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Original Research Article

Diagnostic Accuracy of Ultrasound in Mammographically Dense Breast Taking Histopathology as the Gold Standard

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Abstract: ***Objective:*** To determine the diagnostic accuracy of ultrasound in mammographically dense breast taking histopathology as the gold standard ***Study Design:*** Cross-sectional study. ***Duration and Place of Study:*** Conducted from June to September 2025 at the Department of Radiology, Gambat Institute of Medical Sciences ***Methodology:*** A total of 201 women aged 30–70 years with mammographically dense breasts were included in the study. Patients having Breast Imaging Reporting and Data System category C or D breast density with clinically or mammographically suspected breast lesions were enrolled. Breast ultrasonography was performed using high-frequency linear probe and findings were compared with histopathological examination taken as gold standard. Continuous variables were presented as mean ± standard deviation, while categorical variables were expressed as frequency and percentage. A 2×2 contingency table was used for calculation of sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy. ***Results:*** Mean age of patients was 48.30 ± 10.72 years and mean body mass index was 26.16 ± 3.54 kg/m². Majority of women had heterogeneously dense breasts 138 (68.7%). Histopathology confirmed malignancy in 41 (20.4%) patients, while ultrasound detected malignant lesions in 61 (30.3%) cases. There were 39 true positive, 138 true negative, 22 false positive, and 2 false negative cases. Ultrasound showed sensitivity of 95.12%, specificity 86.25%, positive predictive value 63.93%, negative predictive value 98.57%, and diagnostic accuracy 88.06%. ***Conclusion:*** Ultrasound showed high sensitivity and good diagnostic accuracy in detection of malignant breast lesions in mammographically dense breasts.

Keywords: Breast density; Breast neoplasms; Histopathology; Mammography; Ultrasonography.

INTRODUCTION

Breast cancer is a leading type of cancer among females and also considered as an important cause of mortality and morbidity across the globe.1 Breast cancer occurs as a result of uncontrolled proliferation of breast cells and can further invade other nearby tissues as well as distant body parts, in case it is detected in early stages.2 There are several factors that increase the risk of occurrence of breast cancer, which include advancing age, family history, obesity, use of hormones, early menarche and late menopause.3 Generally, breast mass, nipple discharge, pain in breasts or alterations in breast skin, serve as indicators of the disease; however, in some cases, no symptoms may be seen.4 Early detection of breast cancer becomes crucial for better outcome.

Imaging modalities that are used for detection of breast cancers include mammography, ultrasonography, and MRI. Mammography is the standard diagnostic procedure for screening and it can even help to identify the small tumors and microcalcifications in breasts that have not yet manifested any symptoms.5 But it becomes less sensitive in the case of women who have dense breasts because of the difficulty posed by the dense fibroglandular tissue present in such women.6 In cases where there is uncertainty regarding the nature of the lesion in breast, histopathology serves as the gold standard diagnostic method since it confirms the type of lesion either as benign or malignant.7

Ultrasound imaging plays a crucial role in the diagnosis of mammographically dense breast due to the capability of ultrasound to distinguish between cystic and solid masses as well as detect abnormalities that cannot be detected on mammography.8 Ultrasound imaging is harmless, non-invasive, readily accessible and does not involve exposure to any ionizing radiation. In addition, ultrasound also plays a great role in biopsy guidance and characterization of lesions in terms of characteristics including margins, vascularity and echogenicity.9 Most of the researches conducted indicated that using ultrasound with mammography increases the chances of detecting breast cancer in mammographically dense breast.10

Dense breast tissue on mammography is quite frequent among women and causes reduced sensitivity of mammographic screening for early breast cancer detection. Malignancies can be camouflaged by dense fibroglandular tissue, resulting in late diagnosis and unfavourable prognosis of patients. Ultrasound is now being employed more often as a supplementary examination technique in cases of dense breast, although its reliability could differ between various groups of women. Therefore, this study is needed to determine the diagnostic accuracy of ultrasound in mammographically dense breast taking histopathology as the gold standard, so that early and accurate detection of breast cancer can be improved and unnecessary biopsies can be reduced.

MATERIALS AND METHODS

This cross-sectional study was conducted from 1st June 2025 to 1st September 2025 at the Department of Radiology, Gambat Institute of Medical Sciences. Ethical approval was obtained from the institutional review board of the institute before start of the study. A total of 201 women were included in the study. Sample size was calculated by using prevalence of breast cancer as 19.33%,[11] specificity of ultrasound as 95%,[12] sensitivity as 94.7%,[12] margin of error as 7%, and confidence level of 95%.

Inclusion criteria: Women aged 30 to 70 years, patients having BI-RADS Category C or D breast density on mammography, patients with clinically or mammographically suspected breast lesion, and women willing to undergo biopsy for histopathological confirmation were included in the study.

Exclusion criteria: Patients with previous diagnosis of breast cancer, history of breast surgery including lumpectomy or mastectomy, pregnant or breastfeeding women, patients with coagulopathy or inability to discontinue anticoagulants, and women with breast implants due to medical reasons were excluded from the study.

After obtaining informed consent, demographic details including age, height, weight, body mass index, menstrual status and location of breast lesion according to breast quadrant were recorded. Women referred from surgery or gynaecology department with palpable breast lump or abnormal mammographic findings were enrolled in the study.

Breast ultrasonography was performed by using GE Logiq S7 with XDclear Ultrasound Machine equipped with 7.5–12 MHz linear probe. Patients were placed in supine position with arm raised in contralateral posterior oblique position for proper visualisation of breast tissue. Both breasts were examined in multiple planes by B-mode imaging and lesion characteristics including size, margins, internal echo texture, calcifications, posterior acoustic shadowing, and vascularity were documented. Ultrasound examination was carried out by an experienced radiologist who remained blinded to mammographic findings. After ultrasound examination, True-cut biopsy was performed under ultrasound guidance and biopsy specimens were sent for histopathological evaluation. Histopathological examination was carried out by a pathologist having minimum 5 years experience in breast pathology and findings were considered as gold standard for final diagnosis. All findings were recorded on data collection proforma.

Breast lesion on ultrasonography was considered when any abnormal mass or structure was identified during ultrasound examination with high-frequency transducer of 7–12 MHz. A benign lesion was suspected if the lesion was observed to be round or oval shaped with smooth margins, homogeneous echo pattern inside the lesion, and no posterior acoustic shadowing or calcification within the lesion. The malignancy of the lesion was suspected if the lesion had an irregular or spiculated margin, hypoechoic or heterogeneous echo pattern, posterior acoustic shadowing, microcalcification, or Doppler vascularity within the lesion. The histopathological examination confirmed the presence of a benign lesion when there is a non-malignant lesion such as fibroadenoma, cyst, or fibrocystic disease without atypia or invasion.

Data analysis was performed by using IBM SPSS version 26. Continuous variables were presented as mean ± standard deviation while categorical variables were expressed as frequencies and percentages. A 2×2 contingency table was used for calculation of sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy of ultrasound. Stratification was done for age, body mass index and BI-RADS category.

RESULTS

The study enrolled 201 patients with mammographically dense breasts. The mean age of participants were 48.30 ± 10.72 years, with mean height of 159.54 ± 5.46 cm, mean weight of 66.63 ± 9.80 kg, and mean BMI of 26.16 ± 3.54 kg/m². Regarding breast quadrant involvement, upper outer quadrant was the most commonly affected location with 84 cases (41.8%), followed by lower outer quadrant in 35 cases (17.4%), upper inner quadrant in 31 cases (15.4%), central region in 30 cases (14.9%), and lower inner quadrant in 21 cases (10.4%). For menopausal status, pre-menopausal and post-menopausal groups were nearly equal, comprising 84 (41.8%) and 79 (39.3%) patients respectively, whilst peri-menopausal patients were 38 (18.9%). In terms of BI-RADS categorisation, majority of patients were classified as category C (heterogeneously dense) with 138 cases (68.7%), and remaining 63 cases (31.3%) were category D (extremely dense) (Table-I).

Table I: Patient Demographics

Demographics	**Mean ± SD / n (%)**
Age (years)	48.30 ± 10.72
Height (cm)	159.54 ± 5.46
Weight (kg)	66.63 ± 9.80
BMI (kg/m²)	26.16 ± 3.54
Breast Quadrant	
Upper Outer n (%)	84 (41.8%)
Upper Inner n (%)	31 (15.4%)
Lower Outer n (%)	35 (17.4%)
Lower Inner n (%)	21 (10.4%)
Central n (%)	30 (14.9%)
Menopausal Status	
Pre-menopausal n (%)	84 (41.8%)
Peri-menopausal n (%)	38 (18.9%)
Post-menopausal n (%)	79 (39.3%)
BI-RADS Category	
C – Heterogeneously Dense n (%)	138 (68.7%)
D – Extremely Dense n (%)	63 (31.3%)

On ultrasound, 61 cases (30.3%) were reported as malignant and 140 cases (69.7%) as benign, whereas histopathology

revealed malignancy in 41 cases (20.4%) and benign findings in 160 cases (79.6%) (Table-II).

Table II: Overall Results of Ultrasound and Histopathology in Diagnosis of Mammographically Dense Breast

Findings	Ultrasound	Histopathology
Malignant	61 (30.3%)	41 (20.4%)
Benign	140 (69.7%)	160 (79.6%)
Total	201 (100%)	201 (100%)

When ultrasound findings were compared against histopathological diagnosis, there were 39 true positive, 138 true negative, 22 false positive, and only 2 false negative cases recorded amongst the 201 patients (Table-III).

Table III: Comparison of Ultrasound versus Histopathology in Diagnosis of Mammographically Dense Breast

Ultrasound	Histopathology		Total
	Malignant	Benign	
Malignant	39 (TP)	22 (FP)	61
Benign	2 (FN)	138 (TN)	140
Total	**41**	**160**	**201**

Key: TP = True positive, FP = False positive, FN = False negative, TN = True negative

The sensitivity of ultrasound were 95.12%, with diagnostic accuracy of 88.06%, PPV of 63.93%, and NPV of 98.57% (Table-IV).

Table V: Stratified Analysis of Sensitivity, Specificity, Diagnostic Accuracy, PPV and NPV with Age, BMI and BI-RADS Category

Variable	Group	Diagnostic Parameter	Result
Age (years)	≤50	Sensitivity	85.71%
		Specificity	85.71%
		DA	85.71%
		PPV	28.57%
		NPV	98.90%
	>50	Sensitivity	97.06%
		Specificity	87.27%
		DA	91.01%
		PPV	82.50%
		NPV	97.96%
BMI (kg/m²)	≤25	Sensitivity	0.00%
		Specificity	86.30%
		DA	86.30%
		PPV	0.00%
		NPV	100.00%
	>25	Sensitivity	95.12%
		Specificity	86.21%
		DA	89.06%
		PPV	76.47%
		NPV	97.40%
BI-RADS Category	C (Heterogeneously Dense)	Sensitivity	90.00%
		Specificity	85.94%
		DA	86.23%
		PPV	33.33%
		NPV	99.10%
	D (Extremely Dense)	Sensitivity	96.77%
		Specificity	87.50%
		DA	92.06%
		PPV	88.24%
		NPV	96.55%

Table IV: Sensitivity, Specificity, Diagnostic Accuracy, PPV and NPV of Ultrasound in Diagnosis of Mammographically Dense Breast

Diagnostic Parameter	Result
Sensitivity	95.12%
Specificity	86.25%
Diagnostic Accuracy	88.06%
PPV	63.93%
NPV	98.57%

In stratified analysis by age, patients aged above 50 years showed higher sensitivity (97.06%), specificity (87.27%), diagnostic accuracy (91.01%), PPV (82.50%), and NPV (97.96%) in comparison to those aged 50 years or below, where sensitivity, specificity, and diagnostic accuracy were all recorded as 85.71%, with PPV of 28.57% and NPV of 98.90%. When stratified by BMI, patients with BMI greater than 25 kg/m² demonstrated sensitivity of 95.12%, specificity of 86.21%, diagnostic accuracy of 89.06%, PPV of 76.47%, and NPV of 97.40%, whilst in patients with BMI of 25 kg/m² or less, sensitivity and PPV were both 0.00%, though specificity, diagnostic accuracy, and NPV were 86.30%, 86.30%, and 100.00% respectively. Regarding BI-RADS category, extremely dense breasts (Category D) yielded higher sensitivity (96.77%), specificity (87.50%), diagnostic accuracy (92.06%), PPV (88.24%), and NPV (96.55%) as compared to heterogeneously dense breasts (Category C), which showed sensitivity of 90.00%, specificity of 85.94%, diagnostic accuracy of 86.23%, PPV of 33.33%, and NPV of 99.10% (Table-V)

DISCUSSION

In present study, malignancy was confirmed on histopathology in 41 cases (20.4%), which is considerably lower than the 61 cases (30.3%) reported suspicious on ultrasound, resulting in 22 false positive cases. The high rate of false positive diagnosis may be attributed to the observation that dense breast parenchyma may sometimes mimic an echogenic or hypoechoic mass lesion during ultrasound leading to a low PPV of 63.93%. Stratification according to age demonstrated that the diagnostic accuracy and PPV was higher among women aged above 50 years compared to those who were younger. This is because post-menopausal breast tissue is characterized by fatty involution which leads to reduced background parenchymal density thus improved lesion characterization.

The overall sensitivity of ultrasound in present study were 95.12%, which is comparatively higher than findings reported by Quratulain et al. 13 who found sensitivity of 91.07% and Khan et al. 14 who reported 91.67%, though all three studies consistently confirms the high sensitivity of ultrasound in detecting malignancy in dense breast tissue. This slight variation may be due to difference in sample size, as present study included 201 patients whilst Khan et al. 14 enrolled only 140 women. Similarly, Nisar et al. 15 reported sensitivity of 96.77% which is closely comparable to present study findings, suggesting that ultrasound with BI-RADS classification performs consistently well across different clinical settings.

The diagnostic accuracy of 88.06% recorded in present study is in close agreement with Quratulain et al. 13 who reported 88.11% and Khan et al. 14 who found 88.57%, which strongly supports the reliability of ultrasound in mammographically dense breasts. Rehman et al. 16 also reported sensitivity of 85.3% for ultrasound, which is somewhat lower than present study, and this difference may be attributed to the fact that their cohort included a higher proportion of BI-RADS C cases (59.2%) compared to present study where BI-RADS D cases constituted 31.3% (63 patients), and extremely dense tissue tends to offer better lesion conspicuity on ultrasound.

Histopathology confirmed malignancy in 41 cases (20.4%) in present study, which is lower than 28.3% reported by Rehman et al. 16 though both studies used histopathology as gold standard and enrolled patients with radiographically dense breasts. The PPV in present study were 63.93%, which is notably lower than 89.47% and 89.53% reported by Quratulain et al. 13 and Khan et al. 14 respectively. This lower PPV may be because present study had a relatively lower prevalence of malignancy amongst screened patients, and PPV is well known to be directly influenced by disease prevalence in the study population.

The NPV of 98.57% found in present study is comparatively high and is consistent with findings of Nisar et al. 15 who reported NPV of 94.11% and Robbins et al. 17 who found NPV of 100% in pregnant and lactating women, although the latter population is inherently different. This high NPV suggests that a negative ultrasound finding is highly reliable in excluding malignancy in dense breasts, which has important clinical implications for patient management and avoiding unnecessary biopsies.

Parmar et al. 18 reported ultrasound sensitivity of 95.5% in women aged 45 years or below with dense breasts, which is nearly identical to 95.12% in present study, and both studies together reinforces the role of ultrasound as a preferred first-line imaging tool in

dense breast tissue. Furthermore, Lenihan et al. 19 and Devolli-Disha et al. 20 both highlighted that mammographic sensitivity decreases considerably in dense breasts, dropping as low as 23.7% in heterogeneous dense tissue, which further justifies the use of ultrasound as a supplemental or primary modality in such cases, as supported by present study results.

The current study was carried out in one center, thus limiting the ability to generalize the results to other populations. The study used a relatively small sample size of 201 patients, hence limiting the statistical power of the subgroup analysis especially among the BMI subgroup because of the low number of malignant cases. This being a cross-sectional study, there was no follow up of the patients to determine their long-term results or the occurrence of interval cancers amongst patients who had negative ultrasound results initially. The current study was limited to mammographically dense breasts only.

CONCLUSION

In conclusion, the present study has shown that ultrasound is a very sensitive and precise method of imaging when used to detect malignancy in dense breast tissue where mammography is not expected to be accurate. Ultrasound appears to be effective in all age groups and BI-RADS groups especially in extremely dense breast tissue where the visibility of lesions is better.

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