



Original Research

Imaging findings with clinicopathological correlation in breast carcinoma in young women

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Received: 31 July 2025

Accepted: 27 September 2025

Published: 15 December 2025

DOI

10.25259/IJBI_20_2025

Quick Response Code:



ABSTRACT

Objectives: To evaluate the imaging features of malignant breast masses in young females on imaging modalities. To correlate the morphological features of these masses with histopathology and clinical features.

Materials and Methods: A retrospective study was conducted including 369 patients in whom image-guided core needle biopsy was performed between March 2023 and August 2023, out of which 71 patients under 40 years of age had breast carcinoma. The imaging features across mammography, ultrasonography, and magnetic resonance imaging were independently studied according to American College of Radiology Breast Imaging Reporting and Data System Lexicon criteria. The imaging findings were then correlated with clinical parameters and histopathology, immunohistochemistry, and the Ki67 index. Statistical analysis was performed using GraphPad prism software version 9. The chi-square test was used for all lists of proportions, and significance was assumed for p-values < 0.05.

Results: USG was performed in all 71 patients as the first imaging modality. The commonest finding detected on USG was a mass with an irregular shape and non-circumscribed margins, the most common being spiculated margins. Mammography was performed after clinical or ultrasound suspicion of malignancy. The commonest presentation was a mass with high density, irregular shape, and non-circumscribed margins. Microcalcifications were seen in association with other findings in 32% of the cases. However, isolated microcalcification was not seen in any of the cases in our study. Triple negative breast cancer was found to be the most common molecular subtype in our study.

Conclusion: Breast cancer in young women presents unique challenges due to its aggressive biological behavior, lack of screening, and advanced stage at diagnosis. The cancer usually presents as irregular masses with non-circumscribed margins on imaging. Radiologists and breast clinicians should be aware of the suspicious imaging findings of breast cancer in these young women across various modalities, and a high index of suspicion should be present for timely diagnosis and management, especially in those presenting with palpable lumps.

Keywords: Breast carcinoma, Breast carcinoma in young, Breast imaging, Breast radiology, Mammography

INTRODUCTION

Breast cancer in young women, defined as those under 40 years of age, represents a unique clinical entity with significant challenges due to its aggressive biological behavior, advanced stage at diagnosis, and poorer prognosis compared to older women.^[1] While constituting only 10%–11% of all breast cancer cases, young women often present with high-grade, rapidly proliferating

tumors, including triple-negative breast cancer (TNBC) and human epidermal growth factor receptor 2 (HER2)-positive subtypes. These tumors are associated with worse survival outcomes even at early stages.^[2]

Genetic predisposition, particularly mutations in BRCA1 and BRCA2, significantly increases breast cancer risk in younger individuals. BRCA-associated malignancies often manifest as high-grade, triple-negative tumors with unique imaging characteristics and aggressive clinical courses.^[3] However, 90% of early-onset breast cancers occur in non-carriers who are not subjected to screening, thus resulting in a delay in diagnosis.^[1] Pregnancy-associated breast cancer has further contributed to a higher number of breast cancers in the young.

The diagnosis of breast cancer in younger women poses significant challenges due to their dense breast tissue, which reduces the sensitivity of mammography, the standard screening tool. Ultrasonography (US) is often the preferred modality for initial evaluation, while magnetic resonance imaging (MRI) is used for further characterization and presurgical planning.^[4]

The correlation between imaging and histopathological features is essential for early diagnosis and effective management. Imaging findings often provide valuable clues about tumor biology, aiding in differentiation between subtypes and influencing treatment strategies, such as the association of suspicious calcifications with HER2-enriched tumors and round masses with T2 hyperintense central necrosis and rim enhancement with triple-negative cancers.^[1]

This study aims to summarize the imaging characteristics of breast cancer in young women and their correlation with clinicopathological features. By highlighting the diagnostic challenges and the importance of integrating imaging with pathological insights, the article seeks to improve the understanding of this aggressive disease and foster early detection, individualized treatment, and better outcomes.

MATERIALS AND METHODS

This is a retrospective study of 6 months' duration utilizing medical records of the dedicated breast imaging unit. We included women younger than 40 years with BIRADS 4 or 5 lesions on imaging, with core needle biopsy done at our institute, and the specimen evaluated in the pathology department for histology, immunohistochemistry (IHC), and Ki67 index. Females older than or equal to 40 years of age, those with known biopsy-proven malignancy, and those having pathological evaluation done outside our institute were excluded from our study.

A total of 369 image-guided core needle breast biopsies were performed between March 2023 and August 2023, out of which 71 patients under 40 years of age had breast carcinoma.

The clinical parameters evaluated included patient age, clinical presentation, family history of breast cancer, any known high-risk lesions, personal history of breast cancer, and examination findings by the surgeon.

Imaging Evaluation and Interpretation

All 71 patients underwent an ultrasound of both breasts, axillae, and supraclavicular regions; 66 patients had bilateral mammograms; and three had a dynamic contrast-enhanced MRI. US was performed on an Esaote machine using a 4–15 MHz frequency linear probe. In most of the cases, mammograms were performed after ultrasound revealed BIRADS 4/5 lesions. In a few cases, a mammogram was the first investigation done if there was clinical suspicion of malignancy. Routine craniocaudal and mediolateral oblique views with 2D and tomosynthesis were obtained in all cases undergoing mammograms. Other views, like spot compression or magnification, were obtained as needed. The machine used was Hologic Selenia Dimensions, having 3D Digital Breast Tomosynthesis. MRI is not performed routinely at our institute for diagnostic purposes. Only 3 of the 71 patients underwent MRI for the purpose of problem-solving. A three Tesla GE scanner (Discovery 750 w) was used with a dedicated breast coil. Patients were scanned in the prone position. The following are the sequences obtained and the scan parameters used: an axial, turbo spin-echo T2W sequence (TE/TR of 85/6223 ms, flip angle of 111 degrees, FOV 320 mm, matrix 416 × 320 mm, 2 NEX, slice thickness of 4.5 mm, acquisition time of 3 minutes 20 seconds) and a pre- and dynamic post-contrast sequence using the T1W 3D VIBRANT sequence (TE/TR of 2.1/4.3 ms, flip angle of 10 degrees, 1.2 mm slice thickness with no gap, FOV 330 mm, and matrix 320 × 320). Post-contrast images were obtained after a bolus injection of 0.1 mmol/kg of Omniscan (Gadodiamide). All ultrasound, mammography, and MRI findings were retrospectively interpreted by two radiologists. In cases of disagreement, a consensus was reached by discussion. All lesions were evaluated using the morphological criteria described for all three modalities according to the American College of Radiology (ACR) Breast Imaging Reporting and Data System (BIRADS) atlas, fifth edition. We also correlated imaging descriptors with the index tumor grade and molecular subtypes.

Pathological Analysis

Core needle biopsy using 14G automatic or semi-automatic guns was done under ultrasound guidance from BIRADS 4 and 5 lesions. In case of multiple suspicious lesions, biopsy was done from the most suspicious lesion and the most distant lesion from the index lesion. Lesions in both breasts were biopsied using different biopsy guns; to rule out synchronous malignancy. At least five cores were obtained

and transferred in 10% neutral buffered formalin solution to the pathology department for review. The pathological specimens were reviewed by two pathologists with experiences of more than 10 and 8 years, the former having expertise in breast pathology. The specimens were evaluated for the presence or absence of malignancy, histological type, and histological grade. Estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 status were determined using immunohistochemistry. The Allred scoring system was used to determine the ER and PR status.^[5] The results were classified as positive when the total score was more than or equal to 3. For HER2 status, tumors with a 3+ score were classified as HER2 positive, and tumors with a 0 or 1+ score were classified as negative. In equivocal cases (+2), Fluorescent in situ hybridization (FISH) was done to confirm the HER2 status. In our study, antigen Ki67 was also evaluated, which indicates tumor activity. Using the result of immunohistochemistry, the tumors were classified as ER-positive, HER2 enriched, and triple-negative. ER positive were further divided into luminal A and B based on Ki67 activity using a cutoff value of 15%.^[6]

RESULTS

Clinicopathological characteristics

All 71 patients initially underwent clinical examination by a breast surgeon. The mean age was 35.16 ± 3.85 years, and the age range was from 20 to 39 years. Figure 1 shows the distribution of cases across various age groups. Table 1 summarizes the clinicopathological findings of these cases. Four patients had positive family histories in first-degree relatives. Two had a personal history of breast cancer, one in the same breast and the other in the contralateral breast. Almost 92% of the patients presented with a palpable lump ranging from 1.5 to 5.0 cm on clinical examination. Associated findings, including skin thickening and edema, peau d'orange appearance of the breast, skin ulceration, fixity to skin and chest wall, nipple retraction, and ulceration, were seen in 20.3% of our cases. Palpable axillary nodes were seen in 42.2%, and supraclavicular nodes in 12.6% of our cases. 50 (70%) women presented with locally advanced disease at the time of presentation, and 8 (11%) had metastatic disease.

The most common histological type was intraductal carcinoma, no-specific type (IDC-NST), present in 82.4% of the cases, followed by intraductal carcinoma with lobular differentiation, seen in 5.4% of the patients. The incidence of other types has been summarized in Table 1. Most (65.7%) of the patients had grade 1 tumors as per the Nottingham grading system.^[7] 31.4% had grade 2 tumors, and only 2.8% had grade 3 tumors.

Table 1: Clinicopathological features of the 71 women diagnosed with breast cancer on HPE.

Clinicopathological features	Number (%)
Mean age (mean ± SD)	35.16 ± 3.85 (range: 25–39)
High risk	
Positive family history	4 (5.6)
Personal history of breast cancer	2 (2.8)
Clinical examination	
Palpable lump	68 (91.9)
Associated findings	15 (20.3)
Axillary lymph node+	30 (42.2)
SCLN +	9 (12.6)
LABC	50 (70.4)
Distant metastases	8 (11.3)
HPE type	
IDC	61 (82.4)
IDC with DCIS	2 (2.7)
IDC with medullary feature	1 (1.3)
IDC with lobular differentiation	4 (5.4)
DCIS	2 (2.7)
Myeloid sarcoma	1 (1.3)
Metaplastic cancer	1 (1.3)
Mesenchymal tumor	2 (2.7)
Tumor grade	
Grade 1	46 (65.7)
Grade 2	22 (31.4)
Grade 3	2 (2.8)
IHC	
ER+	35 (47.2)
PR+	28 (37.8)
HER2Neu+	17 (22.9)
TNBC	30 (42.6)

SCLN+: Supraclavicular lymph node present, LABC: Locally advanced breast cancer, IDC: Invasive ductal carcinoma, DCIS: Ductal carcinoma in situ, ER+: Estrogen receptor positive, PR+: Progesterone receptor positive, HER2Neu: Human epidermal growth factor receptor 2, TNBC: Triple negative breast cancer; IHC: Immunohistochemistry, HPE: Histopathological examination.

We used the molecular classification of breast cancer as per the Gallen consensus 2011^[8] and divided the breast cancers into the following four types: triple negative breast cancer was seen in 42.6% of the cases, which was the most common type, followed by luminal type A, seen in 35.2%. The other two types were luminal type B (13.2%), and the least common type was HER2 enriched (9%).

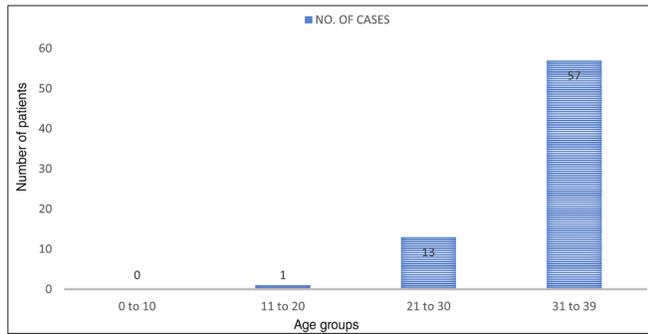


Figure 1: Bar diagram showing distribution of breast cancer cases in our study across various age groups.

Imaging features

Unilateral breast involvement was found in 68 cases, and synchronous malignancies were seen in 3 of the cases, making the total number of breasts with cancer 74. Both breasts had an equal incidence of involvement. Positive ipsilateral axillary nodes were seen in 68.9% of the patients on ultrasound. The frequency of involvement of other lymph nodes is as follows: ipsilateral supraclavicular nodes 18.9%, ipsilateral infraclavicular or level III lymph nodes 18.9%, and contralateral axillary nodal involvement was seen in 8.1% of the cases. The malignancy was multifocal-multicentric in 32 (43.2%) cases. On imaging, skin and nipple involvement was seen in 33 (44.5%) cases, and skin thickening due to infiltration or lymphatic obstruction was noted in 28 (37.8%) cases. All 71 cases were given BIRADS category 4 or 5. BIRADS 5 was the most common final assessment category given in 55 (74.3%) of the cases, BIRADS 4A in 3 (4%), BIRADS 4B in 5 (6.7%), and BIRADS 4C in 11 (14.8%) of the cases. These features are summarized in Table 2.

US

All 71 patients underwent Ultrasound (USG) evaluation, and the findings are shown in Table 3. The mean size of the tumor on ultrasound B-mode was 41.6 ± 21.5 mm. No abnormality was seen on ultrasound in one patient in whom mammography showed an area of architectural distortion. The most common finding was a mass seen in 69 (93.2%) of the 74 breasts. Most of these masses were irregular in shape (60, 81.0%), with a hypoechoic-heterogeneous echo pattern (63, 91.3%), spiculated margins (30, 43.3%), and no posterior features (25, 36.2%) or shadowing (24, 34.8%) [Figures 2-4]. The other less common presentations on USG included dilated ducts (2, 2.7%) and non-mass lesions (2, 2.7%).

TNBC can present as a rounded circumscribed mass with posterior enhancement, which are features of benign tumors. Figure 5a shows a well-circumscribed solid cystic mass with posterior acoustic enhancement. BIRADS 4C category was

Table 2: Associated findings in the 71 females diagnosed with cancer breast on core needle biopsy.

Findings	Number (%)
Positive lymph node	
Ipsilateral axillary	51 (68.9)
Ipsilateral SCLN	14 (18.9)
Ipsilateral ICLN/level III	14 (18.9)
Contralateral axillary	6 (8.1)
Unilateral breast involvement	68 (95.7)
Bilateral breasts involvement	3 (4.2)
Skin/NAC involvement	33 (44.5)
Multifocal/multicentric	32 (43.2)
BIRADS category	
BIRADS 4A	3 (4.0)
BIRADS 4B	5 (6.7)
BIRADS 4C	11 (14.8)
BIRADS 5	55 (74.3)

SCLN: Supraclavicular lymph node, ICLN: Infraclavicular lymph node, NAC: Nipple-areola complex. BIRADS: Breast imaging reporting and data system.

assigned by USG on the basis of the sudden increase in size of the lesion and the presence of suspicious ipsilateral lymph nodes. The lesion came out to be invasive ductal carcinoma, grade 3, TNBC. Figure 6 shows a similar oval-shaped mass lesion with circumscribed margins, internal cystic spaces, and posterior enhancement. Due to the chronicity of the lesion and absence of suspicious lymph nodes, a BIRADS category of 4B was assigned on USG. The lesion turned out to be a benign phyllodes tumor on Histopathological examination (HPE).

Mammography

A total of 66 patients had mammography done, and the findings are shown in Table 4. Most (44, 63.7%) of the breasts were heterogeneously dense as per ACR categories. The most common presentation was mass, seen in 63 (91.3%) of the cases. Most of these masses were irregularly shaped (80.9%), had high density (79.3%), and had spiculated margins (53.9%) in mammography [Figures 2-5]. Other findings included asymmetry and architectural distortion, each seen in three cases (4.3%). Microcalcifications alone were not seen in any of the patients. It was seen in association with mass, asymmetry, or architectural distortion.

MRI

Only 3 out of the 71 patients underwent dynamic contrast-enhanced MRI. 2 of the 3 patients had heterogeneous fibroglandular

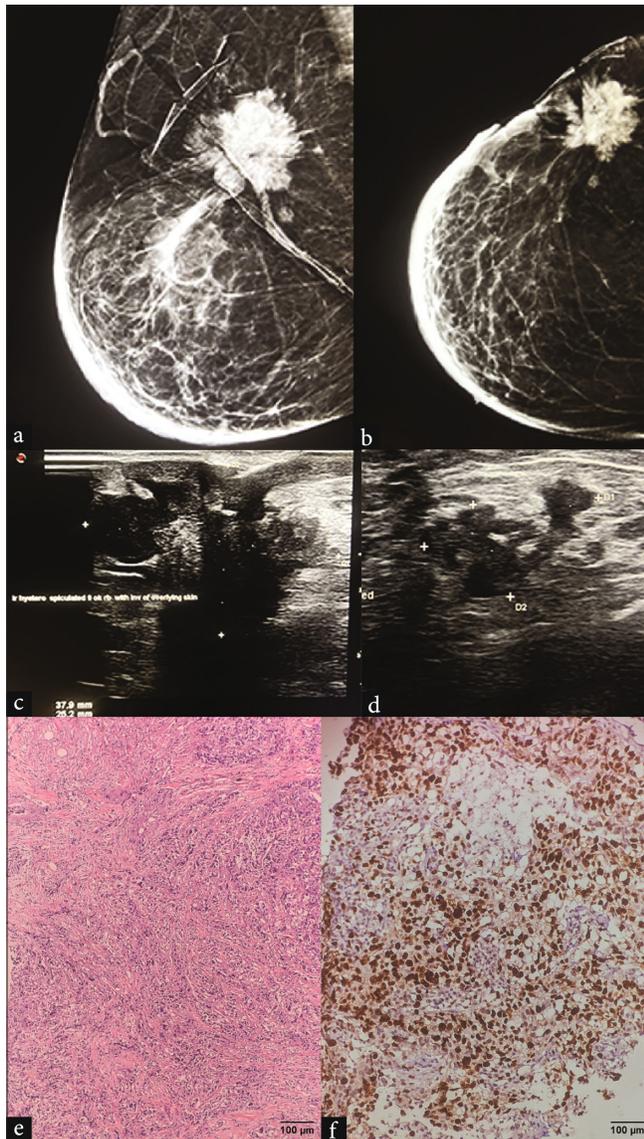


Figure 2: A 38-year-old female presented with a palpable lump in the right breast in the upper outer quadrant. (a-b) MLO and CC view of mammogram of right breast reveal An irregular high-density mass with spiculated margins and associated skin retraction and invasion. Diffuse skin and trabecular thickening noted secondary to lymphatic obstruction. (c) Corroborative grayscale ultrasound shows an irregular heterogeneous mass with spiculated margins and shadowing. (d) USG of the ipsilateral axilla revealed irregular level I lymph node with extracapsular breach. (e) H&E, 20x: grade 3 invasive breast carcinoma, NST. (f) Ki67 labeling index: 70%–80%, grade 3 IBC, NST. MLO: Mediolateral oblique, CC: Cranio caudal, USG: Ultrasound, H&E: Hematoxylin and eosin, NST: Non specific type.

tissue as per ACR categories. The background parenchymal enhancement was mild in two cases and moderate in one case. Two cases presented as masses as shown in Figure 4, and one presented as suspicious non-mass enhancement.

DISCUSSION

Female breast cancer is the most commonly diagnosed cancer worldwide (11.7% of total cases) and in India, surpassing lung cancer.^[9] The incidence of breast carcinoma in women younger than 40 years ranges from 5.6% to 7%^[10,11] in the West to 10%–20% in Asia.^[12] In our study, the incidence of breast cancer in young was 19.2%, which is in accordance with previous data from the Asian population.^[12]

The mean age of the patients in our study was 35.16 ± 3.85 years and ranged from 25 to 39 years. A similar mean age was seen in previous studies.^[13–15]

92% of the cases presented with a palpable lump, which is in line with other studies.^[15–18] Many studies have shown that the imaging features of masses in the young are similar to benign lesions in terms of circumscribed margins, oval shape, and posterior acoustic features. In our study only five patients presented with a mass with an oval shape. All, however, received a BIRADS category of 4A/4B because of non-circumscribed margins, high density, or heterogeneous echotexture and underwent core needle biopsy. Most of the cases had non-benign findings in our study, warranting a higher BIRADS category. An YY *et al.*, in their study, recommended that careful examination of the margins is crucial in oval-shaped masses, as that can decrease the misinterpretation of the masses as benign lesions.^[17]

In general, breast cancer in young women presents in advanced stages.^[19] This is because of a lack of screening in women younger than 40 years and the aggressive biological behavior of the tumors leading to a poor prognosis. The results of this study demonstrated that around 70.4% of the cases were locally advanced, 42.2% presented with lymph node involvement, and 11.3% had distant metastasis at the time of diagnosis.

USG

Similar to previous studies^[16,20,21] ultrasound was highly sensitive (sensitivity of 98.6%) in picking up the abnormalities and showed a negative scan in only one patient, who had architectural distortion on the mammogram. The commonest abnormality on USG was a mass with an irregular shape and non-circumscribed margins, the most common being spiculated margins. This was in congruence with previous studies done by Foxcroft LM *et al.* and Huang J *et al.*^[20,21] The majority of the masses showed either no posterior features or shadowing.

Mammography

Mammography is usually not performed below the age of 40 years because the breasts are dense and obscure findings. In our study, mammography was performed after

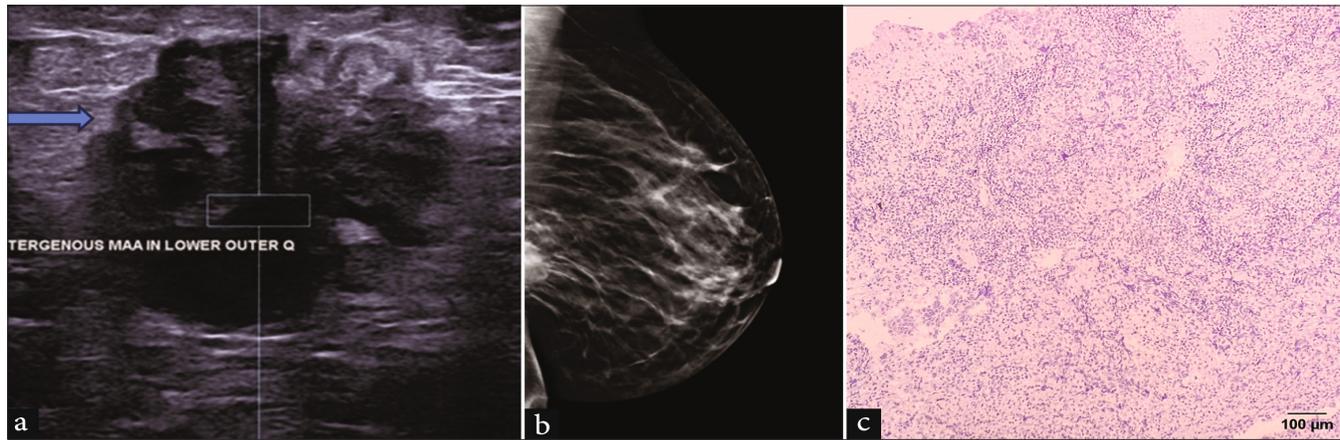


Figure 3: A 33-year-old woman who presented with a palpable lump in the left breast. (a) Grayscale USG image of the left breast shows an irregular shaped, heterogeneous, anti-parallel mass with microlobulated margins (blue arrow) and posterior enhancement. (b) Tomosynthesis slice showed a partially visualized high-density irregular mass in the posterior third of the breast. (c) H&E, 20x: ER/PR: negative (Allred score 0/8), HER2Neu negative in grade 3 carcinoma was found on core needle biopsy of the lump in the above patient. USG: Ultrasound, H & E: Hematoxylin and Eosin, ER: Estrogen receptor, PR: Progesterone receptor.

Table 3: Ultrasound findings in 71 women diagnosed with breast cancer on histopathology.

USG findings (n = 71)	Number (%)
Normal	1 (1.3)
Mean size (mm) (mean ± SD)	41.6 ± 21.53
Mass	69 (93.2)
Others (DE/altered echo/AD)	4 (5.4)
Shape	
Oval	2 (2.8)
Round	1 (1.4)
Irregular	66 (95.6)
Echo-pattern	
Isoechoic	1 (1.4)
Hypoechoic	68 (98.5)
Margins	
Circumscribed	3 (4.3)
Microlobulated	25 (36.2)
Angulated	9 (13.0)
Spiculated	30 (43.4)
Indistinct	2 (2.8)
Posterior features	
PE	10 (14.5)
PS	24 (34.8)
No features	25 (36.2)
Mixed	10 (14.4)

DE: Ductal ectasia, AD: Architectural distortion, PE: Posterior enhancement, PS: Posterior shadowing. USG: Ultrasound.

Table 4: Mammography findings in 66 women diagnosed with breast cancer on histopathology.

Mammography findings (n = 66) (%)	Number (%)
Breast density (ACR)	
A	0
B	11 (15.9)
C	44 (63.7)
D	14 (20.2)
Microcalcifications	
Alone	0
With mass/asymmetry/AD	22 (31.8)
Asymmetry	3 (4.3)
Architectural distortion	3 (4.3)
Mass	63 (91.3)
Margins	
Circumscribed	6 (9.5)
Indistinct	2 (3.1)
Spiculated	34 (53.9)
Microlobulated	21 (33.3)
Obscured	0
Density	
High	50 (79.3)
Equal	13 (20.7)
Shape	
Irregular	57 (90.4)
Oval	5 (7.9)
Round	1 (1.5)

ACR: American College of Radiology, AD: Architectural distortion.

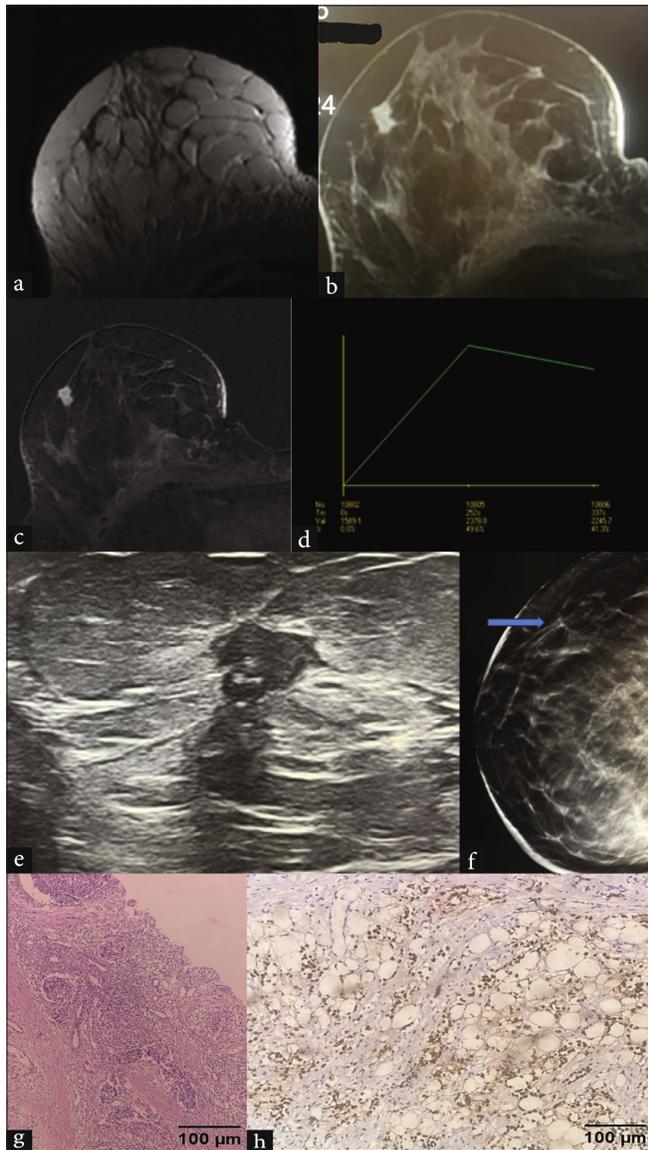


Figure 4: Vague pain as presentation in 39 year old female: Dynamic contrast enhanced MRI revealed an irregular spiculated mass in upper outer quadrant of right breast which was hypointense on (a) T2 and showed heterogeneous enhancement on (b-c) post contrast images with (d) type III kinetic curve. (e) The corroborative USG showed mass as irregular, non-parallel, heterogeneous, spiculated and with no posterior features. It was seen as an area of architectural distortion better appreciated on (f) tomosynthesis. (g) Biopsy confirmed it as invasive ductal carcinoma, NST. H&E, 20x: Photomicrograph showing nests and sheets of tumor cells exhibiting marked nuclear pleomorphism, enlarged nuclei with vesicular chromatin, and increased mitosis—grade 3 invasive breast carcinoma, NST. (h) IHC for ER and PR, 10x: shows ER+/PR+ (Allred score 5 + 3 = 8). MRI: Magnetic resonance imaging, USG: Ultrasound, H&E: Hematoxylin and eosin, IHC: Immunohistochemistry, NST: Non specific type, ER: Estrogen receptor, PR: Progesterone receptor.

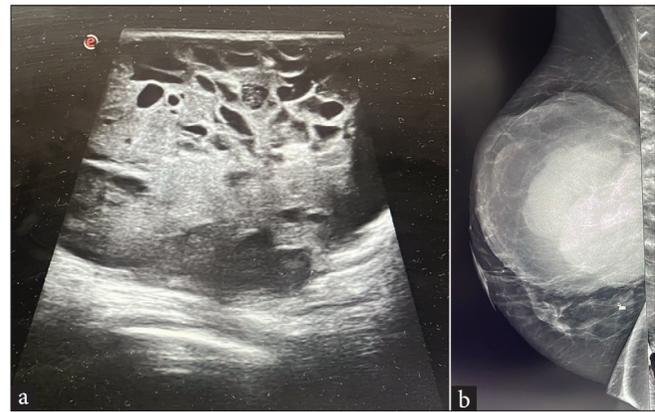


Figure 5: A 25-year-old female presented with a rapidly growing lump in the right breast associated with pain. (a) A grayscale ultrasound of the right breast shows a large, rounded, circumscribed, solid-cystic mass with associated posterior enhancement. (b) The CC view of the mammography shows a large rounded high-density lesion with circumscribed margins occupying all quadrants of the breast. CC: Cranio-caudal.

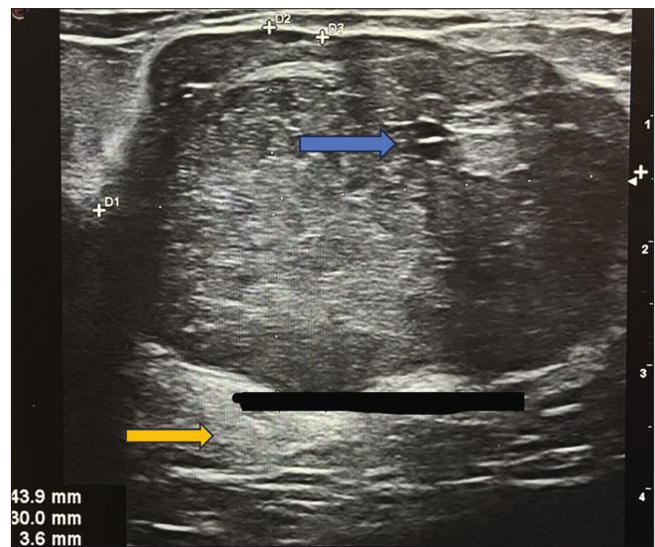


Figure 6: A 37-year-old female presented with a lump in her left breast for 5 years. A grayscale USG of the left breast shows a parallel-oriented oval-shaped lesion with circumscribed margins, heterogeneous echotexture, and posterior enhancement (yellow arrow). Small internal cystic spaces are seen (blue arrow).

clinical or ultrasound suspicion of malignancy. Most of the breasts were heterogeneously dense as per ACR categories of breast densities, as was seen in previous studies.^[17,18,20] The commonest presentation on mammography was mass, which was high density, had an irregular shape and non-circumscribed margins, and was most commonly spiculated. This was in line with previous studies.^[8,13,20–23]

Microcalcifications were seen in association with other findings in 32% of the cases, compared to 26.8%^[17]–49.1%^[18]

seen in other studies. Isolated microcalcification was not seen in any of the cases in this study. One reason for the low number of microcalcifications seen in our study could be the lower number of HER2-enriched molecular subtypes.

MRI

MRI is not routinely performed at our institute for breast cancer before surgeries. It was performed only in three cases in our study and showed a mass in two cases and suspicious non-mass enhancement in one case. The sample size is too low to draw any conclusions.

Molecular Subtypes

As per various studies in the literature, the percentage of TNBCs has been reported to be higher in young patients. This has been corroborated in our study as well, which showed triple negative cancer (42.6%) to be the most common molecular subtype, followed by luminal type A (35.2%).^[12,24] Other studies have reported luminal type A^[14,25,26] and luminal type B^[27] as the most common subtypes in women younger than 40 years. The differences could be attributed to ethnic differences.

Limitations

Our study had certain limitations. Firstly, the sample size was small. Secondly, BRCA mutation testing was not done in any of the patients due to cost constraints. Thirdly, only three patients underwent dynamic MRI, MRI due to logistic issues which also highlights the concerns specific to resource constraint settings.

CONCLUSION

Breast cancer in young women presents unique challenges due to its aggressive biological behavior, lack of screening, and advanced stage at diagnosis. These patients usually present with a palpable mass and at a locally advanced stage. Ultrasound serves as the primary diagnostic modality, demonstrating high sensitivity, with irregularly shaped masses with non-circumscribed margins as the most frequent findings. Despite the challenge of dense breast parenchyma in young women, mammography remains valuable by revealing high-density irregular masses with non-circumscribed margins, as well as detecting architectural distortion, microcalcification, and asymmetry—features that may be missed on ultrasound. Correlation of imaging features with clinicopathological parameters, such as the association of micro-lobulated margins with higher tumor grade and posterior acoustic shadowing with lower tumor grade, enhances diagnostic confidence, helps in assessing prognosis, and guides appropriate management.

Acknowledgement: We would like to acknowledge Dr. Rajeeb Adhikari for his assistance in data collection of this manuscript.

Ethical approval: The study was conducted on a subset of the population recruited under another prospective study with ethical approval number AIIMS/IEC/24/4/8.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship: Nil.

Conflicts of interest: There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation: The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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How to cite this article: Krishnan S, Bhartendu, Syed A, Kaur K, Maharia C, Chowdhury N, *et al.* Imaging findings with clinicopathological correlation in breast carcinoma in young women. *Indian J Breast Imaging*. 2025;3:70–78. doi: 10.25259/IJBI_20_2025