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Research Article

A Comparative Analysis of Breast Density between Normal and Carcinoma Breast Cases

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Abstract

Introduction: *Breast has always been a symbol of womanhood. As a result, both disease and surgery of the breast evoke a fear of mutilation and loss of feminity. Breast cancer is the most side specific cancer in the women and accounts 33% of female cancer[1], and is responsible for 20% of the cancer related deaths in women[2]. Investigators have identified mammographic breast density as a novel independent risk factor (four-to-six fold increased risk) for breast cancer[3]. The purpose of this study was to comparatively analyse Breast Density between Normal and Carcinoma Breast cases above 40 years of age in Indian Setup as characteristics of women's breast density are poorly understood in India.*

Materials and Method: *The present study comprised of 60 patients with various breast complaints. All patients were subjected for mammography/BIRADS staging and classified for breast density as Type A,B,C or D. The patients with BIRADS 4-6were further subjected for trucut biopsy. The patients were thus divided into Group A (Carcinoma) and Group B (Benign) patients. Comparative analysis of Breast Density between Normal and Carcinoma Breast cases was done.*

Results: *In the present study, among all the age groups (ranging between 40 to 80 years) the breast density was found to be Type B in majority of the patients in both the groups(A and B). On comparing the proportion of Group A and Group B with density B it was found to be statistically non significant (P value 0.78)*

Conclusion: *Although breast density is one of the most important risk factors of breast cancer [4], the effect of breast density itself in this study was not significant and the point estimate was much lower than previous meta-analysis which showed about four-six fold increment of breast cancer risk [5].The present study highlights the need for Individualized breast cancer screening guidelines that are appropriate for patient age, breast density, and overall risk for breast cancer. Further studies of women of various ages and risk categories are sorely needed to clarify this important public health issue.*

Keywords: *Breast cancer; mammographic breast density; cancer risk.*

Introduction

Breast has always been a symbol of womanhood. As a result, both disease and surgery of the breast evoke a fear of mutilation and loss of feminity. Breast cancer is the most frequent cancer in women worldwide representing 33% of all malignancies amongst females[1]. Breast cancer is also the second leading cause of death among

women and is responsible for 20% of the cancer related deaths[2]. Screening Mammography has the distinct capabilities of detecting non-palpable lesions thus identifying very early breast cancer lesions[5].The ever rising mortality rate despite of increased awareness and widespread use of mammography has opened avenues for evaluation of factors predicting tumour progress which in turn are necessary to develop adequate therapy regimes for different types of breast cancer[6].

Dense breasts contain more fibrous and glandular tissue (which shows up breast conditions are denser than fat and also appear white on a mammogram)[7]. Mammographic densities reflect the tissue composition of the breast[8]. In general, women of child-bearing age tend to have denser breasts than postmenopausal women. Breasts that are denser may be harder to successfully screen for early signs of tumour genesis, since the white of the fibrous tissue can mask an emerging cancer. Breast density is an important risk factor for breast cancer. Increased density is not only a risk factor for breast cancer, but it results in reducing the sensitivity and specificity of mammography[9]. Breast density on mammography, is determined relatively with measured breast fat and fibro glandular tissue and also in dense breast tissue breast cancer risk is increased 4-6 times more than in non-dense breast tissue[10].

The epidemiology of mammographic density is consistent with its being a marker of susceptibility to breast cancer. It is the intention of the present study to evaluate the association between CA Breast incidence and Breast Density in Indian setup.

Materials and Methods

Comparative prospective hospital based study was conducted in a tertiary health centre of northern India for 12 months after ethical approval and obtaining informed written consent. Patients presenting with the symptoms of breast lump, breast pain, swelling and nipple discharge were included in the study. A total of 60 patients were included and evaluated in this study. Basic Parameters recorded in all patients were age, chief complaint and BMI (Body Mass Index). All patients were thereafter subjected for mammography. Breast density was determined by using Breast Imaging-Reporting and Data System (BI-RADS). Breast density measured by BI-RADS was further classified into 4 Types on the basis of breast composition:-

Type A (0%-25%): mostly fatty breast,

Type B (25%-50%): fibro glandular breast,

Type C (50%-75%): heterogeneously dense breast, and

Type D (75%-100%): extremely dense breast.

Patients with BIRADS 4,5 & 6 were subjected as per BIRADS guidelines for FNAC/Trucut Biopsy. These patients were then divided into two groups: Group (A) included 30 patients with biopsy proven carcinoma of the breast; Group (B) included 30 patients with benign breast lesions or pain breast. Patients less than 40 years, who had undergone any prior Breast surgery or had received Radio-therapy, were excluded from this study. The relevance of result in the light of statistical analysis was displayed and discussed.

Observations

Age

The age of the patients enrolled in the present study varied from 40 years to 80 years. The mean age of patients presenting in Group A was 55.4±10.9 years and the mean age of the patients presenting in Group B was 54±9.84 years respectively.

BMI

In Group A, the BMI of patients ranged between 18.1 kg/m2 to 31.2 kg/m2 with average BMI of 24.8kg/m2 with SD of 3.17.In Group B, the BMI of patients ranged between 19.4 kg/m2 to 27.8 kg/m2 with average BMI of 24.43kg/m2 and SD of 2.17.

BIRADS

In Group A of 30 patients, 10 patients (i.e.33.3%) were BIRADS 4, 14 patients (46.7%) were BIRADS 5 and 6 patients (20%) were BIRADS 6.

All of the 30 patients were subjected for Trucut Biopsy and Histopathological examination. In Group B of 30 patients, 6 patients (i.e.20%) were BIRADS 1, 12 patients (40%) were BIRADS 2 and 12 patients (40%) were BIRADS 3. Out of 30 patients 24 patients were subjected for FNAC whereas 6 patients with BIRADS 1 were not subjected for FNAC.

Biopsy

In Group A of 30 cancer patients Trucut biopsy was done in all and 27 patients were diagnosed with duct cell carcinoma (90%) while 2 patient were reported as lobular carcinoma (6.7%) and 1 patients was diagnosed with tubular carcinoma(3.3%).In Group B out of 30 patients, 2 patients (6.7%) were diagnosed as acute mastitis, 19 patients (63.3%) were diagnosed as Fibroadenosis, 3 patients (10%) were diagnosed as Fibroadenoma, and 6 patients (20%) were not subjected for FNAC due to BIRADS 1 on mammography.

Breast Density

In Group A of 30 cancer patients, 5 patients (16.7%) had breast density of Type A i.e. mostly fatty, while majority of patients i.e 21patients (70%) had breast density of Type B i.e. scattered fibro glandular density and 4 patients (13.3%) had breast density of Type C i.e. consistently dense whereas no patient had Type D density. In Group B, 2 patients (6.6%) had breast density Type A i.e. mostly fatty , while majority 20 patients(66.7%) had breast density Type B i.e. scattered fibro glandular density while in 8 patients (26.7%) the breast density was Type C i.e. consistently dense whereas no patient was of Type D density in this group also(Table No 1).

P Value and Z score

On comparing the proportion of Group A and Group B with density A it was found to be statistically non significant (z score 1.21 and p value 0.23). The proportion of density B was found to be statistically non significant (z score 0.28 and p value 0.78) similarly the proportion of density C was also found to be statistically non significant (z score -1.29 and p value 0.19) (Table no. 2)

Table No. 1

BREAST DENSITY	Group A		Group B	
	No. of Patients	Percentage	No. of Patients	Percentage
A	5	16.7 %	2	6.6 %
B	21	70 %	20	66.7 %
C	4	13.3 %	8	26.7 %
D	0	0 %	0	0 %
Total	30	100 %	30	100 %

Table No. 2

DENSITY	Group A	Group B	Z SCORE	P VALUE
A	5	2	1.21	0.23
B	21	20	0.28	0.78
C	4	8	-1.29	0.19
D	0	0	-	-
TOTAL	30	30	-	-

Discussion

Mammographic breast density is well known and one of the most important non-modifiable risk factors of breast cancer, which increases breast cancer risk by about five times for those with percent density ≥ 75% compared to women with percent density ＜5%[11]. Increased breast density as identified on mammography is also known to decrease the diagnostic sensitivity of the examination, which is of great concern to women at increased risk for breast cancer. Dense tissue has generally been associated with younger age and premenopausal status, with the assumption that breast density gradually decreases after menopause. However, the actual proportion of older women with dense breasts is unknown.

With postmenopausal alteration of glandular breast tissue, the expectation is that the density of a woman's breasts will decrease with increasing patient age. This relationship is generally observed between breast density and age. However, few studies have characterized the incidence of heterogeneously dense or extremely dense tissue in older women.

Breast density is a measurement of the ratio between radio dense epithelium and stroma to radiolucent fatty tissue. Breast density is a mammographic finding not related to the perceived density of breast tissue on palpation. It

is possible to predict with considerable accuracy which women will develop breast cancer and equally important, those who are less likely to develop it based solely on the parenchymal pattern as seen by mammography. Information about breast density enhances the clinician's appreciation of the sensitivity (or lack thereof) of the mammographic examination for an individual patient. It is also possible that breast density reflects characteristics of the stromal component that have not yet been elucidated.However, characteristics of women's breast density are poorly understood in Indian setup.

Age

Maximum patients in this study were in the age group of 40-60year with 45(75%) out of 60 patients in both groups. Both the groups were comparable in terms of mean age of presentation. In another study by Lim Se-Eun et al[12] (2019) the average age for presentation for mammography cases was 46.86 years for study and 48.51 years for controls respectively. This too is comparable with the results of the present study showing maximum females seek hospital care for their ailments in the middle age group whether pathology is benign or malignant.

Complaints

28 patients (93%) with malignant pathologies in breast had lump breast as presenting complaint while 15 patients with benign pathology had breast pain (50%) as their predominant complaint at the time of presentation followed by lump breast in 10(33.33%) patients.

BMI

In Group A, majority of patients i.e 15 were in BMI between18.5-25 kg/m2 (Normal), whereas in Group B majority of patients' i.e 17 patients had BMI between 18.5-25 kg/m2 (Normal) . BMI in both study groups were comparable. Several studies by Yaghjyan .L et al [13] (2015) have revealed that the effect of mammographic density as a non-modifiable factor could be modified by other known breast cancerrisk factors, such as family history, reproductive factors, behavioral factors, or body mass index (BMI) .

BIRADS

In present study with Group A of 30 cancer patients, 10patients (i.e.33.3%) were BIRADS 4, 14 patients (46.7%) were BIRADS 5 and 6 patients (20%) were BIRADS 6 with all patients being subjected for Trucut Biopsy. Similarly In Group B , 6patients (20%) were BIRADS 1, 12 patients (40%) were BIRADS 2 and 12 patients (40%) were BIRADS 3.The density values were almost equally distributed between the lower (BIRADS 1&2) (60%) and upper (BI-RADS 3&4) (73.3%) groupings. BIRADS rating was a strong predictor of presence of malignant pathology in breast as all 30(100%) patients with BIRADS scoring of 4 and above had carcinoma on histopathological correlation while those with lower BIRADS scoring had benign pathologies. Mammography thus appears to be a highly sensitive modality in detect in pathologies of carcinoma breast even in the present scenario with advent of modern imaging techniques such as MRI and Ultrasound.

Breast Density

In group A, majority of patients i.e 21patients (70%) had breast density of Type B i.e. scattered fibro glandular density and 4 patients (13.3%) had breast density of Type C i.e. consistently dense whereas no patient had Type D density. In Group B, majority, 20 patients (66.7%) had breast density Type B i.e. scattered fibro glandular density while in 8 patients (26.7%) the breast density was Type C i.e. consistently dense whereas no patient was of Type D density in this group.Thus the predominant appearance of breasts on mammogram in both the groups was either fibro glandular (Type B) or consistently dense (Type C) with no statistical difference between the two groups in regards to breast density. Even though it is expected that the Group A patients should report with higher breast density as

compared to the Group B, however as a multitude of factors are involved in the causation of carcinoma breast and no single isolated factor can be completely responsible for the pathology it is difficult to make generalizations on basis of a single result of a small sample size study. A large sample size randomized trial might provide more insight into the same.

Age and Density

In group A of our study, between age group of 40-50 years, the breast density was found to be Type B in 8(26.7%) patients and Type C in 4(13.3%) patients. In age group of 51-60 years the breast density was found to be Type A in 2(6.6%) and Type B in 7(23.4%) patients. In age group 61-70 years breast density was found to be Type A in 2 (6.6%) and Type B in 4(13.3%) patients. In the age group 71-80 years the density was Type A in 1(3.3%) and Type B in 2 (6.6%). Hence maximum patients in our cancer group were Type B > A, C

In group B of 30 normal patients, between age group 40-50 years, the breast density was found to be Type A in 1(3.3%) , Type B in 11(36.7%),Type C in 4(13.3%)patients. Between age group 51-60 years,6(20%)patients had breast density of Type B, 2(6.6%)patients had breast density of Type C. Between age group 61-70years , 2 (6.6%)patients had breast density of Type B and 1(3.3%)patient had density of Type C . In the age group 71-80 years the density was Type B in 2(6.6%), Type C in 1 (3.3%) patients. Thus maximum density in benign group was seen in Type B>C>A.Thus, age was not an accurate surrogate for breast density in our study.

In study by Checka et al[14] a total of 7007 screening mammograms were performed. Within each subgroup categorized by decade of age, there was a normal distribution among the categories of breast density. There was a significant inverse relationship between age and breast density.

The mechanism by which increased breast density results in an increased risk for breast cancer is not well understood. One explanation is that an abundance of glandular tissue persists in some menopausal women and this may be reflected as increased mammographic density. However, the overall decrease in breast density with age and clear increase in breast cancer incidence with age would then appear to be contradictory. Since Wolfe's[15] first description of the relationship of breast density and breast cancer risk, multiple studies have attempted to identify the factors that determine density patterns and thereby affect breast cancer risk. These potential causes include genes that control terminal ductal lobular unit differentiation or that act on peripheral fat conversion, exogenous estrogens or other hormones, childbirth, and breast-feeding[16]. Other studies have clearly shown mammographic density as a heritable risk factor [17]. An alternative model of density and risk is the Pike model of "breast tissue ageing." According to that model, the cumulative genetic damage sustained by breast epithelium—rather than a patient's chronologic age—may be the key process in determining tissue density[18]. In addition, Maskarinec et al. [19] have shown that the extent of density at a particular age, rather than the trend over time or rate of decrease in density, is a more significant risk factor.

Increased density renders mammography a less sensitive tool for early detection. The group of women including those in younger age groups with less-dense breasts may not derive a significant benefit from additional imaging modalities because mammography alone may be a sufficiently sensitive tool for the early detection of breast cancer. Although breast density is one of the most important risk factors of breast cancer [4] the effect of breast density itself in this study was not significant and the point estimate was much lower than previous meta-analysis which showed about four fold increment of breast cancer risk [5].

Limitations

The existence of selection bias should be considered. The study population was selected from a single institute with small sample size and would not represent target population. Although

studies measured breast density as continuous variables, this study applied BI-RADS classification as categorical variable because BI-RADS classification is widely available in India and National Cancer Screening Program in India uses BI-RADS system to report the results. Despite the important effect of age on breast density, we did not match age between cases and controls as a whole and in each age group to ensure more number of participants.

Conclusion

In the present study it is concluded that Breast density should be an important consideration in designing an individualized screening protocol, particularly for women with other risk factors for breast cancer. Mammography is still a useful modality to assess breast density and can be used reliably for screening as well as diagnosis of breast pathology. However as etiology of carcinoma breast is multifactorial other investigations along with appropriate individual case assessment might be required. In addition to Mammography, Breast ultrasound and MRI may detect occult cancers and there is growing evidence in the medical literature quantifying the benefits of these techniques for high-risk women. Individualized breast cancer risk assessment is critical to allow clinicians to recommend appropriate screening strategies for their patients. The present study highlights the need for breast cancer screening guidelines that are appropriate for patient age, breast density, and overall risk for breast cancer. Further studies of women of various ages and risk categories are sorely needed to clarify this important public health issue.

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