diffusion restriction absent	Total
Infiltrating Ductal Carcinoma	25 (96.15%)	1 (3.84%)	26
Ductal carcinoma insitu	1 (25%)	3 (75%)	4
Invasive Lobular Carcinoma	3 (75%)	1 (25%)	4
Total	29	5	34

[Table/Fig-6]: Diffusion restriction in various malignant lesions.

Out of 28 patients with MRI BIRADS score IV (eight patients) and V (20 patients), 27 (96.42%) patients were positive for malignancy at FNAC/HPE. Six patients were proven to be malignant at HPE/FNAC before MRI and were given BIRADS score VI [Table/Fig-7].

MRI Diagnosis (BIRADS)	FNAC/HPE		Total
	Positive for malignancy	Negative for malignancy	
I		-	0
II	0	13	13
III	1	4	5
IV	7	2	9
V	19	-	19
VI	6	-	6
Total			52

[Table/Fig-7]: Association of MRI diagnosis (birads category) with histopathological diagnosis.

Sensitivity - 96 .29%, Specificity - 89.47%, Positive predictive value - 92.85%, Negative predictive value-94.44%, Accuracy -93.47%. These parameters were calculated from the 2x2 table [Table/Fig-8].

MRI	Malignancy Present on HPE/FNAC.	Malignancy Absent on HPE/FNAC	Total
Malignant lesion (MRI BIRADS IV and V)	26 (TP)	2 (FP)	28
Non malignant lesion (MRI BIRADS II and III)	1 (FN)	17 (TN)	18

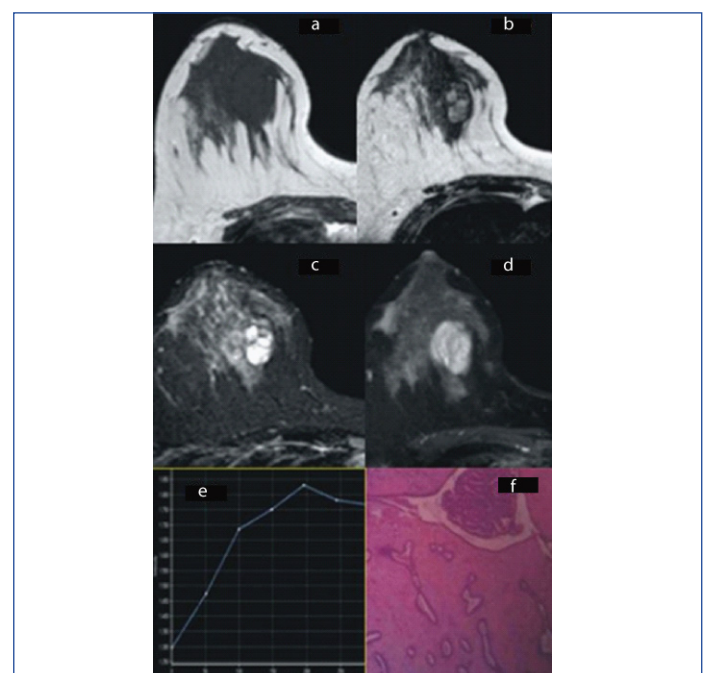**[Table/Fig-8]:** Sensitivity and specificity of MRI breast (2x2 Table).

DISCUSSION

Most of the patients in present study were females in 41-50 years age group, which clearly depicts the change in the trends of breast cancer incidence occurring at earlier age. Lump in the breast was the most common symptom. In present study, the most common pathology was malignant breast tumours. Benign tumours like fibrodenoma of the breast were the second most common pathology; Left breast was the most common side of involvement of the malignant tumours; Upper outer quadrant is the most common quadrant involved in the, malignant breast tumours.

Out of 45 lesions which showed mass like enhancement, kinetic enhancement curves were generated in 40 patients. Enhancement kinetic curves were not generated in five patients who showed rim like enhancement. Kinetic curve i.e., time signal intensity curve for qualitative analysis of DCE-MRI was used.
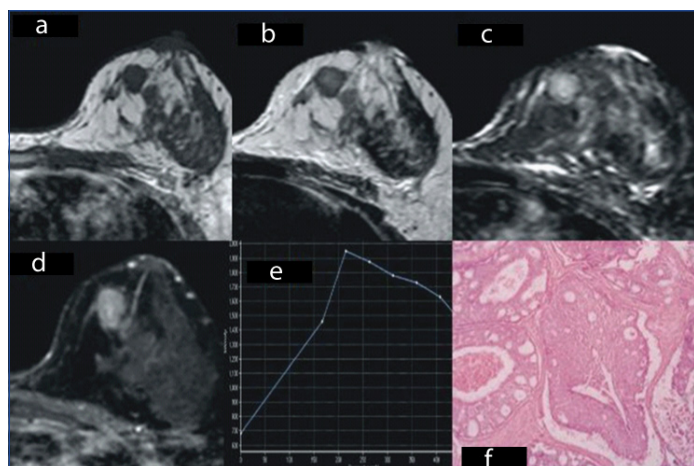
In kinetic curve, the enhacement pattern of a lesion is studied and categorised into three types of curve. The curve has got an initial phase and delayed phase of about 2 and 4 minutes respectively during which the enhancement pattern is observed. In type I curve, the curve rises slowly and continued rise is noted. It indicates least chances of being malignant. In type II curve exhibits slow or rapid rise with plateau in delayed phase [Table/Fig-9]. It has low chances of being malignant. Type III curve shows rapid rise and rapid washout suggestive of malignant lesion [9,10].

Most of the malignant tumours showed mass like enhancement, with heterogenous enhancement being the commonest one. Most
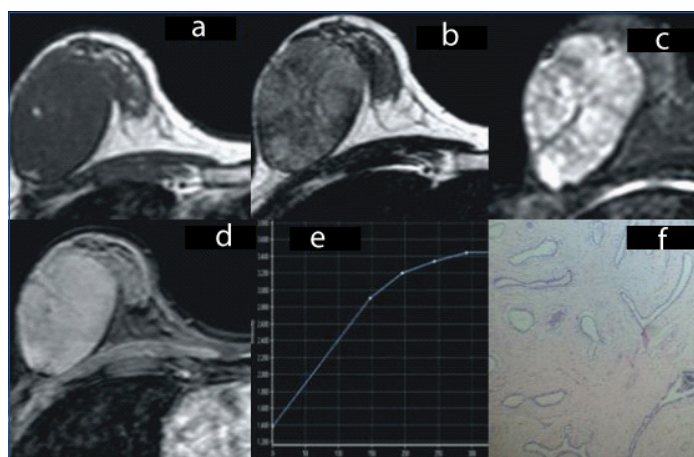

[Table/Fig-9]: a) A 42-year-old female presented with lump in right breast since four months, reveals well circumscribed lesion in right breast appearing iso to hypointense on T1W; b) intermediate to high signal on T2W with hypointense septations; c) hyperintense on STIR; d) sequences and shows homogeneous post contrast enhancement on T1W SPIR with non enhancing septae; e) The lesion shows type 2 enhancement kinetic curve; f) Histopathological slide picture (40x) showing stromal proliferation along with compressed and some patent ducts. One duct shows epithelial lining thrown into folds suggestive of fibroadenoma.

common type enhancement curve in the malignant tumours was the type 3 curve [Table/Fig-10]. Fibroadenoma shows type 1 curve in majority of the cases [Table/Fig-11]. This is in concordance with study by Kuhl CK et al., [11].
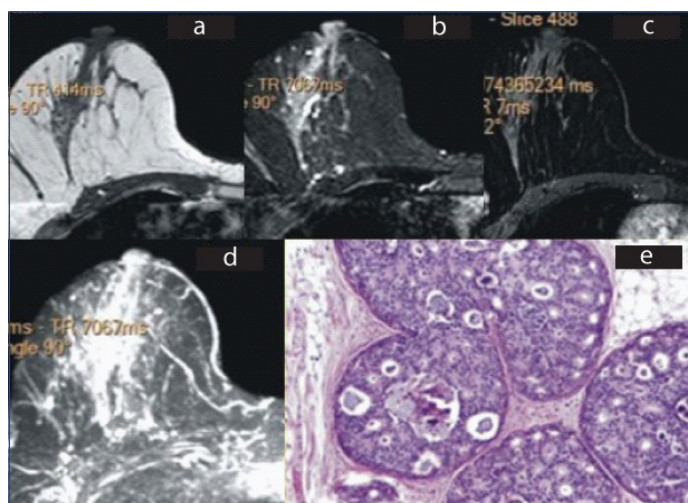

[Table/Fig-10]: a) A 42-year-old female presented with lump in left breast since 2 months, reveals well defined lesion in left breast appearing iso to hypointense on T1W; b) intermediate to high signal on T2W; c) hyperintense on STIR; d) shows heterogeneous post contrast enhancement on T1W SPIR; e) The lesion shows type 3 enhancement kinetic curve; f) Histopathological slide picture (40x) showing Ductal proliferation showing cribriform necrosis and come do necrosis separated by thick fibrous stroma suggestive of Infilterating ductal carcinoma.
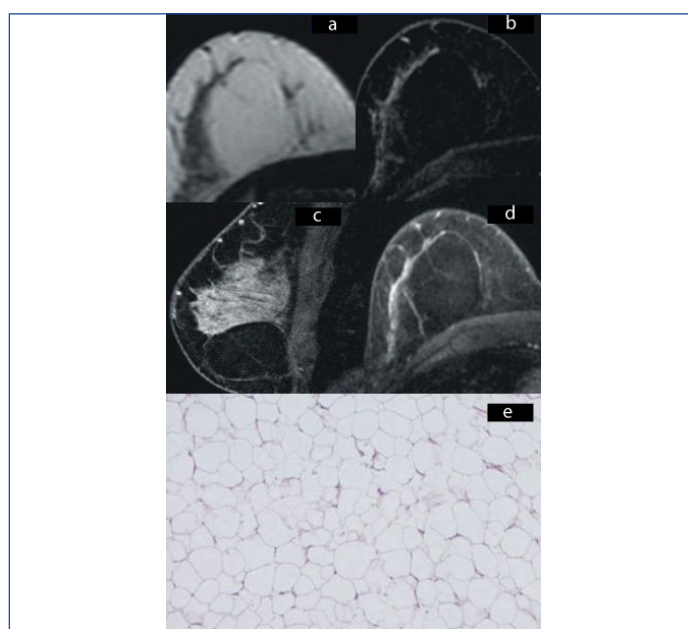

[Table/Fig-11]: a) A 23-year-old female presented with lump in right breast since 6 months reveals well circumscribed lesion in right breast isointense on T1W; b) intermediate to hyperintense on T2W with hypointense septations; c) hyperintense on STIR sequence; d) showing homogenous enhancement on post contrast T1W SPIR; sequence with non enhancing septae; e) Showing Type I enhancement Kinetic curve; f) Histopathological slide picture (40x) showing stromal proliferation along with compressed and patent ducts suggestive of fibroadenoma.

Non-mass like enhancement has a characteristic distribution within the breast. Non-mass like enhancement can be described as a focal area, linear, ductal, segmental, regional, multiregional or diffuse. However in the present study all types of distribution were grouped under non-mass like enhancement [12]. Non mass like enhancement was seen in cases of ductal carcinoma in situ [Table/Fig-12]. Similar results were seen in studies by Rosen EL et al., and Kim JA et al., in which they concluded that non-mass lesions were the dominant MRI findings of pure ductal carcinoma in situ [13-15]. Most common benign tumour was fibroadenoma in present study. There were other few rare benign tumours like Lipoma [Table/Fig-13] and Cystic lymphangioma [Table/Fig-14] of breast. Infiltrating ductal carcinoma was the most common malignancy in present study. Others were lobular carcinoma and ductal carcinoma in situ. In diffusion weighted MRI, the image contrast depends on the motion of water molecules within different tissues. The diffusion in tissues mainly depends on two components, cellularity of the lesion and integrity of the cell membrane [16-19]. The cellular lesions show high signal intensity on diffusion weighted image and corresponding low signal intensity on Apparent Diffusion Coefficient map. In the
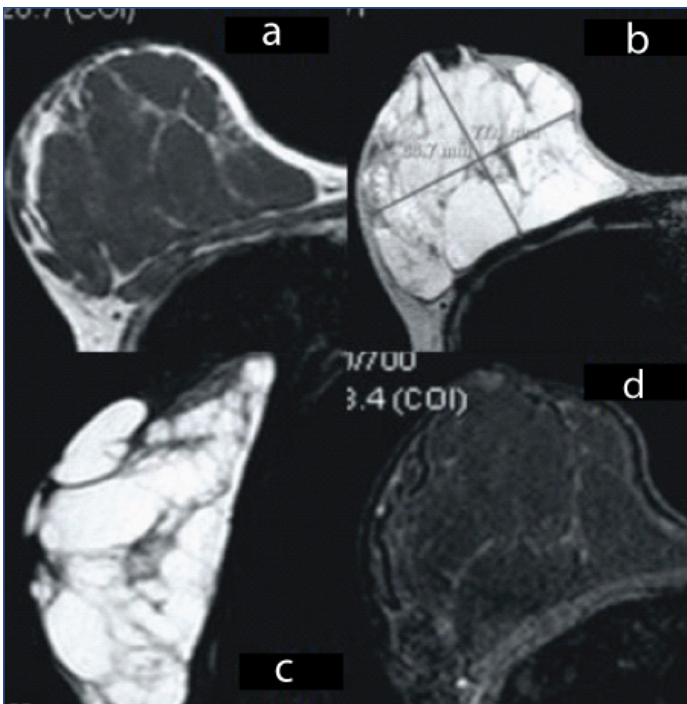

[Table/Fig-12]: a) A 40-year-old female complaining of discharge from right nipple since 1 month reveals ill defined lesion in right breast in retroareolar region extending along the ductal distribution appearing iso to hypointense on T1W; b) hyperintense on STIR sequence; c) showing non mass like enhancement in the segmental distribution in dynamic contrast thrive image; d) STIR MIP image showing high signal intensity in segmental distribution; e) Histopathological slide picture (40x) showing dilated duct spaces lined by intact basement membrane filled with tumour cells arranged in cribriform pattern with punched out spaces suggestive of ductal carcinoma in situ.

[Table/Fig-13]: a) A 40-year-old female presenting with lump in right breast since 3 months reveals ill defined lesion in right breast parenchyma appearing hyperintense on T1W; b,c,d) losing signal on STIR sequence suggestive of fat suppression without any contrast enhancement; e) Histopathology slide (40x) showing immature adipocytes.

present study, Majority of the Malignant tumours showed diffusion restriction on DWI. Benign tumours like fibroadenomas did not showed diffusion restriction. Diffusion restriction is also seen in the breast abscesses and haemangioma but these can be differentiated by morphology and enhancement pattern. In addition to the morphology and enhancement pattern, diffusion restriction in a lesion helps to characterize benign and malignant lesions.

[Table/Fig-12]: a) A 40-year-old female complaining of discharge from right nipple since 1 month reveals ill defined lesion in right breast in retroareolar region extending along the ductal distribution appearing iso to hypointense on T1W; b) hyperintense on STIR sequence; c) showing non-mass like enhancement in the segmental distribution in dynamic contrast thrive image; d) STIR MIP image showing high signal intensity in segmental distribution; e) Histopathological slide picture (40x) showing dilated duct spaces lined by intact basement membrane filled with tumour cells arranged in cribriform pattern with punched out spaces suggestive of ductal carcinoma in situ.

[Table/Fig-14]: a) A 36-year-old female patient with lump in right breast since 2 years reveals large relatively well defined lobulated lesion almost completely replacing the right breast parenchyma appearing iso to hypointense on T1W with hyperintense septations; b) appearing hyperintense on T2W with hypointense septations; c) hyperintense on STIR sequence; d) with enhancing septations on post contrast T1W SPIR sequence suggestive of lymphangioma.

This is in concordance with study by Yabuuchi H et al., [20].

Histopathology could diagnose all the cases accurately. On correlation with histopathology, the sensitivity of MRI in present study was 96.29%, Specificity-89.47 %, PPV-92.85% and NPV-94.44% and Accuracy-93.47%.

CONCLUSION

In the present era, there are many modalites for evaluation of breast masses. Dynamic Contrast Enhanced MRI is far more superior for the diagnosis, detection and monitoring of malignancy. Although DCE-MRI is costly, it is non-invasive and the disease can be evaluated in all the three planes. With fat suppression techniques, a 3D high-quality evaluation of the breasts can be made, regardless of breast density. On post-contrast study changes of heterogenous enhancement suggest about the changes in angiogenic properties even before morphologic alterations occuring in the lesion. Although morphologic analysis alone provides good characterization of breast lesions on MRI as benign or malignant, assessment of the type of contrast enhancement kinetic curve on breast DCE-MRI results in significantly higher diagnostic performance for establishing or excluding malignancy. In addition, DCE-MRI is a powerful tool for screening high-risk patients and for detecting high-grade ductal carcinoma in situ. There was good correlation between the MRI diagnosis and histopathological diagnosis.

LIMITATION

Limitations of the present study include more number of malignant cases compared to benign in the sample which may have cause statistical selection bias.

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