Original Research Article

Characterisation of breast lesions: comparison of digital breast tomosynthesis and ultrasonography

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ABSTRACT

Background: The main aim of the study was to characterize breast lesions using digital breast tomosynthesis and ultrasound and compare the detection and characterization of lesions between both the modalities.
Methods: This was a cross-sectional, observational study that included 150 women who were screened with mammography followed by digital breast tomosynthesis and ultrasound for breast cancer. Patients approaching willingly for screening as per the inclusion criteria underwent mammography and digital breast tomosynthesis followed by ultrasonography. In lesion showing characteristics of malignancy biopsy correlation was done.
Results: About half of the patients had type C tissue composition of the breast (50.67%). Most patients were of age between 35 to 44 years (46%). Malignant lesions were similarly detected by both the modalities. Almost all benign cases were also similarly diagnosed. Sensitivity and specificity of ultrasonography was 94.85% and 92%. Sensitivity and specificity for tomosynthesis was 91.86% and 88.24%. Combined testing showed 100% sensitivity, 97.8% specificity, 98.36% positive predictive value and 100% negative predictive value.
Conclusions: Combining use of tomosynthesis and ultrasonography can make it possible to detect any small lesion, malignancy in its earliest stage (*in situ*) as well as few premalignant conditions like atypical ductal hyperplasia, as in few conditions there is possible sonography negative and mammogram positive calcifications are found.

Keywords: Breast cancer, Mammography, Tomography, Ultrasound

INTRODUCTION

Breast cancer is the most common cancer to occur in women. It accounts for 21% of all cancers in women worldwide and every year 11.7% newly detected cancers. Breast cancer is the second leading cause of cancer death in women. Epidemiological study conducted in recent years in India revealed an age adjusted rate of 25.8 per 1, 00,000 women and a mortality rate of 12.7 per 1, 00,000 women.[1]

Proper and timely diagnosis of the breast cancer will be helpful in reducing the mortality rates. Varying amount of tissue composition in the breast gives the differences in tissue attenuation on radiographic imaging.

Radiographically, fat is lucent and looks dark on a mammogram while epithelium and stroma are radiographically dense and appear light which is referred as mammographic density.[2] Recognition of breast lesion in dense breast may also upsurge the difficulty in breast cancer detection on screening mammography. There is also greater incidence of malignancy in mammographically dense breasts.[1,3-5]

Mammography has been widely adopted as the primary screening tool in breast cancer detection and assessment. However, screening in dense breast makes it difficult to detect lesions on screening.[4] Digital breast tomosynthesis (quasi three-dimensional 3D mammography) generates thin slice reconstructions of the breast out of the low-

dose digital mammographic images that are taken at different angles that expands lesion visibility by decreasing overlapping tissue. In this manner, tomosynthesis has the potential to rise breast cancer detection and to diminish false positive findings.[6] On the other hand, ultrasound is a safe method for screening lesions not detected in mammography but is highly subjective and less sensitive. It shows significant overlap in spectrum of benign and malignant lesions. However it is better than mammography in detection of solid versus cystic lesion and actual tumor size.[7,8] The most commonly used frequencies for high resolution ultrasonography ranges between 7-11 MHz. The aim of this study was to characterize breast lesions using digital breast tomosynthesis and ultrasound and compare the detection and characterization of lesions between both the modalities. The study also evaluated the role of tomosynthesis in morphological analysis of breast lesions and help in BIRADS characterization with comparison with 2D full field mammography, assessed the utility of digital breast tomosynthesis in determining sensitivity in screening of dense breast, determined utility of whole breast ultrasonography as an adjunct in detecting lesions in breast, compared digital breast tomosynthesis with ultrasonography in lesions in screening of breast and histopathological correlation was made whenever applicable. Moreover, we also assessed whether non branching linear calcification can indicate the underlying premalignant condition.

METHODS

This was a cross-sectional, observational study that was conducted at a tertiary care centre in India from August 2018 to September 2020. Total 150 women from an unselected population were screened with mammography followed by digital breast tomosynthesis and ultrasound. All female patients above the age of 35 years who came for breast screening and patients with breast pain, palpable lump or discharge for presence and characterization of presented lesion/lesions were included. Female patients aging <35 years, patients who are known case of carcinoma breast, post-operative, post biopsy cases and post radiation cases and male patients with breast related complaint were excluded from the study. Informed consent was obtained from all the patients. Patients approaching willingly for screening as per the inclusion criteria underwent mammography and digital breast tomosynthesis followed by ultrasonography. In lesion showing characteristics of malignancy biopsy correlation was done. Follow up of the patients with histological reports was done if the biopsy/FNAC were performed.

Procedures

Mammography

44 years (46%). Baseline demographics have been detailed in Table 1. The distribution of type C and type D

Screening of breast was done on Selena Dimention-Hologic 3D mammography machine with plate size of 11×14 inch. Mammography routinely started with standard mediolateral-oblique and craniocaudal projections with 3.7 sec scan time for each view.

Ideal positioning of the breast (nipple in profile and pectoral nipple distance (PND) within 1 cm prompts an ideal positioning for CC projection and lower end of pectoralis muscle at the level of PNL or below, PND less than 1 cm and nipple in profile is the ideal positioning of MLO projection.) was ensured in performing mammography to reduce patient exposure as well as reduce tissue overlap in the field.

Digital tomosynthesis

DBT images were acquired on the digital mammography unit with rotation of the X-ray tube through angular range of 15 degree (-7.5 0 to +7.5 0) while the breast was given standard compression in MLO and CC projections.

15 projections were acquired with approximately 1 degree interval while tube is still in motion. Auto filter is used in machine to automatically select kV, filter and mAs. Image acquisition was performed with a pulsed, short exposure during continuous motion of the X-ray tube, with an acquisition time of 5 seconds or less for one view. Image reconstruction was performed immediately after image acquisition. Slice thickness 1 mm, time of reconstruction 2-5 seconds and a reconstructed pixel size of about 100 micrometer.

Ultrasonography

Screening study of breast was done using high frequency linear transducer of Samsung Medison Accuvix XG machine with frequency of 5-13 MHz.

Statistical analysis

Descriptive statistics like numbers and percentages were calculated using the statistical package SPSS (statistical package for the social sciences) version 20 (IBM Corp., NY, USA). Standard diagnostic indices including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) were calculated as per standard method of analysis.

RESULTS

Of total 150 females included in the study, about half of the patients had type C tissue composition of the breast (50.67%), followed by type B, type D and type A. Majority of patients complained of having lump in their breasts (44%). Most patients were of age between 35 to

lesions according to age groups has been depicted in Figure 1.

Upon diagnosis through various modes, lesion characteristics were detected and classified as benign, malignant, suspicious and normal. Diagnosis through screening mammography and tomography, ultrasonography and collective diagnosis were performed. Through all the diagnostic modes, about one third of lesions were detected as normal, and one third were benign. The detailed have been presented in Table 2. Tomographic findings in patients under study is indicated in Figure 2. Through tomography, focal benign or malignant types of lesions contributed about half of the lesions (52.67%).

Table 3 shows the comparison of findings between tomography and ultrasonography in differentiating malignant and benign lesions. Malignant lesions were similarly detected by both the modalities. Almost all benign cases were also similarly diagnosed. Comparison of findings between only ultrasonography and final imaging diagnosis based on combined ultrasound and tomosynthesis have been demonstrated in Table 4. Upon combining the diagnostic modes, almost all types of

lesions were diagnosed similar to that of ultrasonography diagnosis. Only 5 benign cases were detected as suspicious in ultrasonography whereas they were actually found to be benign in final diagnosis.

Agreement of findings between ultrasonography and histopathological diagnosis is indicated in Table 5. Table 6 denotes the agreement of findings between tomography and histopathological diagnosis. Moreover, Table 7 shows agreement of findings between combined imaging diagnosis and histopathological diagnosis. All detection methods have showed comparable results in detecting the benign and malignant lesions.

Table 8 shows diagnostic indices of ultrasonography, tomography and combined testing in differentiating malignant and benign lesions. Sensitivity, specificity, PPV and NPV were lower in case of individualized diagnosis using ultrasonography or tomography. Whereas, combined testing showed 100% sensitivity, 97.8% specificity, 98.36% PPV and 100% NPV.

Table 1: Baseline characteristics of patients (N=150).

Characteristics	Patients (N=150) (%)
Breast density (tissue composition on mammogram)	
A	13 (8.67)
B	38 (25.33)
C	76 (50.67)
D	23 (15.33)
Complaints	
Screening	57 (38)
Lump	66 (44)
Pain	23 (15.33)
Discharge	11 (7.33)
Redness	5 (3.33)
Skin thickening/nipple retraction	18 (12)
Age group (in years)	
35-44	69 (46)
45-54	44 (29.33)
55-64	22 (14.67)
65-74	14 (9.33)
>74	1 (0.67)

Table 2: Lesion characteristics detected by various modes.

Characteristics	Detection rate of lesion in screening population (N=57) (%)	Diagnosis based on mammography and tomography findings (N=150) (%)	Diagnosis based on ultrasonography findings (N=150) (%)	Final diagnosis based on collective findings (N=150) (%)
Benign	8 (14.04)	47 (31.33)	46 (30.67)	55 (36.67)
Malignant	1 (1.75)	18 (12)	23 (15.33)	23 (15.33)
Suspicious	3 (5.26)	32 (21.33)	31 (20.67)	27 (18)
Normal	45 (78.95)	53 (35.33)	50 (33.33)	45 (30)

Table 3: Comparison of findings between tomography and ultrasonography in differentiating malignant and benign lesions.

Diagnosis by tomography	Ultrasound diagnosis			
	Benign	Malignant	Normal	Total
Benign	31	0	4	35
Suspicious	5	6	1	12
Malignant	0	15	0	15
Normal	7	0	42	49
Total	43	21	47	111

Table 4: Comparison of findings between only ultrasonography and final imaging diagnosis based on combined ultrasound and tomosynthesis.

Diagnosis by ultrasound	Final diagnosis			
	Malignant	Suspicious	Benign	Total
Malignant	23	0	0	23
Suspicious	0	25	5	30
Benign	0	0	46	46
Total	23	25	51	99

Table 5: Agreement of findings between ultrasonography and histopathological diagnosis*.

Diagnosis by ultrasonography	Final/histopathological diagnosis			
	Benign	Malignant	Normal	Total
Benign	37	0	0	37
Suspicious	15	10	0	25
Malignant	2	21	0	23
Normal	5	0	45	49
Total	59	31	45	135

*With exclusion of infective/inflammatory/inconclusive lesion on histopathology.

Table 6: Agreement of findings between tomography and histopathological diagnosis*.

Diagnosis by tomography	Final /histopathological diagnosis			
	Benign	Malignant	Normal	Total
Benign	39	1	0	40
Suspicious	12	16	0	28
Malignant	0	14	0	14
Normal	8	0	45	53
Total	59	31	45	135

*With exclusion infective/inflammatory/inconclusive lesion on histopathology.

Table 7: Agreement of findings between combined imaging diagnosis and histopathological diagnosis*.
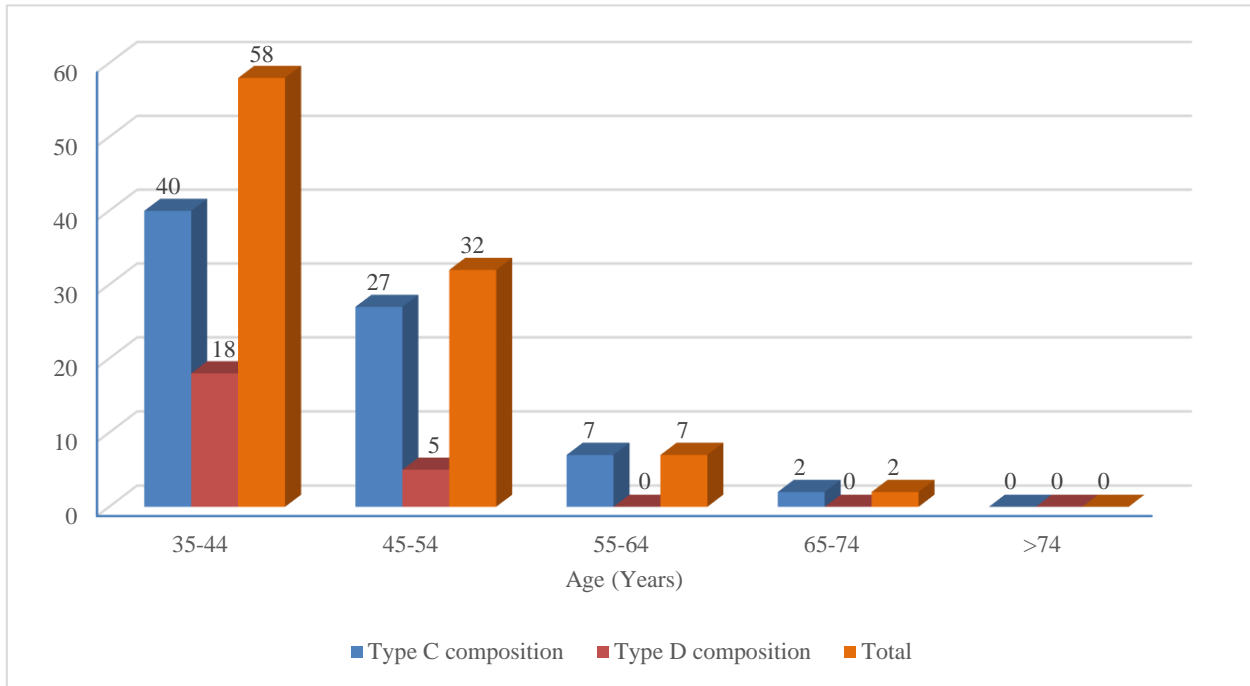
Diagnosis by combined imaging modality	Final /histopathological diagnosis		
	Benign	Malignant	Total
Benign	38	1	39
Suspicious	13	10	23
Malignant	0	22	22
Normal	1	0	1
Total	52	33	85

*With exclusion of small typically benign lesions that has not been followed up by histopathology, infective/inflammatory/inconclusive lesion on histopathology.
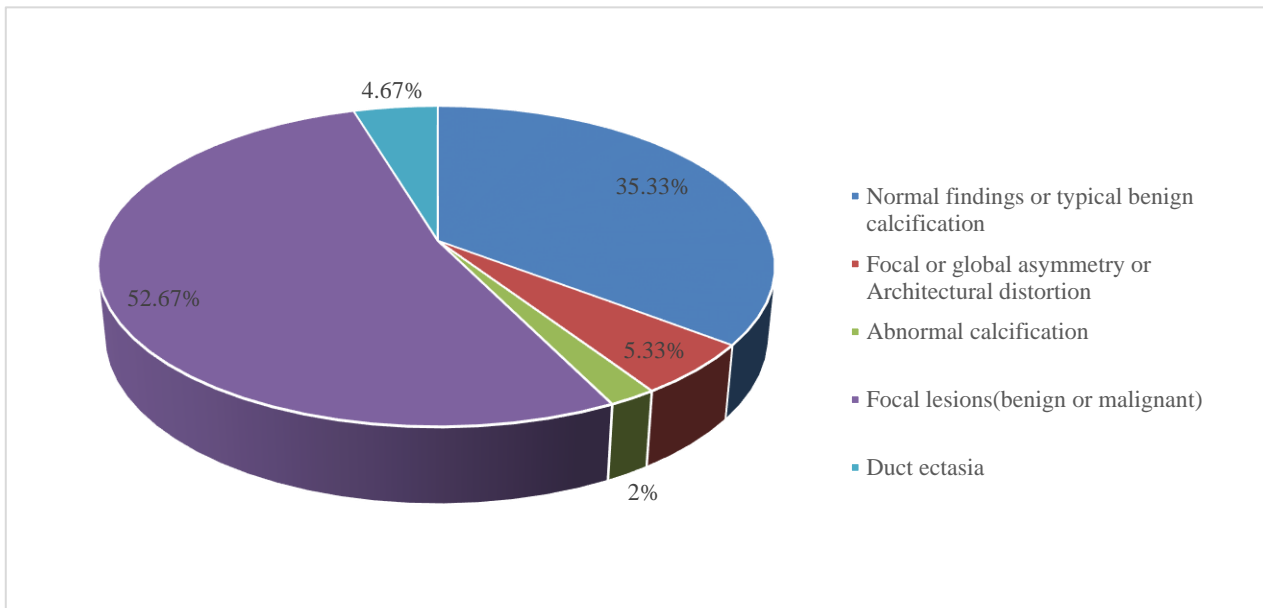
Table 8: Diagnostic indices of ultrasonography, tomography and combined testing in differentiating malignant and benign lesions.

Diagnostic indices	Diagnostic indices of ultrasonography (%)	Diagnostic indices of tomography (%)	Diagnostic indices of tests combined (%)
Sensitivity	94.85	91.86	100
Specificity	92	88.24	97.8
PPV	96	93	98.36
NPV	90	87	100

Note: for purpose of calculating demographical parameters like sensitivity and specificity, moderately or highly suspicious lesions are considered as malignant category and probably benign and low suspicious lesions are considered as benign lesion category.
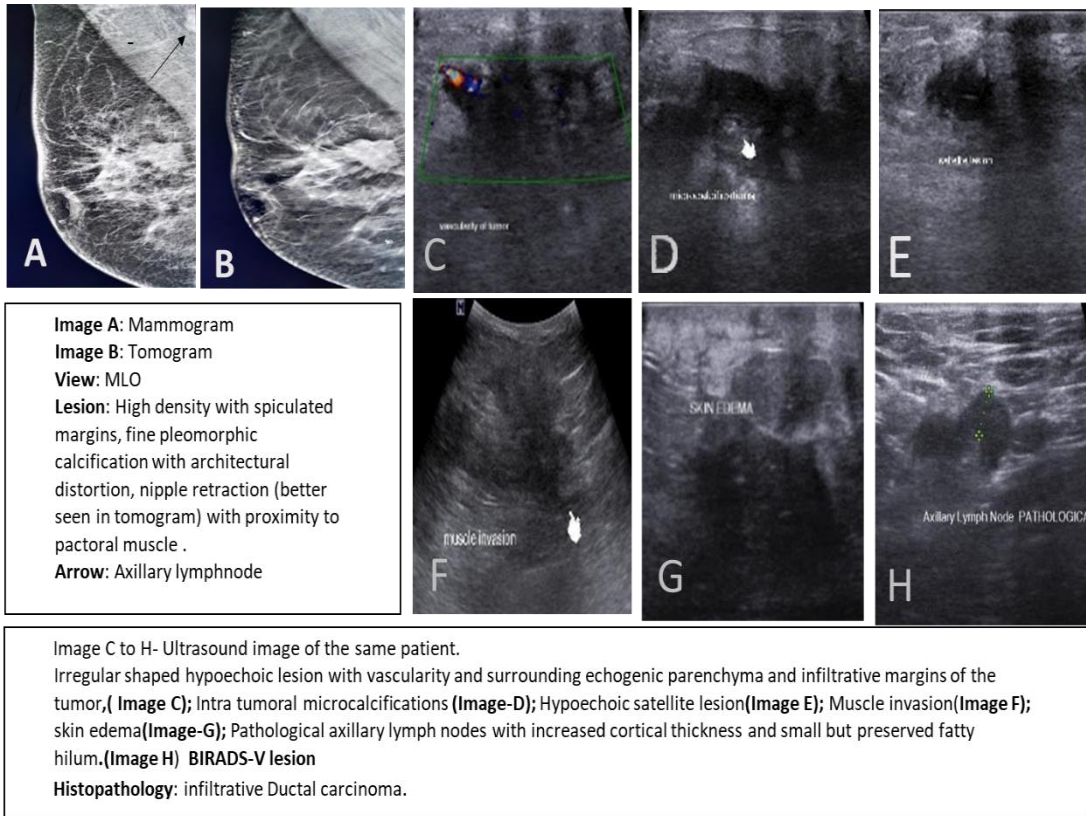

Figure 1: Age distribution of breasts with dense composition (type C and D).
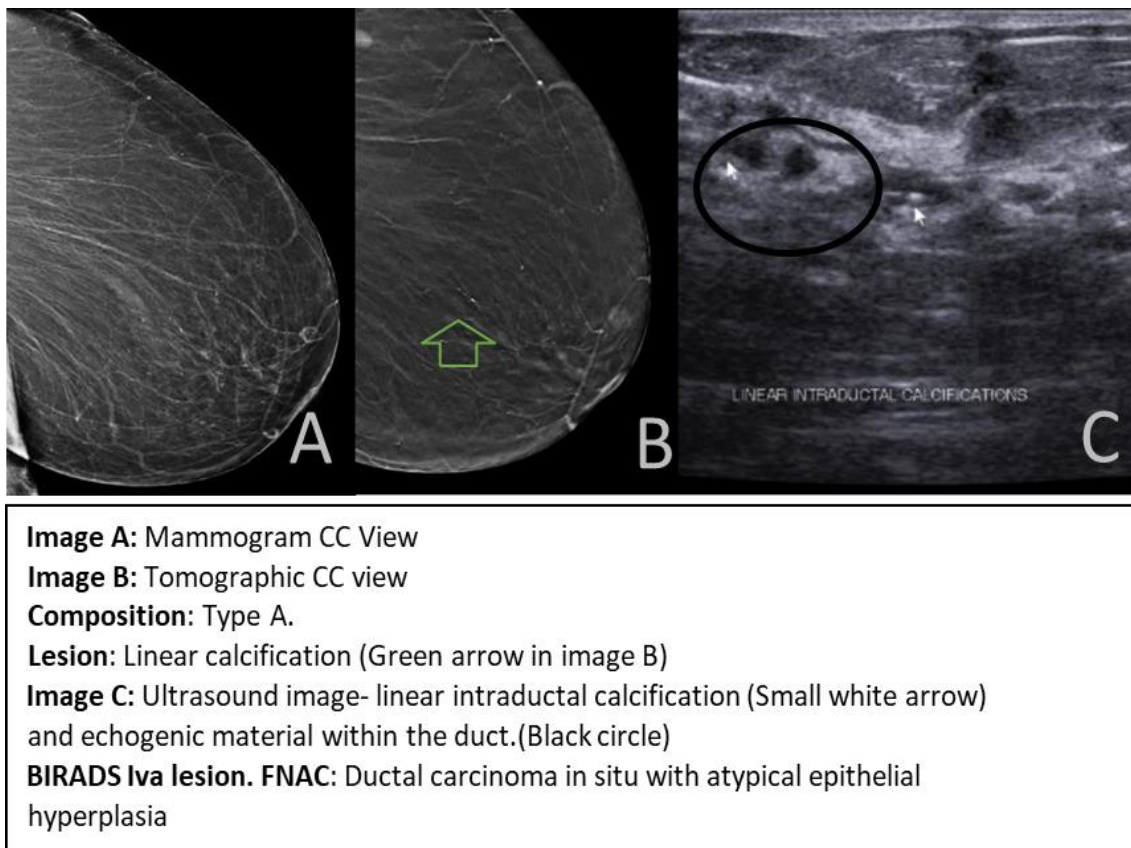

Figure 2: Tomographic findings in patients under study.

Image A: Mammogram
Image B: Tomogram
View: MLO
Lesion: High density with spiculated margins, fine pleomorphic calcification with architectural distortion, nipple retraction (better seen in tomogram) with proximity to pactoral muscle .
Arrow: Axillary lymphnode

Image C to H- Ultrasound image of the same patient.
Irregular shaped hypoechoic lesion with vascularity and surrounding echogenic parenchyma and infiltrative margins of the tumor,(Image C); Intra tumoral microcalcifications (Image-D); Hypoechoic satellite lesion(Image E); Muscle invasion(Image F); skin edema(Image-G); Pathological axillary lymph nodes with increased cortical thickness and small but preserved fatty hilum.(Image H) BIRADS-V lesion
Histopathology: infiltrative Ductal carcinoma.

Figure 3: Illustrative case number 1.

Image A: Mammogram CC View
Image B: Tomographic CC view
Composition: Type A.
Lesion: Linear calcification (Green arrow in image B)
Image C: Ultrasound image- linear intraductal calcification (Small white arrow) and echogenic material within the duct.(Black circle)
BIRADS Iva lesion. FNAC: Ductal carcinoma in situ with atypical epithelial hyperplasia

Figure 4: Illustrative case number 2.

Image A: Mammogram; **Image B**: Tomogram; **View**: MLO
Lesion: High density with smooth lobulated margins, fine pleomorphic calcification in segmental distribution with architectural distortion, nipple involvement without retraction (better seen in tomogram).
Arrow: Axillary lymph node

Image C to image F: Ultrasound and doppler image
Solid vascular lesion with internal necrosis (with fine echoes)(Image D); Lobulated margin, fine calcification and posterior acoustic enhancement (Image C); Pathological axillary lymph node with increased cortical thickness and loss of fatty hilum(Image E) and low resistant blood flow pattern(Image F)
BIRADS-V lesion
Histopathology: Squamous cell carcinoma

Figure 5: Illustrative case number 3.

Image A: Mammogram CC View right breast
Image B: Tomographic CC view right breast
Composition: Type C.
Lesion: Focal architectural distortion in outer quadrant.
Image C: Ultrasound image focally dilatated duct with echogenic material within; there is presence of minimal vascularity within the material, suggests a solid lesion.
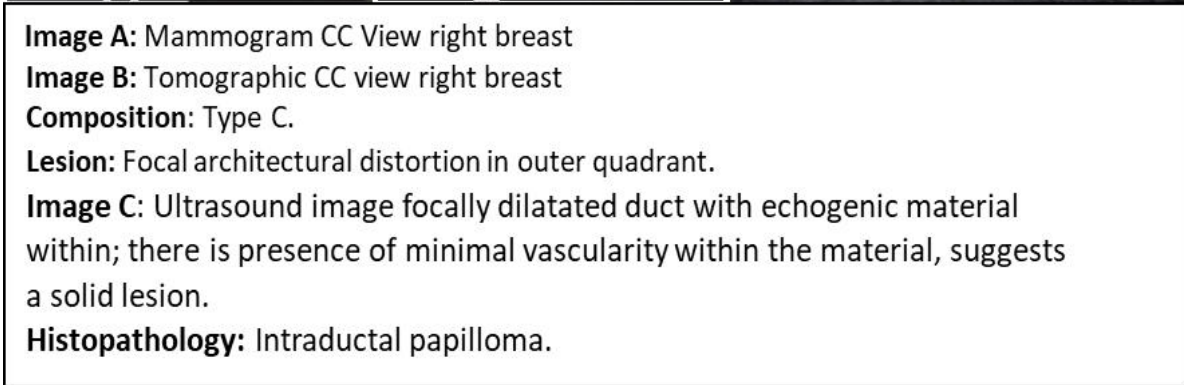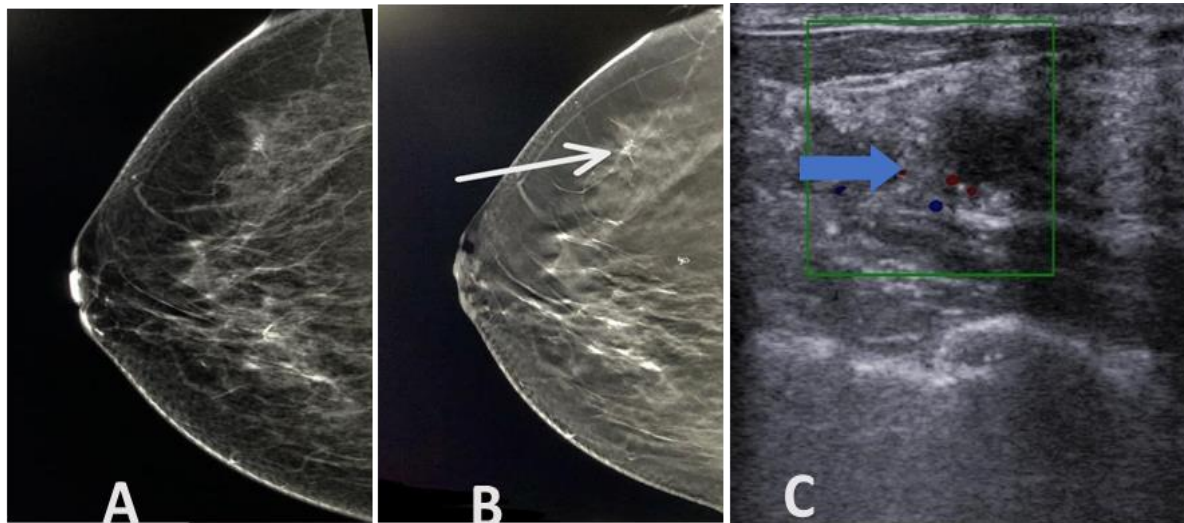**Histopathology:** Intraductal papilloma.

Figure 6: Illustrative case number 4.

DISCUSSION

The breast cancer is the main cause of mortality amongst women in developing countries and it is the second-leading cause of mortality in developed countries. Since there is no factor that prevents breast cancer, the possible way to reduce mortality is its early detection and prompts treatment. Screening techniques such as mammography, digital breast tomosynthesis and ultrasound play a key role in the early detection of breast lesions and thus reduction of mortality. The DBT and ultrasound have been used as adjunct to mammography to further evaluate women with dense breasts. Advantages of the ultrasound are lack of radiation exposure and real time imaging and vascularity of the lesions.

In the present study, the women undergoing mammosonography for screening or for diagnosis of breast pathology in cases with clinically palpable lump or breast related complaints like mastalgia, discharge and redness. Of 150 women satisfying the inclusion criteria out of which 13 (8.67%) had type A entirely fatty breast, 38 (25.33%) had type B breast with scanty fibro glandular tissue, 76 (50.67%) had type C heterogeneously dense breast while the remaining 23 (15.33%) had type D very dense breast. Age distribution of study participants with dense breast composition, type C and type D breast composition on mammogram revealed majority of the females are in the age group of 35 to 44 years with frequency being 58 (58.60%). This finding has successfully replicated the finding by Vikas C et al in their study on mammographic breast density patterns.[9]

On digital breast tomosynthesis the diagnostic indices in differentiating malignant and benign lesions were found to demonstrate sensitivity of 92%, a specificity of 88%, PPV of 93% and NPV of 87%. In the present study diagnostic indices of ultrasound in differentiating malignant and benign lesion revealed a sensitivity of 95%, a specificity of 92% and PPV of 96% and NPV of 90%. Digital breast tomosynthesis has a higher sensitivity and specificity than mammography in diagnostic setting in dense breast whereas an increase in cancer detection rate was noted in combining digital breast tomosynthesis and mammography in dense breast.[10-12]

Few of the lesions show axillary lymph nodes on tomography. On further evaluation by ultrasound and Doppler study, lymph nodes could be classified according to its benign and malignant nature. Typical benign lymph nodes show preserved fatty hilum and thin cortex. Malignant lymph nodes show thickening with bumpy appearance of cortex, raised low resistant medullary vascularity, may or may not show complete loss of fatty hilum. Internal mammary lymph nodes or any supra clavicular lymph nodes can also be evaluated. Any vascular involvement secondary to the lesion (for example thrombosis) can easily be assessed.

Most common type of cancer on histopathology was found to be invasive ductal carcinoma. Amongst the malignant lesions found on histopathology, majority of them was subtypes of invasive ductal carcinomas and other types detected amongst which were squamous cell carcinoma, lobular carcinoma, Non-Hodgkin's lymphoma and mucinous carcinoma. The squamous cell carcinoma has a very rare occurrence rate of about 0.01%. Figure 3-6 represent some illustrative cases included in the study. Amongst the benign calcification majority were found to be vascular calcification followed by round calcifications. Amongst the malignant calcification majority were found to be fine pleomorphic calcification followed by coarse heterogeneous. Calcifications were better appreciated on mammography and tomosynthesis than on ultrasound. Of the 23 suspicious lesion collectively diagnosed on mammography, digital breast tomosynthesis and ultrasound, 10 were confirmed to be malignant on histopathological evaluation. The remaining two lesions were proven to be of benign etiology on HPE. Two of the highly suspicious lesions on combined diagnostic tests were turned out to be atypical ductal hyperplasia with possible changes of *in situ* carcinoma. Ultrasound breast better detected cancer than tomosynthesis in mammographically negative dense breast. However, ultrasound was found to have more false positives in comparison to tomosynthesis.[13] Another study by Yadav et al conducted in 164 females also reported similar results and concluded that breast ultrasound and digital breast tomosynthesis had shown equivocal significance in identifying breast lesion upon screening.[14]

As seen in the study, there are special cases in which the lesion has typical suspicious characteristics but turn out to be having benign infectious or inflammatory etiology like acute or chronic mastitis, sclerosing mastitis or abscess. These lesions have not been included in final calculations as that can lead to falsely low demographical indices. Tomosynthesis also helps in better characterization of margins of the lesions which are obscured in dense breast in mammogram, thus improving the diagnostic accuracy of tests. Few suspicious densities found on mammogram, were not seen on tomogram or seen as a well-defined small lesion with distinct margins. Thus tomosynthesis helps in reducing unnecessary FNAC and aid in ruling out any asymmetry which is seen on mammogram due to faulty overlap of fibro glandular tissue.[15] Skin involvement is better depicted on tomosynthesis image to look for presence of dermal calcification or clinically puckered skin for detecting underlying pathology. In this study dense breasts caused some lesions to be obscured due to soft tissue overlap on mammogram, they were further detected on ultrasonography and tomography which had statistical significance. This proved that combined DBT and ultrasound helped in detecting and better characterizing breast pathology study.

CONCLUSION

From the results of the study, it can be concluded that by combining tomosynthesis and ultrasonography, it is possible to detect any small lesion, malignancy in its earliest stage (*in situ*) as well as few premalignant conditions like atypical ductal hyperplasia, as in few conditions there is possible sonography negative and mammogram positive calcifications are found. Follow up and targeted biopsy is helpful in such cases.

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