Cross-sectional study of mammographic breast density of Pakistani women and its association with breast cancer

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Abstract

Objective: To explore if a positive association existed between breast cancer and increased breast density.

Method: The retrospective cross-sectional study was conducted at Shifa International Hospital, Islamabad and comprised data from July 10, 2018, to July 10, 2020, of all patients who underwent mammography for screening or diagnostic purposes. Data was collected by reviewing patients' charts, and was divided into diagnostic group A and screening group B according to mammography target. Breast Imaging Reporting and Data System category was also noted. Data was analysed using SPSS 21.

Results: Of the 1,035 women with mean age 46.8±2.5 years (range: 35-82 years), 928(89.7%) were in group A and 107(10.3%) were in group B Prevalent breast densities overall were category A 67(6.3%), B 349(33.7%), C 530(51.2%) and D 89(8.5%). In group A, a lump was detected in 542(58.4%) patients. Of them, 367(67.7%) lesions were malignant and 175(32.3%) were benign. Breast density and malignant tumours had significant association (p<0.05).

Conclusion: Mammographic breast density wsa found to have a significant association with breast cancer.

Key Words: Breast density, Bcancer, BIRADS, Malignant, Mammography.

Introduction

With the establishment of breast cancer (BC) registries in Asia, the BC burden is being more accurately reported.[1] Therefore, the difference in BC incidence in Asian and Western countries is reducing.[2] In Asian countries, age-related BC incidence is the highest.[3] Compared to its neighbouring countries, the BC incidence in Pakistan is about 2.5 times greater, with one in every 9 women at risk of being diagnosed with BC in her lifetime.[3-5] The International Agency of Research reported 34,066 new BC cases in Pakistan in 2018. This increased incidence is coupled with advanced stage and increased mortality.[6, 7] This difference is most likely due to variations in the biological expression of aetiological factors.[7,8] In addition to the well-established risk factors for mammographic breast density, measures of epithelium and stroma have been reported as significant factors for BC by several systematic reviews, with majority of studies in such reviews having been performed in the West on white women, but breast density may be different in different races.[9,10] There are significant differences in mammographic breast density (MBD) measures in various ethnicities of the world probably because of some genetic basis.[9,10] In younger women, BC usually develops in extremely dense breasts. Because of lower sensitivity of the test in younger women with dense breasts, presentation is delayed till locally advanced stages.[9, 10]

The current study was planned to explore if a positive association existed between BC and increased breast density in the local context.

Patients and Methods

The retrospective cross-sectional study was conducted at Shifa International Hospital, Islamabad and comprised data from July 10, 2018, to July 10, 2020, of all patients who underwent mammography for screening or diagnostic purposes. After approval from the institutional ethics review committee, the sample size was calculated using Raosoft calculator.[11] Data was collected by reviewing patients' charts after taking consent from the patients through telephone calls.

Data retrieved related to female patients aged >35 years who underwent mammography for screening or diagnostic purposes. None of the mammographies were done exclusively for the current study. Data excluded related to cases with bilateral synchronous BC, and cases in which a screen-film mammogram without radiological signs of cancer were not available. Data of patients who had had mastectomy, breast implants or reduction mammoplasty was also excluded.

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MDB assessment was performed by an experienced radiologist using the standardised clinical assessment form using the American College of Radiology's Breast Imaging Reporting and Data System (BIRADS) classification categories A, B, C and D, where C and D are considered dense.[11] In the event of discordance in the density of the right and left breast, the case was classified according to the higher density classification. Oblique, medio-lateral and cranio-caudal views of both breasts were used for mammographic assessment.

The data was collected using a predesigned proforma. Breast density was recorded along with age, family history, size of tumour and histopathology reports. The data was divided into diagnostic group A and screening group B according to mammography purpose and target.

Data was analysed using SPSS 21. Data was expressed as frequencies and percentages or means and standard deviation, as appropriate. For evaluation of association between BC and MBD, logistic regression analysis was used. P<0.01 was considered statistically significant.

Results

Of the 1,035 women with mean age 46.8±2.5 years (range: 35-82 years), 928(89.7%) were in group A and 107((10.3%)
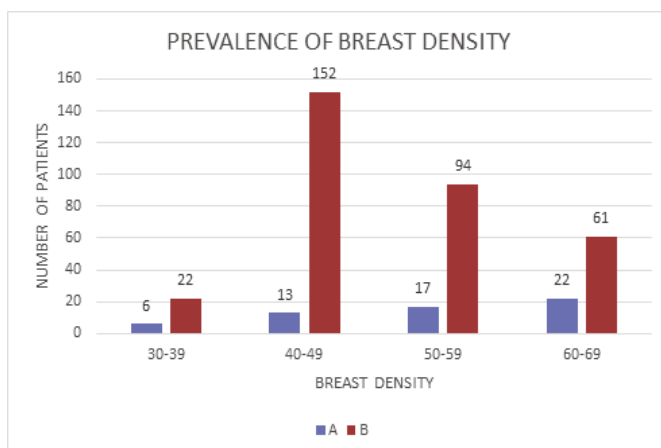

Figure-1: Breast density

were in group B. Prevalent breast densities overall were BIRADS category A 67(6.3%), B 349(33.7%), C 530(51.2%) and D 89(8.5%) (Figure 1). Positive BC family history was found in 255(24.6%) patients. Breast density was also compared in terms of age and bodymass index (BMI), and BIRADS C was the most common category, followed by BIRADS B (Table 1).

In group A, a lump was detected in 542(58.4%) patients, while 386(41.5%) had no lump. Also, 429(79%) patients underwent stereotactic or ultrasound-guided core biopsy for breast lumps, 105(19.5%) had fine needle aspiration cytology (FNAC) followed by excision biopsies, and 8(1.5%) had incisional biopsy. Of them, 367(67.7%) lesions were malignant and 175(32.3%) were benign.

There was significant association of breast density with malignant lesions (p<0.05) (Table 2). Patients with either benign or malignant lesions had
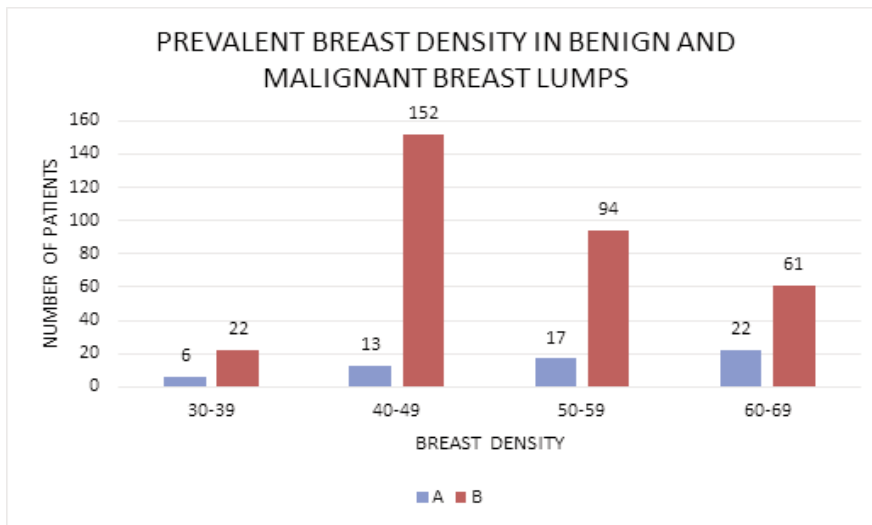
Table-1: Association of breast density with age, family history and body mass index (BMI) (n=1035).

Breast density	Variables	Type A (67) (6.3%)	Type B (349) (33.7%)	Type C (530) (51.2%)	Type D (89) (8.5%)
Family history					
	Positive (n=255) (24.6%)	21(8.2%)	67(26.2%)	133(52.1%)	34(13.3%)
	Negative (n=780)(75.3%)	46(5.8%)	282(36.1%)	397(50.8%)	55(7.5%)
Age					
	30-39 years (n=134)(12.9%)	6(4.4%)	22(16.4%)	75(56%)	31 (23.1%)
	40–49 years (n=433)(41.8%)	13(3%)	152(35%)	221(51%)	47(11%)
	50-59 years (n= 257)(24.8%)	17(7%)	94(36.5%)	135(52.5%)	11(4.2%)
	60–69 Years (n=163)(15.7%)	22(13.4%)	61(37.4%)	80(49%)	0(0%)
	>70years (n= 48) (4.6%)	9(19%)	20(42%)	19(40%)	0(0%)
BMI					
	<25 (n=278)(27%) 16(5.7%)	93(33.4%)	143(51.4%)	27(10%)	
	25–29 (n=396)(38.2%)	29(7.3%)	136(34.3%)	205(52%)	34(9%)
	30+ (n=345)(33.3%)22(6.3%)	120(35%)	182(53%)	28(8.1%)	

Table-2: Association of breast density with histopathology (n=542).

	BIRADS A	BIRADS B	BIRADS C	BIRADS D	p-value
Histopathology					
Benign (n=175) (32.2%)	10 (5.7%)	56 (32%)	87 (49.7%)	22 (12.5%)	<0.01
Malignant (n=367) (68%)	19 (5.1%)	138 (37.6%)	193 (52.5%)	17 (4.6%)	<0.01
Ductal Carcinoma in Situ 5 (1.3%)	1 (20%)	2 (40%)	2 (40%)	0	<0.01
Invasive Mammary Carcinoma 345 (94%)	17 (4.9%)	134 (38.7%)	182 (52.4%)	14 (4%)	<0.01
Invasive Lobular Carcinoma 17 (4.6%)	1 (6.6%)	6 (35.2%)	9 (52.9%)	1(6.6%)	<0.01

BIRADS: Breast imaging reporting and data system.

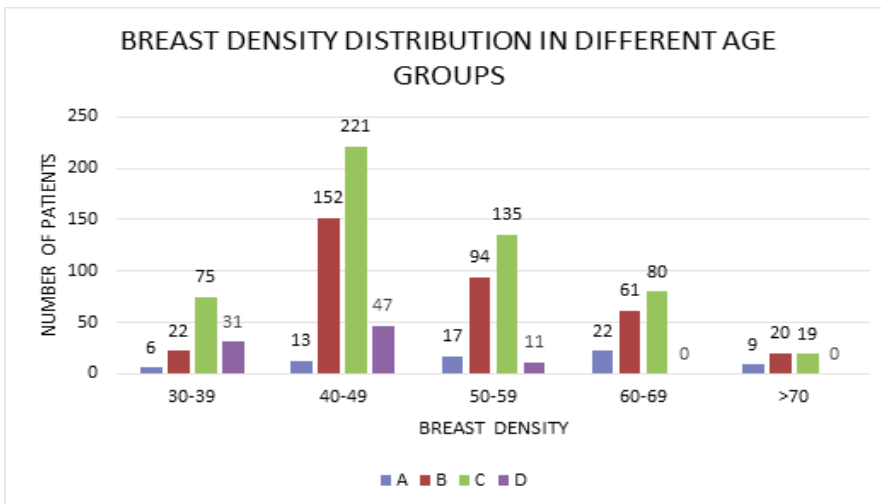**Figure-2:** Breast density in benign & malignant breast lumps.

Figure-3: Breast density across age groups

increased breast density (Figure 2), with BIRADS C being the most common category. BIRADS C was the most frequently reported breast density in patients aged 40-60 years (Figure 3).

Discussion

In 2012, the annual age-standardized incidence rate (ASIR) for BC stood at 43.3/100,000 females at the global level, and at 50.3/100,000 in Pakistan.[12] Idrees et al. in their meta-analysis showed BC incidence in different areas of Pakistan ranging from 20% to 50%.[13] The difference in incidence could be mainly because of genetic differences in the study populations. Factors responsible for this high incidence are unknown and need to be investigated.[12] Hisam et al. showed that BC

developed in most Pakistani women despite having protective factors against BC, like menarche after 12 years (92.5%), menopause before 50 years (88.8%), age at first full-term pregnancy <35 years (98.8%), nulliparity (10%) and positive breastfeeding (77.5%). Hormone replacement treatment (HRT) was absent in all 100% patients of the study.[14]

The concept of MBD as a BC risk factor was first proposed in 1976.[15] Women with high MBD have more stromal and epithelial cells and less fatty adipose tissue, and are more likely to develop BC in their lifetimes compared to women with low MBD.[16-18] The current retrospective study investigated the mammographic density patterns, and assessed its significance as a BC risk factor. To our knowledge, the current study is the first in Pakistan to explore MBD as a risk factor for BC in Pakistani women.

Mariapun et al. studied differences in percent mammographic density among Asians of different ethnicities living in the same region. In contrast to postmenopausal women, differences in MBD of premenopausal women of various ethnic groups were independent of age, BMI and parity. The difference in MBD of various ethnic groups may have a genetic basis.[19] In the current study, the most prevalent breast density in patients diagnosed with malignant breast lumps was BIRAD C (52.5%), followed by BIRAD B (37.6%). Women with a higher breast density are 4- to 6-fold more likely to develop BC than those with low breast density.[20] Women presenting with locally advanced BC having positive lymph nodes (LNs) were found to have higher breast density.[21] In Asia, Pakistan has the highest BC incidence and yet there is a scarcity of studies investigating MBD as a risk factor in the local population.[22] In Pakistan, BC patients mostly present at advanced stages either because of delayed presentation or because of aggressive tumour behaviour.[23] A meta-analysis of studies carried out in the United States, Europe and Canada found a significant increase in the risk associated with more

extensive percent mammographic density (PMD) after adjustment for other risk factors.[24] Mammographic density shows individual differences and is strongly affected by age, BMI, hormonal status and parity. With advancing age, obesity, menopause and increased parity, epithelial and stromal tissues in the breasts are replaced with fat, and these histological changes are reflected in the mammographic images.[25] The current study population had higher breast density in all age groups (Figure 3), and the study was able to establish higher breast density as a BC risk factor (Table 1). In the current study, patients aged 45-55 were most commonly diagnosed with malignant breast lump. Patients in this age group were found to have higher breast density irrespective of their age, family history and BMI. Park et al. demonstrated that there was a 5-time higher risk of developing BC in women with extremely dense breasts compared to women who had entirely fatty breasts,[26] showing increased breast density as an independent BC risk factor irrespective of age or menopausal status. However, the association of breast density with BC risk was greater in younger, premenopausal women.[27]

The current study has several limitations as it was hospital-based and was done at a single centre. While the study fund MBD to be a BC risk factor, further studies are required to determine if it is an independent risk factor.

Conclusion

There was a positive association between increased absolute breast density measured by mammography and breast cancer in Pakistani women. Prevalent breast density in the population was BIRADS C across all age groups.

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Conflict of Interest: None.

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