ORIGINAL ARTICLE

Comparative Evaluation of Mammographic Parenchymal Density in Biopsy-Proven Breast Cancer Patients and Age-Matched Normal Subjects in Maiduguri, Northeastern Nigeria

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ABSTRACT

Background: Breast parenchymal density is an important imaging biomarker associated with both an increased risk of breast cancer and reduced diagnostic accuracy in mammography. Despite its significance, there is a lack of comparative data on breast density patterns between breast cancer patients and healthy individuals in our setting. **Objectives:** To compare mammographic breast parenchymal density in women with biopsy proven-breast cancer and age-matched normals. **Method:** This comparative cross-sectional study of mammographic breast pattern comprising150 women with biopsy-proven breast cancer and 150 age-matched women with normal mammogram between 35-80 years was conducted at the University of Maiduguri Teaching Hospital (UMTH). **Results**: The Mean ± (SD) for each group was 48.37 ± (11.67) and 48.49 ± (11.17) years, respectively. The predominant age-group was 40-49 years for both groups accounting for 33% of the study population. The most common type of mammographic parenchymal density was BIRADS 2 (scattered fibroglandular) comprising 48.7% and 46.7% for women with biopsy-proven breast cancer and age-matched normals respectively. **Conclusion**: There was no statistically significant difference in mammographic breast parenchymal density in women with biopsy-proven breast cancer and age-matched normal subjects.

Key words: Mammography, Breast, Density pattern, Cancer

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Introduction

Breast parenchymal density, a measure of the extent of radiodense fibroglandular tissue in the breast; has the potential to be used as a predictor of breast cancer risk.[1] There are numerous methods of assessing mammographic density, and this can be qualitative or quantitative.[2] The Breast Imaging Reporting and Data System (BIRADS) method for density assessment developed by American College of Radiology (ACR) is one of the most commonly used approaches. It consists of four patterns (almost entirely fatty, scattered fibroglandular densities, heterogeneously dense and extremely dense).[3]

Breast cancer can affect any tissue in the breast, but mainly affects the ducts and lobules. The most common type of breast cancer is invasive ductal carcinoma (IDC) which affects the terminal ductal lobular unit (TDLU), invasive lobular carcinoma (ILC) which arises from terminal ductules of breast lobules and ductal carcinoma in situ.[4]

Breast cancer is the most invasive cancer in women worldwide. It accounts for 16% of all female cancers, 22.9% of invasive cancers in women and 18.2% of all cancer deaths worldwide are from breast cancer.[4] In Nigeria, breast cancer is the most common malignancy among women accounting for 22.7% of all new cancer cases.[5]

Women who have dense breast tissue occupying greater than 50% of the area of their mammographic breast image have high density and are at 3-5 fold greater risk of breast cancer than women with less than 25% dense area.[3]

Mammography, Breast Ultrasound Scan (BUS) and Magnetic Resonance Imaging (MRI) can be used to assess parenchymal density in women. However, the imaging modality used for baseline screening or diagnostic assessment of the breast in women is mammography because it is a cheap, safe and readily available tool for evaluating the patients. It is also important in monitoring the disease progression.

The study is aimed to compare the breast parenchymal density of women with biopsy-proven breast cancer and age-matched normal subjects.

Method

This prospective cross-sectional comparative study was conducted from June 2016 to August 2017 in the University of Maiduguri Teaching Hospital using purposive sampling, a type of non-probability sampling technique. This study was carried out on 300 female patients aged 35 years and above, made up of 150 women with biopsy-proven breast cancer and 150 age-matched women with normal mammograms (normal subjects) who voluntarily accepted to participate in the study and who met the inclusion criteria for the study. The examination was explained to each subject and a brief history was obtained. A data collection form was used that contains columns for the patient's age, parity and mammographic findings.

Excluded from this study were women less than 35years and those with abnormal mammograms but not proven to be malignant.

The imaging of the breast was carried out using GE-Senograph DMR X-ray mammography machine. The procedure comprises the use of full film digital mammography (FFDM) to acquire images of the breast which consists of 2 screening views per breast, a mediolateral oblique (MLO) and craniocaudal (CC) views for all patients. Additional views when required were obtained; spot compression views for masses and spot magnification for suspected Microcalcifications. Extended CC views were done for patients with large breasts.

The mammographic breast density was categorised using the ACR BI-RADS. Breast composition categories which were converted to numerical values as follows: BI-RADS 1: almost entirely fatty; BI-RADS 2: scattered fibroglandular density; BI-RADS 3: heterogeneously dense pattern and BI-RADS 4: extremely dense breast patterns.

Data obtained was analysed using SPSS version 16 (Chicago IL, USA). The results were expressed as mean ± standard deviation (SD) and presented in forms of tables and charts as appropriate. Statistical significance between breast parenchymal density and selected demographic variables were assessed using Pearson's and Gamma correlation for various groups. Simple linear regression was used to correlate patients' age, parity and BIRADS classification. P value <0.05 was considered statistically significant at 95% confidence level. The study was approved by the Ethical Committee of the hospital.

Results

The age range was 35-80 years for both groups and mean ± (SD) ages were 48.37 ±(11.67) and 48.49± (11.7) for those with biopsy-proven breast cancer and age-matched normals respectively.

Breast parenchymal density using the ACR-BIRADS classification in determining breast parenchymal density in women with biopsy-proven breast cancer is presented in Table 1. The most frequently encountered was BIRAD 2 (48.7%) and the least common was BIRADS 4 (1.3%).

Table 1: ACR-BIRADS classification of mammographic density in women with biopsy-proven breast cancer.

ACR-BIRADS classification	Frequency	Percentage %)
BIRADS1-predominantly fatty	48	32
BIRADS 2-scatterd fibroglandular	73	48.7
BIRADS 3-Heterogenously dense	27	18.0
BIRADS 4-Extremely dense	2	1.3

The most frequent breast parenchymal density encountered was BIRADS 2 accounting for 46.7% and the least frequent is BIRADS 4 accounting for 2% (Table 2) occurring in age-matched normal women.

Table 2: ACR-BIRADS classification of mammographic density in age matched normal women.

ACR-BIRADS classification	Frequency	Percentage %)
BIRADS1-predominantly fatty	45	30.0
BIRADS 2-scatterd fibroglandular	70	46.7
BIRADS 3-Heterogenously dense	32	21.3
BIRADS 4-Extremely dense	3	2.0

The distribution of the mammographic breast parenchymal density using ACR-BIRADS category shown in the Table 3 and Figure 1 reveals BIRADS 2 (scattered fibroglandular) as the most frequent pattern seen in both groups (48.7%) and (46.7%) in women with biopsy-proven breast cancer and age-matched normal subjects respectively. It was followed by BIRADS 1; predominantly fatty (32%) and (30%) respectively, then BIRADS 3; heterogeneously dense (18%) and (21.3%) respectively. The least common was the BIRADS 4 extremely dense; 1.3% in women with biopsy-proven breast cancer and 2% in aged-matched normal women.

Table 3: Comparison of mammographic density between women with biopsy-proven breast cancer and age-matched normals.

BIRADS	Biopsy-proven breast cancer (%)	Age-matched normal (%)
1	48 (32)	45 (30)
2	73 (48.7)	70 (46.7)
3	27 (18.0)	32 (21.3)
4	2 (1.3)	3 (2)
Total	150 (100)	150 (100)

Figure 1 below, shows the bar chart illustrating the distribution of mammographic parenchymal density between women with biopsy-proven breast cancers (case) and age-matched women with no biopsy-proven breast cancers (normal) subjects.

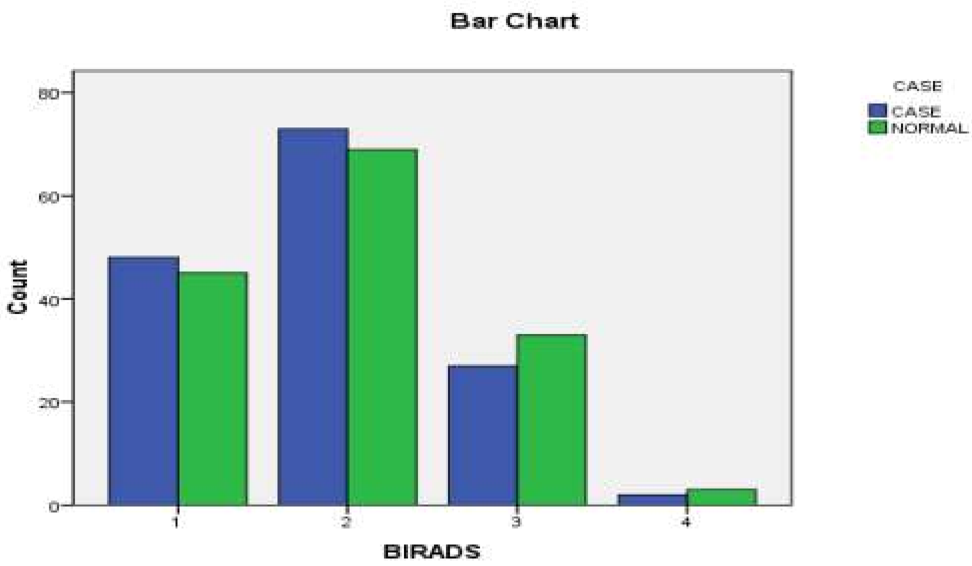

Figure 1: Distribution of mammographic parenchymal density between women with biopsy-proven breast cancers and age-matched normal subjects.

There was no statistically significant difference in breast parenchymal density between women with biopsy-proven breast cancer and age-matched normal p = 0.402 using Pearson's correlation. Asymptotic standard error = 0.058.

The predominant age group of the study population was 40-49 years 30% and 36% for women with biopsy-proven breast cancer and age-matched normal subjects respectively; comprising 33% in the overall study population (Table 4). The least number of subjects was seen in 70-80 years accounting for 9.3% and 7.3% in women with biopsy-proven breast cancer and age-matched normal respectively; comprising 8.3% in the overall population.

Table 4: BIRADS classification for each age group of the study population

BIRADS	AGE-GROUP					
	<40	40-49	50-59	60-69	70-80	Total
1	0	21 (21.2%)	26 (37.7%)	22 (71%)	24 (96%)	93 (31%)
2	24 (31.6%)	68 (68.7%)	40 (58%)	9 (29%)	1 (4%)	142 (47.3%)
3	47 (61.8%)	10 (10.1%)	3 (4.3%)	0	0	60 (20%)
4	5 (6.6%)	0	0	0	0	5 (1.7%)
Total	76 (25.4%)	99 (33%)	69 (23%)	31 (10.3%)	25 (8.3%)	300

There was decrease in parenchymal density pattern progressively from the age group <40years in which 0% had predominantly fatty breasts through to 70-80 years in which 96% had predominantly fatty breast pattern.

There is an inverse relationship between the age and BIRADS classification; as the age increases the BIRADS classification is seen to decrease. There was a statistically significant correlation between the age group and density pattern p=0.000 using Pearson's correlation. A simple linear regression analysis showed a positive correlation between age group and breast parenchymal density ($r = 0.728$; $r^2 = 0.529$; $p = 0.000$).

Table 5 shows the relationship between breast parenchymal density and parity. Range of parity is 0-13 for both groups, mean and standard deviation for biopsy-proven breast cancer and age-matched normal are 4.67± (2.55) and 4.6± (2.67) respectively. There was statistically significant correlation between the breast density pattern with parity, (P = 0.000) using Pearson's R correlation.

A simple linear regression analysis with parity as an independent variable showed weak positive relationship between parity and breast parenchymal density;(r=0.363, r^2 =0.132 and adjusted R= 0.126).

The highest parity in the overall study population was seen in BIRADS 2 (scattered fibroglandular) with 75 women having 1-4 children, 64 women having 5-9 children and 2 women having 10-13 children and 2 women being nulliparous respectively.

The least number of children was seen in BIRADS 4 (extremely dense); 3 women having 5-9 children; 1 woman having 1-4 children and none being nulliparous or having 10-13 children. Least number of children (nulliparity) was seen in BIRADS 3 (heterogeneously dense), while highest number was with 7 having 10-13 children seen in BIRADS 1 (predominantly fatty). This shows that the more the number of children, the less the parenchymal density and vice-versa.

Table 5: Relationship between BIRADS classification and parity

BIRADS	NULLIPAROUS	PARITY			Total(%)
		1-4	5-9	10-13	
1	0	22	63	7	92 (30.7%)
2	2	75	64	2	143 (47.7%)
3	10	46	4	1	61 (20.3%)
4	0	1	3	0	4 (1.3%)
Total	12	144	134	10	300

Discussion

Mammographic breast parenchymal density alone and in combination with other demographic variables have been studied for years by several researchers in an attempt to investigate its relationship with the risk of developing breast cancer.[6] Breast parenchymal density has been proven to be one of the strongest breast cancer risk factors and an independent predictor of breast cancer.[7]

The study population consisted of 150 women with biopsy-proven breast cancer and 150 age- matched normal subjects in the age range of 35-80 years. Highest number of participants was found within the age group of 40-49 years (33%) which was similar to studies done in Kano, Enugu and Ibadan; Nigeria.[8-10]

However, the above finding was at variance with a study in the USA which showed the highest population of women in the age range of 50-59 years.[11] This is most likely because their local studies show that breast cancers predominantly occur a decade earlier in Nigeria than in Caucasians and justify the need to start screening by age 40 years.[10]

The most common BIRADS density pattern found in this study was BIRADS 2 (scattered fibroglandular) which was in concordance with the study done in Enugu and Ilorin, Nigeria.[9,12,13]This was at variance with the study done in Ibadan and Kano, Nigeria which revealed BIRADS 1 (predominantly fatty) to be most common followed by BIRADS 2 (scattered fibroglandular).[10,8]

Another study done in Ado Ekiti found BIRADS 3 (heterogeneously dense) to have the highest distribution of breast parenchymal density followed by BIRADS 1 (predominantly fatty).[14]

A study in the USA found BIRADS 3 (heterogeneously dense) to be the most common breast density pattern followed by BIRADS 2 (scattered fibroglandular) and predominantly fatty being the least common.[11]

It has been shown that Caucasian women generally have a higher breast density pattern when compared with their African or African American counterparts; indeed breast density has been said to be genetically predetermined or hereditary.[8] Screening effectiveness is said to decrease for the so called high risk mammographic breast pattern that degrades the sensitivity of mammogram and also houses high grade breast cancer.[4]

There was no statistically significant difference in breast parenchymal density of subjects with biopsy proven-breast cancer and age-matched normal which was similar to a study done in India.[15] However, a study done in Uganda showed prevalence of high breast density among cases was higher compared to the control group.[16]

This study showed statistically significant correlation between the age group and breast density pattern p = 0.000. It also showed inverse linear relationship between age and mammographic density. This was similar to studies done in Maiduguri, Northeastern Nigeria, Uganda and USA.[11,16,17]

The average percent mammographic density in the population decreases with increasing age, which seems paradoxical that breast cancer incidence increases with age.[18,19] This may be explained by the Pike model which is based on breast tissue exposure which refers to the exposure to hormones, and growth factors, and to the effects that menarche, pregnancy and menopause have on these exposures and on the susceptibility of breast tissue to carcinogens.[18] Breast tissue exposure is highest at the time of menarche, decreases at the time of pregnancy, is further reduced during the perimenopausal period, and is lowest after menopause. [18]

There was a significant relationship between parity and breast parenchymal density (p = 0.000). This was in conformity with various other studies. A study in Kano, stated an association of decreased parenchymal density on mammograms with increased parity. However, a study in Ibadan found decrease in proportion of women with BIRADS 3 and 4 which appeared to decrease with history of children.[10] A study in USA by Vachon *et al*.[20] found that increase breast density was associated with nulliparity and late age at first child birth while Yaghjyan *et al*.[21] found that breast density was inversely associated with parity. Women with more than one child showed significant 2.6% faster decline in densities than women who had 0 to 1 child.[22] At variance was a study done in Uganda which found that there was an increase in breast density with increasing parity among the cases and controls.[16]

The inverse association of parity with breast density could be explained by biological changes that take place in breast tissue during a full-term pregnancy that leads to permanent gene expression changes to type 3 lobules making them less susceptible to hormone influences and carcinogenesis.[23]

Conclusion

Mammographic density pattern is mainly classified using the ACR-BIRADS in our Centre. The commonest in this study was BIRADS 2 (scattered fibroglandular). There was no significant difference in breast parenchymal density between women with biopsy-proven breast cancer and age-matched normal subjects.

The association between mammographic density with both age and parity has been statistically confirmed to be significant.

Recommendation

Future large-scale studies in mammographic density pattern and other variables such as BMI, combined oral contraceptive pills and use of hormone replacement therapy is advocated.

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Conflict Of Interest

No conflict of interest

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