RESEARCH ARTICLE

Benign and malignant breast diseases during pregnancy and lactation: a diagnostic challenge

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Abstract

Objective: To determine the frequency of breast cancer associated with pregnancy and lactation, and to evaluate the lesions on ultrasound.

Method: The descriptive, observational study was conducted at the Dow Institute of Radiology, DUHS, Karachi from December 2020 to August 2021, and comprised of pregnant and lactating women with clinically palpable breast lumps and/or painful breast. The margins, orientation, echo pattern and associated features of the lesions were studied on ultrasound and were assigned a Breast Imaging Reporting and Data System grade. All the lumps were followed and ultrasound-guided core needle biopsy for histopathology was done of grades IV and V cases. Incidence and Accuracy of ultrasound for diagnosis of pregnancy-associated breast cancer was estimated. Data was analysed using SPSS 26.

Results: Of the 237 women, 19(8%) were pregnant and 218(92%) were lactating. The overall mean age was 28.4±5.5 years. Ultrasound findings for lactating and pregnant women were significantly different (p=0.05). Significant association of Breast Imaging Reporting and Data System grades III, IV and V lesions with heterogeneous echo texture of mass was seen (p<0.001). Biopsy was performed in 20(8.4%) cases, and 12(60%) of them had benign results on histopathology.

Conclusion: A variety of benign and malignant breast diseases were found in women during pregnancy and lactation phases.

Key Words: Pregnancy, Breast cancer, Lactation, Diagnosis, Ultrasound, Core biopsy

(JPMA 73: 1192; 2023) **DOI: 10.47391/JPMA.6111**

Submission completion date: 01-02-2022— **Acceptance date:** 04-02-2023

Introduction

Breasts during pregnancy and lactation (P&L) phase undergo various changes, including ductal dilatation, glandular hyperplasia, water retention and engorgement due to altered physiology, which hinders in the palpation of small developing lumps.[1] To make matters worse, people have the misconception that breast pain in pregnancy and lactation is due to physiological changes or milk engorgement. Cancer is not the initial differential when facing such discomfort, and if any suspicion is raised it is a substantial emotional challenge for women who is expecting to have, or has just welcomed a new family member. The prevalence of breast cancer (BC) in females is increasing gradually with a shocking change in prevalence among young women.[2] However, there is increased incidence of pregnancy-associated breast cancer (PABC) theoretically because of elevated cortisol, decreased T-lymphocyte and immunoglobulin (IG) levels as well as circulatory and lymphatic hyper vascularisation. PABC, also known as gestational breast cancer (GBC), is defined as the development of breast cancer during pregnancy, in the first postpartum year or later during lactation[3]. PABC is considered to be a rare BC type and only consists of 0.2-0.4% of all BCs.[4] However, it is the most commonly seen cancer during pregnancy and is diagnosed in around 15-35 per 100,000 births.[5]

PABC poses many challenges for patients, clinicians and radiologists. The diagnostic algorithms and strategies have been defined. Mammography is not indicated in pregnancy to avoid foetal radiation exposure, and it fails to detect abnormalities due to increased density of the breasts. Also, adequate compression cannot be made because of engorged breasts.

Ultrasound (US) plays a key role in the detection of PABC, and has been noted to be 100% accurate in detecting a mass in such patients. The sensitivities of US and mammography were reported to be 86% and 83.3%, respectively.[6] There has been a slight overlap among different pathological lesions on US. For example, galactocoele and puerperal sepsis mimics BC, and inflammatory BC closely mimics inflammatory mastitis.

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Therefore, follow-up US and US-guided intervention remain the only means to detect carcinoma. Moreover, close integration of clinician and radiologist is required for early diagnosis with appropriate counselling. A recent study has described detailed sonographic and histological features of all lesions detected during P&L phase, ranging from benign to malignant, and it also highlighted the role of core biopsy for PABC[7].

The current study was planned to determine the incidence of BC associated with pregnancy and lactation, and to evaluate the lesions on US in a tertiary care setting.

Patients and Methods

The descriptive, observational study was conducted at the Dow Institute of Radiology, DUHS, Karachi from December 2020 to August 2021. After approval from the institutional ethics review board, the sample size was calculated using Power Analysis and Sample Size (PASS) version 15 (NCSS, Kaysville, Utah, USA),[8] software, chi-square test for association with 95% confidence of interval (CI), 80% power of the test, 0.4707 effect size with degree of freedom 4, and using association between breast diseases during P&L phase in line with literature[5]. The sample was raised using consecutive non-probability sampling technique from among pregnant and lactating women with clinically palpable breast lumps and/or painful breast who had been referred for radiological evaluation. Patients with known breast lumps whether benign or malignant prior to pregnancy were excluded.

After taking informed consent from each patient, US of breast and axilla was done (Aplio 300) with high-frequency probe by an experienced radiologist having >10 years of experience in women imaging. The margins, orientation, echo pattern and associated features of the lesions were studied on US and were assigned a Breast Imaging Reporting and Data System (BIRADS) grade for lesion characterisation[9]. As defined by the American College of Radiology, BIRADS I is a normal finding, BIRADS II is benign, BIRADS III means <2% risk of malignancy, BIRADS IV means 2-95% risk of malignancy, and BIRADS V implies >95% risk of cancer[9].

All BIRADS III cases were followed up after 6 weeks, while all BIRADS IV and V cases underwent US-guided core needle biopsy (CNB) with 14-gauge needle. The histopathology record was obtained.

Data was analysed using SPSS 26. Continuous variables were presented as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. Association of lactating women with US findings, BIRADS category and axillary lymph nodes (LNs) was checked. Fisher exact test was applied. To see the proportion difference of positive cases from biopsy and histopathology, Mc-Nemar test was used. P<0.05 was considered statistically significant.

Results

Of the 237 women, 19(8%) were pregnant and 218(92%) were lactating. The overall mean age was 28.4±5.5 years. Of the total, 95(40.1%) women were affected on the right side, 77(32.5%) left side, and 65(27.4%) bilateral (Table 1). Besides, 140(59%) women had no mass (Figure 1).

Table-1: Descriptive data.

Characteristics	n = 237 (%)
Age (years)	
Mean ±SD	28.4±5.5
Min – Max	17 – 50
Side	
Right	95 (40.1)
Left	77 (32.5)
Bilateral	65 (27.4)

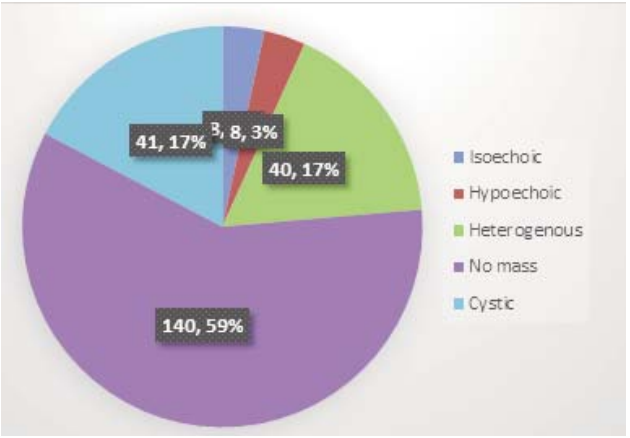

Figure-1: Echogenicity distribution.

Table-2: Clinical characteristics

Clinical Characteristics	n = 237 (%)
Clinical Presentation	
Pain	125 (52.7)
Nodule/lump	75 (31.6)
Swelling	34 (14.3)
Nipple discharge	3 (1.3)
Associated Features	
Skin thickening and oedema	27 (12.3)
Skin thickening	8 (3.7)
Oedema	3 (1.4)
Intra-mammary lymph nodes	1 (0.5)
None	180 (82.2)
Lump Size (length x width) (cm) (n=105) Mean± SD	3.6±2.1 x 2.4±1.6
Ducts Diameter (mm) (n=116) Mean± SD	3.4±1.9

SD: Standard deviation.

More than half the women had pain 125(52.7%), followed by nodule/lump 75(31.6%), and 180(80%) women had no associated features. Mean lump size (length x width) was 3.6±2.1cm x 2.4±1.6cm in 105(44.3%) women, and mean ducts diameter was 3.4±1.9mm in 116(49%) women (Table 2).

Ultrasound findings for lactating and pregnant women were significantly different (p=0.05). Significant association of BIRADS grades III, IV and V lesions with heterogeneous echo texture of mass was seen (p<0.001). There was no significant difference between axillary LNs and lactating women (p=0.540) (Table 3)

Table-3: Association of ultrasound, BIRADS, and axillary lymph nodes (LNs) with pregnant and lactating women.

Parameters	Pregnant (n = 19)	Lactating (n = 218)	Total (n=237)	P-value~
Ultrasound Findings				
Normal	5 (31.3%)	11 (68.8%)	16	0.051
Clear ducts	7 (8.8%)	73 (91.3%)	80	
Ducts with internal echoes	1 (2.8%)	35 (97.2%)	36	
Galactocoele	1 (3.3%)	29 (96.7%)	30	
Fibroadenoma	1 (8.3%)	11 (91.7%)	12	
Abscess	0 (0%)	8 (100%)	8	
Cyst	1 (6.3%)	15 (93.8%)	16	
Collection	0 (0%)	21 (100%)	21	
Suspicious mass	3 (17.6%)	14 (82.4%)	17	
Lactating adenoma	0 (0%)	1 (100%)	1	
BIRADS				
I	6 (42.9)	8 (57.1)	14	<0.001
II	5 (7.2)	64 (92.8)	69	
III	4 (3)	129 (97)	133	
IV	4 (20)	16 (80)	20	
V	0 (0)	1 (100)	1	
Axillary Lymph nodes				
Positive (Enlarge)	2 (4.8)	40 (95.2)	42	0.540
Negative (Normal Size)	17 (8.7)	178 (91.3)	195	

~Fisher Exact Test; BIRADS: Breast Imaging Reporting and Database System.

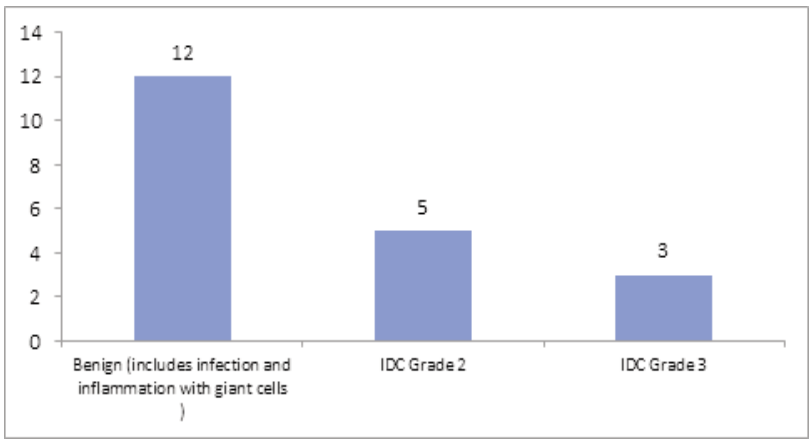

Figure-2: Histopathology findings..

There were 12(5%) Fibroadenoma cases that were labelled BIRADS II when they were interval stable or with coarse, popcorn calcifications, and III on the basis of recent onset, except 1(8.3%) case which was labelled BIRADS IV due to rapid interval increase in size. Biopsy was performed in 20(8.4%) cases, and 12(60%) of them had benign results on histopathology. Among the malignant cases, 5(62.5%) had infiltrating ductal carcinoma (IDC) grade 2, and 3(37.5%) had IDC grade 3 (Figure 2).

Discussion

In the past few years, quite a high incidence of PABC has been noted at the tertiary care centre even though it is a rare disease. This provoked the researchers to plan the current study. Diagnosis of BC among women in P&L phase is challenging for both clinicians and radiologists. The mean age of patients in the current study was 28.4 years which is close to a recent study which reported 30.3 years.[6]

The incidence, epidemiology, and sono-pathological features of lesions during P&L detected on US was observed in the current study. In prior studies, the incidence of PABC was estimated to be between 0.2% and 3.8%, and was reported to occur in 1:10,000 to 1:3,000 pregnancies.[10] The current study found an incidence rate of 3.4%. A recent study in Pakistan reported PABC incidence of 4.56% in 899 diagnosed BC cases.[11]

In 2016, Bano et al. reported 29.8% incidence of PABC[12]. The delay in childbearing to the 30s or 40s either due to personal or professional reasons is a key factor behind increasing incidence of PABC.

The most common presentation in the current study was pain (52.7%). This nonspecific symptom causes delay in consultation and diagnosis. The second important presentation was palpation of lump (31.6%). The nodularity, tenderness and hormonal changes of the parenchyma during P&L hinders the diagnosis of the palpable mass.[13,14] The mean size measured on US was 3.6cm which also shows the aggressive nature of the disease and the consequence of the delayed diagnosis.

A comparative study of 206 pathologically confirmed breast lesions over 8 years in

both pregnancy and non-pregnancy groups reported a variety of lesions.[15] Compared to non-pregnancy cases, overall benign lesion diameter and higher BIRADS grade for fibroadenomas and mastitis/abscesses were detected in the pregnancy group[15]. In the study, galactocoele was the most common benign lump and all lesions were clinically more evident in the lactation phase because of pronounced hormonal changes and secretory phase of breasts.

A recent international study said the most common BC type in pregnancy was IDC, and pregnancy-associated malignancies had more aggressive behaviour.[16]

In recent literature, different benign lesions have been reported, including galactocele, fibroadenoma and lactating adenoma[7]. In the current study, overlapping clinical features of benign and malignant lesions were found. CNB is the gold standard for PABC diagnosis with sensitivity up to 90%. In literature, most common histological type of breast carcinoma during P&L is IDC in aggressive pattern, which is not different from BCs in non-pregnant women. Majority had higher incidence of grade 3 tumours (40-95%) with lympho-vascular invasion and oestrogen receptors (ER) negativity. In one PABC study, human epidermal growth factor receptor 2 (HER2-neu) positivity was seen in a higher percentage of cases.[17] In the current study, HER2-neu, ER and progesterone receptor (PR) status was not analysed.

Typical US features of PABC, like hyper-vascular irregular solid mass, were described in a case report of a 40-year-old woman with 36 weeks of gestation[18]. In the current study, BIRADS IV and V lesions had heterogeneous echo texture. Langer et al. also emphasised that all the benign lesions, such as galactocele, adenoma and breast abscess, can have overlapping features with PABC; each needs to be followed up and intervened until the suspicion of malignancy has been eliminated.[19]

Masroor et al. studied 282 patients who underwent CNB, and reported that 60.9% and 37.2% of breast lesions were concordant malignant and benign, respectively, and 0.7 and 0.3% were discordant malignant and benign, respectively[20]. In the current study, diagnostic accuracy and concordance / discordance for breast lesions was not calculated because of limited number of biopsies performed, which is a limitation. Another limitations of the current study is that it did not cover management and treatment of patients with benign and malignant diseases. Further research needs to be done in this regard.

Conclusion

Variety of benign and malignant breast diseases were found in women in the P&L phase. Possibility of BC should also be considered during the phase. US and CNB are the best tools for the assessment of breast lumps in P&L phase.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

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