

Diagnostic accuracy of ultrasound in detection of pregnancy associated breast cancer

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¹ Data analysis and interpretation of data drafting

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Article Info.

Conflict of interest: Nil

Funding Sources: Nil

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A B S T R A C T

Introduction: Some unique physiological changes occur in breast volume and water content during pregnancy which makes the radiological evaluation of the breast difficult. As a result, diagnosis of Pregnancy Associated Breast Cancer. is often delayed.

Objective: To find out the diagnostic accuracy of ultrasonography in detection of pregnancy associated breast cancer taking histopathology as gold standard.

Methodology: Present cross-sectional study was carried out at the Department of Diagnostic Radiology of INMOL Hospital, Lahore. Ultrasound of 200 women was performed using the equipment Toshiba Aplio 500. Before the examination, patient was explained about the procedure.

The patient was laid supine and then turned slightly in oblique position to scan the breast with high frequency linear probe (7.5-10 MHz). The contra-lateral breast and both axillae were also scanned in the same way. Findings were categorized on the basis of Breast Imaging Reporting and Data System (BI-RADS) assessment categories. Subsequently the breast tissue was sent to histopathology laboratory for tissue diagnosis. The pathologist was blinded of the results of ultrasonography.

Results: Mean age was 34 ± 11.36 years. Twenty-eight percent patients were primi-para while 72% patients were multi-para. Diagnostic accuracy of ultrasonography taking histopathology as gold standard was analyzed and ultrasonography had sensitivity 84.78%, specificity 98.05%, positive predictive value 92.85%, negative predictive value 95.56% and diagnostic accuracy was 95%. Invasive ductal carcinoma was most commonly observed ($P < 0.001$) malignant histopathology. On the other hand, significantly high ($P = 0.033$) number of benign lesions were Fibroadenomas.

Conclusion: The high sensitivity and specificity along with easy availability, and non-invasive nature makes ultrasonography a very useful technique for the diagnosis of Pregnancy Associated Breast Cancer.

Keywords: Diagnostic accuracy, ultrasonography, pregnancy associated breast cancer, histopathology.

Cite this article as: Mehmood Z, Shahzad R, Fatima I, Shahid A. Diagnostic accuracy of ultrasound in detection of pregnancy associated breast cancer. JSTMU. 2021; 4(1):3-8.

Introduction

Pregnancy associated breast cancer (PABC) refers to the breast cancer which is diagnosed during pregnancy or in the first 12 months' post-partum, or at any time during

lactation. Incidence of PABC is about 300 per million pregnancies. Approximately, 0.2 - 2.5% of all breast cancers are linked with pregnancy.¹⁻³

As childbearing trends are greatly changing and most of the women in recent times delay childbearing until their 30s or 40s. The incidence of PABC may show drastic increase, since old age is already a known risk factor for breast cancer. So, the proper workup of breast related complaints during pregnancy and lactation is becoming increasingly important.⁴

During pregnancy, some unique physiological changes occur in breast volume and water content which make the radiological evaluation of the breast difficult. These underlying changes in breast tissue and the use of imaging with ionizing radiations which is contraindicated during pregnancy may result in delayed detection of PABC. A non-invasive test is required in these situations.⁵ Ultrasonography is considered to be the first-line modality in evaluation of a palpable breast mass during pregnancy or lactation.^{1, 6}

This study aims to determine the accuracy of ultrasound in detecting breast malignancy in pregnant and lactating women of this region as there is scarcity of local data in this regard. This study might prove to be useful in establishing the role of ultrasound in early detection of pregnancy associated breast cancer as ultrasound is an easy, affordable and non-invasive radiological investigation.

Methodology

The present cross-sectional study was conducted at the Department of Diagnostic Radiology, of INMOL Hospital, Lahore during June -December 2019. Sample size was calculated by using sensitivity & specificity sample size calculator (open epi.com) taking sensitivity of the test as 57% with 15% margin of error. Specificity of the test as 81.8% with 85% margins of error and expected prevalence as 14.9%.⁴ Confidence level was set to 95% and precision required was adjusted to 10%. The sample size calculated came out to be 200. Non-probability consecutive sampling technique was used.

Pregnant or lactating women presenting with symptomatic breast (symptoms may include any or all of the following i.e. palpable lump, pain, skin or nipple retraction, nipple discharge) aged between 18-45 years were included. Patients with prior history of breast cancer and patients who were not willing to participate in the study were excluded.

Permission and approval of the study was sought from the hospital ethics committee for conducting the study. Patients were enrolled as per inclusion criteria with prior informed written consent. Ultrasound was performed using the equipment Toshiba Aplio 500. The patient was explained about procedure prior to the examination. The patient was laid supine, arm raised and placed under the head to keep the breast firm on to the chest wall and then turned slightly in oblique position to scan the breast with high frequency linear probe (7.5-10 MHz). The contralateral breast and both axillae were also scanned in the same way. Findings were categorized on the basis of Breast Imaging Reporting and Data System (BI-RADS) assessment categories. BI-RADS category 1 to 3 was labelled as negative for malignancy whereas category 4 and above was labelled as positive for breast cancer (Figure 2 & 3).

Subsequently the breast tissue was sent to histopathology laboratory for tissue diagnosis. Breast tissue which was labelled as benign on histopathology was taken as negative for breast cancer, whereas breast tissue having atypical or malignant cells was taken as positive for breast cancer on histopathology. The pathologist was blinded of the results of ultrasonography. All the gathered information was entered in the proforma.

Data were entered in SPSS version 20. Quantitative variables like age was measured as mean \pm SD. Qualitative variables like symptoms, positive/negative on ultrasound and histopathology was measured as frequency and percentages. A 2x2 Table was constructed to determine the sensitivity, specificity, PPV, NPV and accuracy of ultrasound. Effect modifiers like age, parity, tumour size, BMI were controlled by stratification. Post stratification diagnostic accuracy was measured. Chi square test was applied for the determination of significance in categorical variables. P <0.05 was considered significant.

Results

Mean age was 34 years with SD \pm 11.36. Parity distribution among 200 patients showed that 56 (28%) patients were primi-para while 144 (72%) patients were multi-para and 116 (58%) patients had tumor size >2 cm (Table 1). Status of obesity among 200 patients was analyzed as 90 (45%) patients were non obese while 110

(55%) patients were obese. Patient characteristics are described in Table 1.

Table 1: Patient characteristics

Variable	Subgroup	Frequency (%)
Age	18-30 years	76 (38%)
	31-45 years	124 (62%)
Mean age: 34.0 ± 11.36 (18-45) years		
Parity distribution	Primi para	56 (28%)
	Multi para	144 (72%)
Tumor size	≤ 2 cm	84 (42%)
	>2 cm	116 (58%)
Mean tumor size: 2.0 ± 1.82 cm		
Obesity	Non obese	90 (45%)
	Obese	110 (55%)

Ultrasonography findings for breast cancer among the patients were positive in 42 (21.0%) patients and were negative in 158 (79.0%) patients (Figure 1).

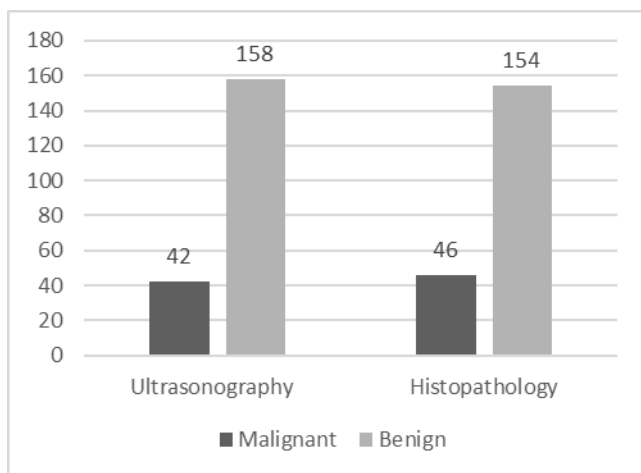


Figure 1: Comparison of ultrasonographic findings with histopathology for differentiating benign and malignant lesions.

Ultra-sonographic features of the patients with PABC histopathologically diagnosed with Invasive ductal carcinoma are shown in Figure 2 & 3. Histopathology was performed for all the patients. Histopathology findings among 200 patients were analyzed and breast cancer was positive in 46 (23.0%) and negative in 154 (77.0%) patients (Figure 1). Out of 42 patients with positive Ultrasonography Findings 3 had negative histopathology results depicting false positivity (Table 2). On the other hands 7 patients with negative ultra-sonographic findings had positive histopathology i.e., false negative (Table 2).

Table 2: Breast Cancer Histopathology Vs Ultrasonography Findings (n=200)

Ultrasonography	Histopathology			
		Positive	Negative	Total
	Positive	39	3	42 (21%)
	Negative	7	151	158 (79%)
Total	46 (23%)	154 (77%)	200	

In malignant patients, Invasive ductal carcinoma (IDC) was the significantly high histological type (P<0.001). It was observed in 39 out of 42 cases (92.85%). Two (4.76%) patients were diagnosed with Invasive Lobular Carcinoma (ILC) and one (2.38%) had medullary carcinoma.

On the other hand, benign lesions (n=158) were predominantly Fibro adenomas i.e., 43 (27.2%) followed by Mastitis/Abscess in 37 (23.4%) and Galactocele in 31(19.6%) patients. Lactating adenomas were seen in 28 (17.7%) and Fibrocystic changes were observed in 19 (12.0%) patients. Statistically significant difference was observed in the presentation of benign lesions too, with P=0.033 applying chi square test.

Diagnostic accuracy of ultrasonography taking histopathology as gold standard was analyzed. Ultrasonography had sensitivity of 84.78%, specificity 98.05%, positive predictive value 92.85%, negative predictive value 95.56% and diagnostic accuracy was 95%. Stratification of diagnostic accuracy of ultrasonography taking histopathology as gold standard was done with respect to age, parity, tumor size and obesity.

Patients were stratified into two groups i.e., 18-30 Years (n=76) and 31-45 years (n=124) with respect to age. It was observed that ultra-sonographic findings were consistent with respect to age. In the patient group 18-30 years, sensitivity, specificity, PPV, NPV and diagnostic accuracy were 83.35, 96.42, 87.5, 95.0 and 93.42% respectively. It was 82.75, 97.89, 92.30, 94.89 and 94.35% respectively in the patients ranging between 31-45 years. Similar observations were made in Primi para and multi para women. In primi para (n= 56), sensitivity of ultrasound was 84.61 vs. 84.84% in multi para in diagnosing PABC. Specificity of the modality was 97.67 vs. 98.19%, PPV remained 91.66 and 93.33% while, NPV and diagnostic accuracy were 95.45 vs. 95.61% and

94.64 vs. 95.13% respectively in both prima para and multi para patients.

Tumor size ≤ 2 cm (n=84) and >2 cm (n=116) was also compared for the determination of any potential difference in diagnostic efficiency of ultrasound in diagnosing PABC. Sensitivity was 84.21 vs. 84.84%, specificity was found to be 96.92 vs. 97.75%, PPV was 88.88 and 91.66%, NPV 95.45 vs. 94.56% and diagnostic accuracy was 94.04 and 93.96% with respect to the tumor size <2 cm and >2 cm respectively.

In non-obese (n=90) and obese (n=110) women, the sensitivity of ultrasound was 80.95 vs. 84.0%, specificity was 97.10 and 97.64%, PPV and NPV were 89.47 vs. 91.30% and 94.36 and 95.40% respectively. Diagnostic accuracy was 93.33 and 94.54% in both non obese and non-obese women respectively. The study shows comparable sensitivity, specificity, PPV, NPV and diagnostic accuracy of ultrasound with respect to above mentioned factors.

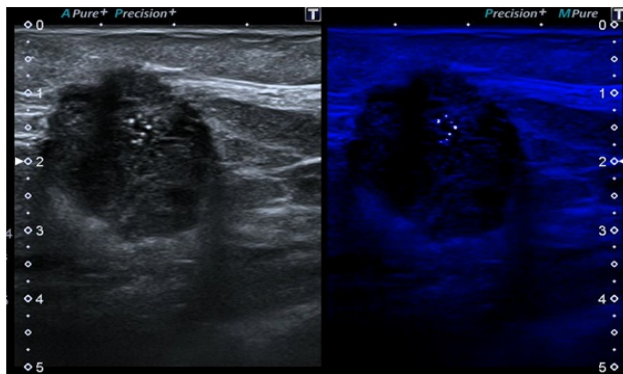


Figure 2: Pregnancy-associated breast cancer in a 34-year-old lactating woman, 7 months' post-partum, presented with a palpable mass in the left breast. Ultrasonography showed an irregular-shaped, hypoechoic mass at 12 o' clock position in left breast with micro lobulated margins and micro calcifications within the mass. Core needle biopsy revealed invasive ductal carcinoma. The patient received neoadjuvant chemotherapy followed by breast-conserving surgery.

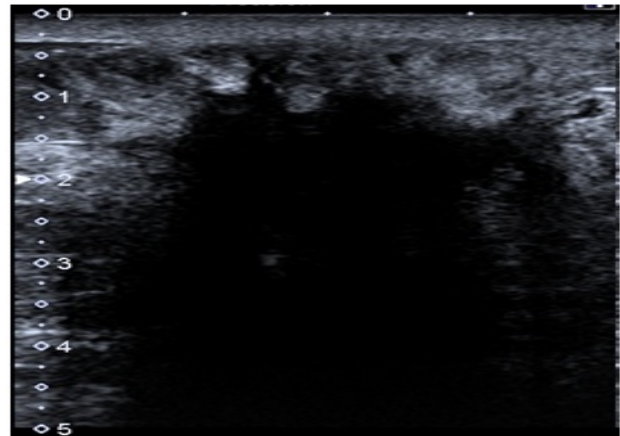


Figure 3: Pregnancy-associated breast cancer in a 38year old lactating woman, 10 months postpartum presented with a palpable mass in her right breast for the prior 2 months. Ultrasonography showed a hypoechoic mass at 10 o' clock position in right breast having irregular infiltrative margins and dense posterior acoustic shadowing. Core needle biopsy revealed invasive ductal carcinoma.

Discussion

Palpable breast mass during pregnancy which resides for more than two weeks should be investigated.⁷ Radio-dense nature of breast tissue during pregnancy or lactation, results in decreased sensitivity of standard diagnostic techniques i.e., mammography. Ultrasound is non-invasive diagnostic technique which was initially used to determine the cystic nature of mass. Its use in detection of breast lesions has increased in recent years. The absence of ionized rays in ultrasound makes it low risk for pregnant and lactating women.⁸

Breast ultrasound is the first-line imaging technique and excellent modality in PABC. It has the highest sensitivity during pregnancy and lactation. If a palpable mass in breast is observed, sensitivity of USG is 100% and specificity is 86% in such cases.⁹⁻¹¹ We have designed our present study to observe the diagnostic accuracy of ultrasound in the detection of PABC. We included 200 pregnant or lactating with symptomatic breast. Mean age of patient population in our study was 34 ± 11.36 years. Average age reported in literature is between 32 to 38 years which is similar to our population.^{4, 12-13}

We have observed PABC in 23% of our subjects and obesity was predominant in our patient population i.e., 110 (55%). Kim et al. conducted a study about clinic pathological features of PABC and also observed that PABC patients were more likely to be overweight (≥ 23.0 kg/m²).¹⁴ Specificity of ultrasound in our study was 98.05%, with NPV, PPV and diagnostic accuracy of 95.56, 92.85 and 95.0% respectively. These values are concordant with literature.^{4, 12-14} Sensitivity of the ultrasound in our study is 84.78% for diagnosing PABC. Wang et al have studied the clinic pathological features and diagnosis of PABC. They have found the sensitivity of ultrasound as 86.0%.¹⁵ Sensitivity of our study is consistent with their study and similar studies who report that PABC usually shows a falsely reassuring pattern on ultrasound. However, the ultrasound is preferred over mammography in PABC. Due to high breast density in PABC mammography is not suitable technique.¹⁶⁻¹⁸

We have observed that diagnostic accuracy of ultrasound is not affected by age, parity, tumor size or obesity. It has shown high sensitivity and specificity of younger to middle aged women. Similarly, in obese or non-obese women the diagnostic accuracy of the modality remained appreciably high. Similar pattern was observed with parity and tumor size.

Our study has a limitation that being a single institution study we could recruit only those patients who were referred to our hospital. Generalization to a larger set of population could not be achieved.

Conclusion

Our study concludes that the ultrasound has high sensitivity, specificity, PPV, NPV and diagnostic accuracy in detection of PABC. It had sensitivity of 84.78%, specificity 98.05%, positive predictive value 92.85%, negative predictive value 95.56% and diagnostic accuracy 95%. The high sensitivity and specificity along with easy availability, low cost, noninvasive and radiation free nature makes ultrasonography a very useful technique for detection of PABC. Moreover, it retains its high diagnostic accuracy with respect to age, parity, obesity and tumor size.

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