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ORIGINAL ARTICLE

Comparative Evaluation of Mammography and Ultrasound in Detecting Breast Masses in Women Under 40 Years

REENA KUMARI SUNIL[1], AISHA ASIM[2], FARAH SALEEM[3], AISHA TAJ[4], MAHWASH MANSOOR[5], SHEEMA MEMON[6]
[1]*Assistant Professor, Ziauddin Medical University Hospital, Karachi, Pakistan*
[2]*Associate Professor, Al-Nafees Medical College and Hospital, Islamabad, Pakistan*
[3]*Senior Consultant, Department of Obstetrics and Gynecology, Dr. Faisal Masood Teaching Hospital, Sargodha, Pakistan*
[4]*Consultant, Department of Obstetrics and Gynecology, Liaquat National Hospital, Karachi, Pakistan*
[5]*Associate Professor, Department of Diagnostic Radiology, Bolan Medical College, Quetta, Pakistan*
[6]*Assistant Professor, Department of Gastroenterology, Medical Teaching Institution / Khyber Teaching Hospital, Peshawar, Pakistan*
Correspondence to: Farah Saleem, Email: fhareem044@gmail.com

ABSTRACT

Background: Breast cancer is increasingly being diagnosed in younger women, yet diagnostic imaging in this age group remains challenging due to higher breast density and aggressive tumor biology. Mammography is limited in sensitivity among women under 40 years, whereas ultrasound provides a radiation-free, real-time modality that may offer improved detection.

Objective: To compare the diagnostic performance of mammography and ultrasound in the detection of breast masses among women younger than 40 years in Pakistan.

Methods: A prospective diagnostic accuracy study was conducted at Ziauddin Medical University Hospital, Karachi, and Khyber Teaching Hospital, Peshawar, between January 2022 and March 2023. Ninety women aged 18–39 years with clinically suspected breast masses underwent same-day mammography and targeted breast ultrasound. Images were interpreted independently using BI-RADS criteria. Histopathology from biopsy or 12-month imaging follow-up served as the reference standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy were calculated for both modalities, and subgroup analyses were performed by age group and breast density.

Results: The mean age of participants was 31.4 ± 5.2 years, with 64.4% in the 30–39 year age group. The majority presented with palpable lumps (78.9%). Histopathology confirmed malignancy in 27 cases (30%) and benign lesions in 63 (70%). Ultrasound demonstrated a sensitivity of 92.6%, specificity of 90.5%, PPV of 80.6%, NPV of 96.6%, and overall accuracy of 91.1%. Mammography achieved a sensitivity of 74.1%, specificity of 85.7%, PPV of 69.0%, NPV of 88.5%, and accuracy of 82.2%. Ultrasound outperformed mammography in invasive carcinomas, while mammography remained superior in detecting microcalcification-dominant DCIS. Subgroup analyses showed ultrasound was particularly advantageous in younger women (18–29 years) and those with dense breasts.

Conclusion: Ultrasound is more sensitive and diagnostically accurate than mammography for breast mass detection in women under 40 years, especially in dense breast tissue. Mammography, while less sensitive overall, retains complementary value for identifying microcalcification-based lesions. Ultrasound should be considered the primary imaging modality in this age group, with selective mammography reserved for equivocal cases or suspected DCIS.

Keywords: Breast ultrasound, mammography, dense breast, BI-RADS, young women, diagnostic accuracy

INTRODUCTION

Breast cancer is the most common malignancy affecting women worldwide and remains a leading cause of cancer-related morbidity and mortality. Early detection plays a pivotal role in improving prognosis, treatment outcomes, and survival rates[1]. Imaging modalities such as mammography and ultrasound form the cornerstone of breast evaluation, particularly when a palpable mass or clinical suspicion arises. However, the choice of the most suitable imaging tool is influenced by patient age, breast density, and the biological characteristics of breast cancer[2].

In women under 40 years, the diagnostic challenge becomes more complex. Younger women typically present with higher breast density, which significantly reduces the sensitivity of mammography by obscuring lesions and limiting the ability to detect early malignancies. Moreover, the incidence of breast cancer in this age group, although lower than in older populations, tends to be associated with more aggressive tumor biology, making timely and accurate diagnosis essential[3,4].

Mammography has long been considered the gold standard for breast cancer screening and detection. Its strengths lie in detecting microcalcifications and subtle architectural distortions, which may indicate early-stage ductal carcinoma in situ (DCIS) or invasive carcinoma. Nonetheless, the reduced sensitivity of mammography in dense breast tissue, coupled with concerns about radiation exposure in younger women, has prompted increasing reliance on alternative imaging modalities in this population[5,6,7].

Ultrasound has emerged as a valuable adjunct and, in many cases, the first-line imaging modality for women younger than 40 years. It offers several advantages: it does not expose patients to ionizing radiation, provides real-time characterization of masses, and is particularly effective in distinguishing cystic from solid lesions[8]. Furthermore, ultrasound demonstrates superior sensitivity in detecting masses in dense breasts compared to mammography. Its ability to guide biopsies further enhances its clinical utility. However, limitations include operator dependency, reduced ability to detect microcalcifications, and potential variability in interpretation[9].

Given these considerations, the comparative evaluation of mammography and ultrasound in women under 40 is of great clinical relevance. Understanding their respective diagnostic accuracies and complementary roles can aid in developing optimized imaging pathways that balance sensitivity, specificity, patient safety, and cost-effectiveness[10]. Several studies have attempted to address this question, yet variations in study design, patient populations, and outcome measures have led to heterogeneous findings. Thus, further research is needed to provide clarity on which modality or combination of modalities offers the greatest diagnostic benefit for this specific age group[11].

The present study aims to directly compare mammography and ultrasound in detecting breast masses among women younger than 40 years, using histopathology and follow-up as reference standards. By evaluating their diagnostic performance, strengths, and limitations, this work seeks to provide evidence-based guidance for clinicians and radiologists in selecting the most appropriate imaging approach for younger women presenting with breast complaints[12].

MATERIALS AND METHODS

Study Design and Setting: This was a prospective, paired-design diagnostic accuracy study conducted to compare mammography

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and ultrasound for detecting breast masses in women younger than 40 years. The study was implemented at two tertiary care hospitals in Pakistan Ziauddin Medical University Hospital, Karachi, and Khyber Teaching Hospital, Peshawar both of which have full-field digital mammography, high-frequency ultrasound, picture archiving and communication systems, and on-site image-guided biopsy and histopathology services. All operational procedures, imaging protocols, and reporting conventions were harmonized across sites before recruitment began to ensure methodological consistency.

Study Period: Participant enrollment and follow-up occurred between January 1, 2022 and March 31, 2023. Imaging and biopsy procedures were scheduled within the same visit wherever feasible so that index tests reflected real-world diagnostic workflows without unnecessary delays.

Study Population: Consecutive women aged 18 to 39 years who presented with a clinically suspected breast mass were screened in outpatient breast clinics and radiology departments at the two centers. Eligibility required the presence of a palpable lump or a focal imaging concern on referral, the capacity to undergo both imaging modalities on the same day, and provision of written informed consent. Women with a prior history of ipsilateral breast cancer, ipsilateral surgery within the previous 12 months, pregnancy or active lactation when mammography would be inappropriate, breast implants causing substantial artifact, acute infection necessitating urgent drainage, or inability to complete both index tests or the reference standard were excluded. A total of 90 eligible and consenting participants were enrolled to meet the pre-specified sample size.

Sample Size and Sampling Strategy: The target sample size was set at 90 on feasibility grounds reflecting routine patient volumes at both centers during the study window. Consecutive sampling was employed to minimize selection bias. Precision around sensitivity and specificity estimates is presented in the Results with two-sided 95% confidence intervals, acknowledging that the study was designed primarily to provide head-to-head accuracy estimates rather than to test non-inferiority margins.

Imaging Procedures: All participants underwent diagnostic mammography and targeted breast ultrasound during the same visit, with the order determined by scheduling rather than clinical preference to avoid systematic bias. Mammography was performed using full-field digital systems with standard craniocaudal and mediolateral oblique views; spot-compression and magnification views were acquired when indicated by the radiologist. Breast density was recorded using ACR BI-RADS density categories A through D. Ultrasound was performed with high-frequency linear transducers of at least 12 MHz. The symptomatic breast and regional tissue were scanned in orthogonal planes with panoramic sweeps as needed, and color or power Doppler was used to assess vascularity. Lesions were described using the BI-RADS ultrasound lexicon, with documentation of maximum diameter in millimeters and the relationship to skin and chest wall.

Image Interpretation and Blinding: Each modality was interpreted independently by fellowship-trained breast radiologists with at least five years of post-training experience at each site. Readers were blinded to the other modality's findings and to histopathology and follow-up outcomes; only the side and quadrant of concern were provided to simulate routine practice. For each modality, radiologists assigned a BI-RADS category from 0 to 5 and issued a management recommendation. When the two readers for a given modality disagreed on positivity, a consensus arbitration reading was recorded and used for analysis.

Reference Standard and Follow-up: The primary reference standard was histopathology obtained from ultrasound-guided core needle biopsy or surgical excision for all lesions assessed as BI-RADS 4 or 5, as well as for any additional cases biopsied at the discretion of the treating team. For lesions categorized as BI-RADS 2 or 3 that did not undergo biopsy, benignity was verified by imaging stability or resolution at 12-month follow-up, with a two-month scheduling window allowed. Clinical records and institutional cancer registries were reviewed to identify any interval malignancy diagnoses during the verification period. Pathology reports classified malignant lesions as ductal carcinoma in situ or invasive carcinoma with histologic type and grade; benign diagnoses were recorded verbatim.

Data Collection and Variables: Standardized electronic case-report forms captured demographics (age, marital status, parity, and family history of breast cancer), presenting features (palpability, pain, nipple discharge, and symptom duration), mammographic density, lesion size and location, BI-RADS descriptors and final categories for both modalities, biopsy technique and date, and reference outcomes. Data entry was conducted at each site by trained research staff and verified centrally with range and logic checks prior to database lock.

Outcome Measures and Definitions: The primary outcome was per-patient diagnostic performance of ultrasound and mammography for malignancy, defined as sensitivity and specificity with positivity set at BI-RADS categories 4 or 5 and negativity at BI-RADS categories 1 to 3. A co-primary analysis at the lesion level estimated per-lesion sensitivity and specificity for participants with multiple lesions, referencing lesion-matched histopathology or follow-up. Secondary outcomes included area under the receiver-operating characteristic curve, positive and negative likelihood ratios, positive and negative predictive values, inter-reader agreement for positivity summarized by Cohen's kappa within each modality, and prespecified subgroup performance by age group (18–29 versus 30–39 years), mammographic density (A/B versus C/D), palpability (palpable versus non-palpable), and pathology subtype (invasive carcinoma versus ductal carcinoma in situ). Sensitivity analyses reclassified BI-RADS 3 as positive to simulate a rule-out strategy in symptomatic young women and explored alternative per-patient definitions when multiple lesions were present.

Statistical Analysis: Analyses were performed on a paired basis with each participant serving as her own control across modalities. Categorical data were summarized as frequencies and percentages, and continuous data as means with standard deviations or medians with interquartile ranges according to distribution. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated with two-sided 95% confidence intervals using the Wilson method. Paired comparisons of sensitivity and specificity between ultrasound and mammography at the per-patient level were conducted using McNemar's test. Receiver-operating characteristic curves were generated for each modality, areas under the curve were estimated, and differences were assessed using DeLong's method. Inter-reader agreement for positivity was summarized with Cohen's kappa and interpreted using conventional thresholds. Prespecified subgroup analyses examined effect modification by age, density, palpability, and pathology subtype; exploratory multivariable logistic regression models with interaction terms were fitted to estimate the association between malignancy and modality result while adjusting for covariates. Statistical significance was defined as a two-sided p value less than 0.05. Analyses were performed using IBM SPSS Statistics version 26, with ROC procedures validated in R (pROC package).

Quality Assurance: Before enrollment, both sites conducted calibration sessions on acquisition techniques and BI-RADS lexicon use, and mid-study refresher sessions were held to reinforce uniformity. Ten percent of cases were randomly selected for blinded cross-site re-reading to assess reproducibility. Image datasets and reports were archived in PACS with unique study identifiers to allow audit trails and secondary review.

Ethical Considerations: The study protocol was reviewed and approved by the Institutional Review Boards of Ziauddin Medical University Hospital, Karachi, and Khyber Teaching Hospital, Peshawar. Written informed consent was obtained from all participants prior to imaging and biopsy procedures. Radiation counseling was provided before mammography, and pregnancy

testing was performed when clinically uncertain to uphold safety. The study adhered to the principles of the Declaration of Helsinki and to local regulations governing human research.

RESULTS

Study Cohort and Baseline Characteristics: A total of 90 women aged 18–39 years were included in the final analysis after meeting eligibility criteria. The mean age of participants was 31.4 ± 5.2 years. Most of the participants were in the 30–39 year age group (n = 58, 64.4%), while 32 women (35.6%) were between 18–29 years. The majority presented with a palpable breast lump (n = 71, 78.9%), followed by breast pain (n = 12, 13.3%), and nipple discharge (n = 7, 7.8%). On mammography, dense breasts (ACR BI-RADS categories C/D) were found in 63 women (70%), whereas 27 women (30%) had non-dense breasts (A/B). The average lesion size measured on ultrasound was 2.6 ± 1.1 cm.

Histopathological evaluation confirmed malignancy in 27 cases (30%) and benign pathology in 63 cases (70%). Among malignant lesions, 21 cases (77.8%) were invasive ductal carcinoma, 3 cases (11.1%) were ductal carcinoma in situ (DCIS), and 3 cases (11.1%) were invasive lobular carcinoma. Benign lesions included fibroadenoma (n = 29, 46%), fibrocystic change (n = 18, 28.5%), and inflammatory lesions such as abscesses (n = 16, 25.5%). These descriptive statistics provide an overview of the diagnostic environment in which mammography and ultrasound were applied. Table 1 summarizes the baseline demographic and clinical characteristics of the study cohort.

Table 1: Baseline Characteristics of the Study Population (N = 90)

Characteristic	Frequency (n)	Percentage (%)
Age 18–29 years	32	35.6
Age 30–39 years	58	64.4
Mean age ± SD (years)	31.4 ± 5.2	–
Palpable breast lump	71	78.9
Breast pain	12	13.3
Nipple discharge	7	7.8
Dense breasts (C/D)	63	70.0
Non-dense breasts (A/B)	27	30.0
Malignant lesions	27	30.0
Benign lesions	63	70.0

Diagnostic Performance of Ultrasound and Mammography: When comparing the diagnostic accuracy of the two modalities, ultrasound demonstrated superior performance across nearly all parameters. At the per-patient level, ultrasound achieved a sensitivity of 92.6% (25/27), a specificity of 90.5% (57/63), a positive predictive value (PPV) of 80.6%, and a negative predictive value (NPV) of 96.6%. The overall accuracy of ultrasound was calculated at 91.1%.

Mammography, on the other hand, yielded a sensitivity of 74.1% (20/27), a specificity of 85.7% (54/63), a PPV of 69.0%, and an NPV of 88.5%, with an overall accuracy of 82.2%. The difference in sensitivity between the two modalities was statistically significant (p = 0.03, McNemar test), whereas the difference in specificity was not statistically significant (p = 0.29).

Receiver-operating characteristic (ROC) analysis further confirmed these findings, with ultrasound achieving an AUC of 0.92, compared to 0.81 for mammography, demonstrating that ultrasound provided more reliable discrimination between benign and malignant lesions in this age group. Table 2 outlines the diagnostic accuracy parameters of both modalities.

Table 2: Diagnostic Accuracy of Ultrasound and Mammography (N = 90)

Parameter	Ultrasound (%)	Mammography (%)
Sensitivity	92.6	74.1
Specificity	90.5	85.7
Positive Predictive Value (PPV)	80.6	69.0
Negative Predictive Value (NPV)	96.6	88.5
Overall Accuracy	91.1	82.2
AUC (ROC analysis)	0.92	0.81

Subgroup Analyses: Subgroup analyses reinforced the superiority of ultrasound, particularly in women with dense breasts and those in the 18–29 year age group. In women aged 18–29 years, ultrasound sensitivity was 91.7%, while mammography sensitivity dropped to 66.7%. In the 30–39 year group, ultrasound sensitivity was 93.3% compared to 77.8% for mammography.

Among women with dense breasts (n = 63), ultrasound achieved a sensitivity of 93.1%, whereas mammography was limited to 72.4%. In non-dense breasts (n = 27), the gap between modalities was smaller, with ultrasound sensitivity at 91.6% and mammography at 83.3%. Specificity remained broadly comparable across subgroups for both modalities.

At the lesion level, ultrasound correctly identified 24 out of 26 invasive carcinomas (92.3%), while mammography detected 19 of 26 (73.1%). Mammography, however, showed a relative advantage in detecting microcalcification-dominant DCIS, identifying all 3 cases (100%), compared to 1 out of 3 (33.3%) detected by ultrasound. This highlights the complementary nature of the two imaging modalities ultrasound being superior for invasive masses, while mammography retains its importance in evaluating calcification-based lesions.

These results are detailed in Table 3, which presents subgroup-specific diagnostic performance.

Table 3: Subgroup Performance of Ultrasound and Mammography

Subgroup	Ultrasound Sensitivity (%)	Mammography Sensitivity (%)	Ultrasound Specificity (%)	Mammography Specificity (%)
Age 18–29 years (n = 32)	91.7	66.7	89.3	83.3
Age 30–39 years (n = 58)	93.3	77.8	91.2	87.5
Dense breasts (n = 63)	93.1	72.4	90.0	85.0
Non-dense breasts (n = 27)	91.6	83.3	91.6	88.0

Inter-Reader Agreement: Inter-reader agreement was high for both modalities, though slightly higher for ultrasound. Cohen's kappa for BI-RADS categorization was 0.86 for ultrasound (almost perfect agreement) compared with 0.79 for mammography (substantial agreement). This indicates that ultrasound interpretations were more consistent across radiologists, further supporting its reliability in this younger patient population.

In summary, ultrasound outperformed mammography in sensitivity, NPV, and overall diagnostic accuracy in women under 40 years, particularly in those with dense breasts and in the 18–29 year age group. Mammography, while less sensitive overall, retained value in the detection of microcalcification-dominant DCIS. Thus, the combined use of both modalities provides complementary benefits, with ultrasound as the primary diagnostic tool and mammography as an adjunct in selected cases.

DISCUSSION

The present study highlights that ultrasound outperformed mammography in detecting breast masses among women younger than 40 years, particularly in terms of sensitivity, negative predictive value, and overall accuracy[13]. These findings are in line with the well-documented challenges of mammography in dense breast tissue, which is predominant in younger women. In our study, ultrasound achieved a sensitivity of more than 90% compared with approximately 74% for mammography, reflecting its superior ability to identify solid, non-calcified lesions despite parenchymal density. Mammography, however, retained an important complementary role, especially in identifying ductal carcinoma in situ characterized by microcalcifications, where ultrasound was less reliable[14].

The diagnostic superiority of ultrasound demonstrated here mirrors international evidence. Lehman and colleagues in an American Journal of Roentgenology study reported that ultrasound sensitivity in symptomatic women aged 30–39 years reached 95.7%, compared with 60.9% for mammography[15]. Similarly, meta-analyses have confirmed that ultrasound provides higher lesion-based sensitivity than mammography in younger cohorts, while mammography maintains value in calcification-dominant pathology. These consistencies reinforce the robustness of our findings and underscore the importance of tailoring imaging strategies according to patient age and breast density[16].

From a clinical perspective, the implications of this study are highly relevant. Younger women often present with more aggressive tumor subtypes, and diagnostic delays can worsen outcomes. Ultrasound offers a rapid, radiation-free, and widely accessible modality that not only identifies lesions effectively but also guides real-time biopsies, thereby streamlining diagnostic workflows[17]. In the context of Pakistan and similar low- and middle-income settings, ultrasound is more feasible as a frontline tool due to its lower cost, portability, and absence of radiation risks. This makes it particularly valuable in resource-limited healthcare systems where mammography availability is restricted[18].

Nevertheless, mammography should not be completely replaced in this age group. Our findings, consistent with others, demonstrate that mammography is indispensable when evaluating suspected microcalcifications, subtle architectural distortions, or when ultrasound findings are equivocal[19]. This duality supports the concept that ultrasound should be the primary modality in women under 40, with mammography used selectively as an adjunct when clinical suspicion persists or when certain pathologic features are suspected. Importantly, our subgroup analyses confirm that this approach is especially critical in dense breasts and among women under 30, where mammographic sensitivity is particularly low[20].

Strengths of this study include its prospective, paired design, which allowed direct within-subject comparison of modalities, reducing confounding. Conducting the study across two tertiary centers increases generalizability and strengthens the evidence base for national diagnostic protocols. High inter-reader agreement also attests to the reproducibility and reliability of the results. Limitations, however, must be acknowledged[21]. The sample size, while adequate for detecting significant differences in diagnostic accuracy, was relatively small and may not capture rarer subtypes. Furthermore, verification bias may exist because not all benign lesions underwent histopathology, with some relying on 12-month imaging follow-up. Finally, advanced imaging modalities such as digital breast tomosynthesis or MRI were not assessed, which might have provided additional insights into comparative diagnostic accuracy[22].

Overall, our findings strongly support the integration of ultrasound as the first-line diagnostic modality for women younger than 40 presenting with breast masses, with mammography reserved for complementary use. This pragmatic approach balances diagnostic sensitivity with patient safety, reduces unnecessary radiation exposure, and is aligned with international best practices while also addressing the needs of resource-limited healthcare environments[23,24,25].

CONCLUSION

In conclusion, this study demonstrates that ultrasound provides superior sensitivity, negative predictive value, and overall diagnostic accuracy compared to mammography in women under 40 years of age with breast masses. Mammography, while less sensitive in this age group due to breast density, remains valuable for detecting microcalcification-dominant lesions such as ductal carcinoma in situ. Thus, ultrasound should be adopted as the primary imaging modality in younger women, with mammography used selectively as a complementary investigation in cases of suspected calcifications or inconclusive ultrasound findings. Adopting such an approach can improve early detection, reduce unnecessary radiation exposure, and optimize patient outcomes. In countries like Pakistan, where breast cancer often presents at a younger age and healthcare resources are variable, prioritizing ultrasound as the frontline tool offers a practical, cost-effective, and evidence-based diagnostic pathway.

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Availability of Data and Materials: The datasets generated and analyzed during this study are available from the corresponding author upon reasonable request.

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Authors' Contributions

- **R.K.S.**: Conceptualization, study design, data collection, and manuscript drafting.
- **A.A.**: Patient enrollment, data acquisition, and manuscript revision.
- **F.S.**: Imaging interpretation, methodology development, and analysis.
- **A.T.**: Statistical analysis, literature review, and results interpretation.
- **M.M.**: Supervision, technical input, and manuscript editing.
- **S.M.**: Final review, validation, and approval of the manuscript.

All authors have read and approved the final version of the manuscript.

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