Original Article

# Age-related ultrasonographic mammary gland density patterns: Implication for breast cancer risk

Nicholas Kayode Irurhe, Nwachukwu Mike Ibeabuchi[1], Omodele Abosede Olowoyeye, Ogechi Augustina Ihekuna[2], Oluwaseyi Jessy Balogun[3], Caleb Itopa Yakubu[4], Francis Ikechukwu Duru[1]

Departments of Radiation Biology, Radiotherapy and Radiodiagnosis, [1]Anatomy, [2]Biochemistry and [3]Biotechnology, College of Medicine, University of Lagos, [4]Department of Radiodiagnosis, Lagos University Teaching Hospital, Lagos, Nigeria

## Abstract

**Introduction:** Mammary gland/breast density is important because it is a known biomarker for breast cancer risk. However, the sensitivity of mammography decreases with high breast density found in younger age group. Ultrasound is considered as the first-line examination in the classification of breast density and in the detection and characterization of breast lesions. This study aims to evaluate the relationship between age and ultrasonographic breast density pattern and its implication for breast cancer risk.

**Materials and Methods:** This was a community-based cross-sectional, exploratory, descriptive study involving 658 females. Breast ultrasonographic scans were performed using a Sonoace X1 Machine with a 7.5 MHz transducer. The lesions detected and classified by ultrasonography as benign or malignant were further subjected to cytopathology.

**Results:** Modal age group of the participants ranged from 33 to 43 years representing 29.8%. There was significant correlation ($P<0.01$) between ultrasonographic mammary gland density pattern and age, the age group of <33 years demonstrated predominant fibroglandular density pattern with mostly benign lesions, while the age group of 33–53 years demonstrated predominant heterogeneous breast density pattern with most of the malignant lesions in this age group, making it the high-risk group for breast cancer.

**Conclusion:** The relationship between age and ultrasonographic breast density is inversely proportional and not absolute. It also concludes that ultrasonography is a reliable screening tool in the diagnostic process for mammary gland lesions, and as an imaging tool, it is the preferred modality in dense breast. The heterogeneous fibroglandular pattern emerged as the high-risk group for breast cancer, especially in middle age.

**Keywords:** Age, breast cancer, density pattern, mammary gland, ultrasound

**Address for correspondence:** Dr. Nicholas Kayode Irurhe, Department of Radiation Biology, Radiotherapy and Radiodiagnosis, College of Medicine, University of Lagos, Lagos, Nigeria.
E-mail: nirurhe@unilag.edu.ng

**Submitted:** 31-Mar-2021 **Revised:** 14-Sep-2021 **Accepted:** 10-Nov-2021 **Published:** 11-Feb-2022

## INTRODUCTION

The female mammary gland or breast consists of glandular, fatty, and connective tissues. While rudimentary in males, the development in females commences in response to estrogen stimulation at the onset of puberty.[1,2] Imaging the mammary gland to distinguish between normal and/or

Access this article online

Quick Response Code:

Website: www.wajradiology.org

DOI: 10.4103/wajr.wajr_10_21



**How to cite this article:** Irurhe NK, Ibeabuchi NM, Olowoyeye OA, Ihekuna OA, Balogun OJ, Yakubu CI, *et al*. Age-related ultrasonographic mammary gland density patterns: Implication for breast cancer risk. West Afr J Radiol 2021;28:31-5.

abnormal morphology is increasingly important, with the high incidence of breast cancer reported among females, especially in developing countries such as Nigeria, with over 15% of breast cancer cases occurring in females over 30 years in Lagos.[3,4]

Some recent studies in Nigeria have recommended that females aged 40 years and above should undergo annual X-ray mammographic screening for breast cancer.[5] In the past four decades, mammary gland parenchymal density on X-ray mammography has been graded using Breast Imaging Reporting Archiving Data system (BI-RADS) lexicon.[6] However, in dense breast, X-ray mammography has limited sensitivity and specificity.[7-9] In addition, the increased risk of fetal injury from exposure to ionizing radiation during mammography precludes its application in pregnant women, while the increased glandularity of the breast in lactating mothers reduces its sensitivity and specificity in this group.

Ultrasonography is increasingly being used in mammary gland imaging because of its high sensitivity and specificity in the glandular breast.[9,10] It is currently considered by clinicians as the first-line imaging modality in the detection and characterization of breast lesions, including the evaluation for breast cancer.[11] Whole mammary gland ultrasonography is useful for evaluation in both normal and diseased breast;[1,12] this means that all females can be screened with ultrasound, irrespective of age.

Researchers have identified mammary gland density patterns as the independent biomarkers for different risk levels of breast cancer.[11,13] As glandular tissue changes with age, it is expected that the mammary gland density will decrease with increasing age. However, this is not always the case as investigations have documented contrary reports, where high mammary gland density pattern is seen in older women and low mammary gland density pattern is seen in younger women.[14]

The purpose of the study is to evaluate the relationship between age and ultrasonographic mammary gland density pattern and its implication for breast cancer risk.

## MATERIALS AND METHODS

This was a prospective community-based cross-sectional, exploratory, descriptive study, involving 658 female participants aged 13–83 years. The participants were selected from local government councils in seven states in Southern Nigeria. The study was carried out in the local government council health centers in seven states, namely Lagos, Ondo, Ogun, Delta, Anambra, Abia, and Imo states.

Adequate room space to facilitate participant interaction with the researcher and physical and ultrasonographic examinations was made available at each location where the study was carried out. These facilities were specifically provided in the designated centers where a breast cancer awareness program was being organized. Admission of the participants into the study was strictly at their convenience.

### Inclusion/exclusion criteria

This study sample included both asymptomatic (that is, individuals with no breast-related complaints) and symptomatic (that is, individual with breast-related complaints). Individuals with breast atresia or amastia were excluded.

The ultrasonographic mammary gland scans were performed on both right and left breasts using Sonoace X1™ machine (made in South Korea) with a 7.5-MHz transducer probe connected to a display monitor. The procedure used to scan the participants was similar to that of Gundry, 2016.[15]

The ultrasonographic mammary gland density patterns were categorized according to BI-RADS classification.[16] On detection of any mass, the final BI-RADS for lesions was classified using ACR-BI-RADS lesion classification.[16]

Tissue sample collection was carried out at each of the centers where ultrasonography demonstrated breast lesion. After identification, a fine-needle aspiration biopsy was carried out on the examination couch after which the test samples were processed, stored, and transported in a specimen transport box following standard protocols,[17] from each study center to the Cytopathology Laboratory of the Department of Anatomic and Molecular Pathology of the College of Medicine, University of Lagos, and Lagos University Teaching Hospital, Idi-Araba, Lagos, Nigeria. All samples were then viewed under a Leica-500™ microscope and reported by a consultant pathologist.

The cytopathological report on the fine-needle aspirate biopsies indicated a definitive diagnosis categorized as either a benign or malignant tumor.

### Statistical analyses

Data obtained were collated and entered into the spreadsheet of Statistical Package for the Social Sciences (SPSS™) version 20.0 and analyzed for descriptive and inferential statistics. Frequency distribution was measured for the sociodemographic variables. Chi-square test compared

mammary gland density patterns, age, and breast cancer risk at 95% confidence level.

## RESULTS

The study results are presented as tables, graphs, and charts. The breast pattern distribution of females in Southern Nigeria using the ACR-BI-RADS classification clearly delineates the various patterns of ultrasonographic mammary gland parenchymal density in Southern Nigeria women, with the homogenous fatty breast pattern being the least common (25.8%), the homogeneous fibroglandular breast pattern (28%), and the heterogeneous fibroglandular breast pattern being the most common (46.2%).

Figure 1 shows the age distribution of the participants in this study.

The modal age group (33–42 years) of the participants represents the highest frequency of 30%.

Table 1 shows that mammary gland density pattern is significantly influenced by chronological age ($P < 0.01$) at the time of investigation. The homogenous fibroglandular (BI-RADS C) pattern was more pervasive in younger age group of <33 years (81%), the heterogeneous fibroglandular pattern (BI-RADS B) was most common in the middle age group of 33–43 years (94.4%), while the homogenous fatty pattern (BI-RADS A) was predominant at older age group of 53–62 years (96.7%) and >63 years (100%).

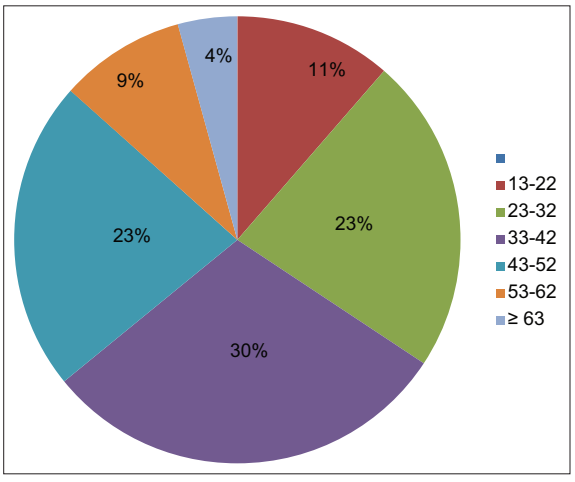


**Figure 1:** Age distribution of participants in this study

In this study, it was observed that age group of <33 years demonstrated predominant fibroglandular density pattern with mostly benign lesions, while the age group of 33–53 years demonstrated predominant heterogeneous breast density pattern compared to fatty breast density with most of the malignant lesions in this age group, making it the high-risk group for breast cancer, and the age group of >53 years mainly has fatty breast density pattern.

## DISCUSSION

The association of mammographic parenchymal pattern of women with breast cancer risk has been extensively studied.[18,19] However, the literature on ultrasonographic parenchymal distribution pattern and breast cancer risk in Nigeria is sparse.[20] Further, increasing clinical use of ultrasonography has highlighted the need to standardize the operational terminologies to facilitate accurate and consistent reporting, interpretation, and communication between clinicians.[21]

Our data showed that participants in this study were mainly in the young and middle-aged groups representing 64.1% of the overall participants. This may be due to the awareness, willingness, and knowledge level of breast cancer, which was seen in this group. This findings is similar to the findings of Nwaneri *et al.* (2017)[22] where he observed that the willingness and awareness to participate in breast cancer screening were more in young and middle age females. A large proportion of this group of females may not have the opportunity to be screened for breast lesions due to age since the conventional breast cancer screening imaging modality is mammography which is recommended only to females aged 40 years and above in Nigeria. This has further highlighted the need for ultrasonographic breast cancer screening, especially with a large population that would otherwise not have had the prospect of being screened.

The mammary gland parenchymal patterns have been used as markers of varying risk of breast cancer with

**Table 1: Categorization of age and ultrasonographic mammary gland density distribution patterns**

| Age | Homogenous fatty breast pattern (%) | Heterogeneous fibroglandular pattern (%) | Homogenous fibroglandular pattern (%) | $\chi^2$ | *P* |
|---|---|---|---|---|---|
| <33 | 0 | 43 (19) | 183 (81) | 838.567 | *P*<0.01 |
| 33-42 | 10 (5.1) | 185 (94.4) | 1 (0.5) | | |
| 43-52 | 74 (50) | 74 (50) | 0 | | |
| 53-62 | 58 (96.7) | 2 (3.3) | 0 | | |
| >63 | 28 (100) | 0 | 0 | | |

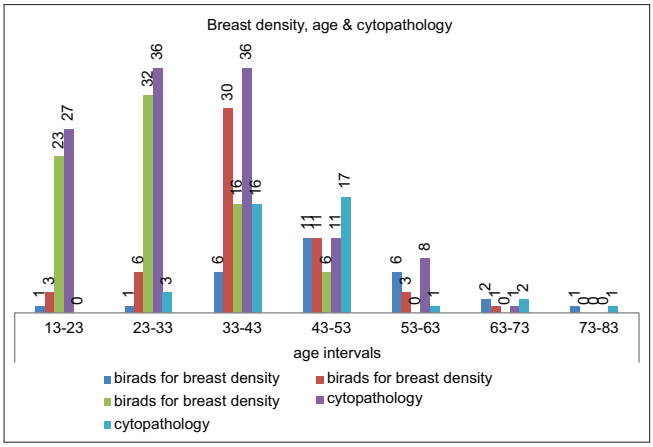


**Figure 2:** Pictorial bar charts showing the distribution of mammary gland density pattern and cytopathology status

mammography.[13] This study clearly delineated the various patterns of ultrasonographic mammary gland parenchymal density in Southern Nigeria women. BI-RADS B was observed to be the predominant density pattern (46.2%). This study showed that mammary gland density pattern is significantly influenced by age ($P < 0.01$) at the time of investigation. This is consistent with the findings of Obajimi *et al*.[20] in Ibadan, where 53% of the participants were documented as heterogeneous fibroglandular pattern with 573 participants and Olarinoye-Akorede *et al*.[23] in Zaria, where 49.1% of the participants were documented as heterogeneous fibroglandular pattern with 503 participants.

A few of the older or post-menopausal women in this study were discovered to have dense breast pattern this may suggest that age may not always influence or determine breast density (figure 2), this is similar to the findings of Checka *et al*., 2012.[14] Although with a few older women in the dense breast pattern category, this may suggest that density pattern is not only influenced by age, and other potential influencers of breast density have been postulated by other researchers.[24-26] The factors responsible for regulating the proportion of density in tissues are still not well understood. Furthermore, some researchers have reported that the proportion of density at a specific age is an important risk factor, while others believe that the rate of reduction in density is the major risk factor.[25]

Ultrasonography was able to successfully discriminate between normal/negative (BI-RADS 1) classifications (75.8%) from the abnormal mammary gland parenchymal patterns (24.2%), that is, those with lesions (BI-RADS 2–6). This suggests that ultrasonography, as an imaging modality for breast lesion, is reliable; this is in agreement to the findings of Huay-Ben.[11]

This study showed that benign lesions were predominantly located in the BI-RADS C density pattern that is largely dominated by the <33years age group while the malignant lesions were majorly located in BI-RADS B pattern and found mainly in the 33-52 years category [Figure 2]. This demonstrated that the BI-RADS C pattern found in the younger age group has high probability of breast lesion being benign and BI-RADS B pattern found in the middle age group has high probability of breast lesions being malignant; this may be partly due to late presentation and possibly from financial constraints, distance to the center, or sheer ignorance on the part of the participants.

The process by which high density increases breast cancer risk is yet to be understood. A situation where abundant glandular tissue persists in some menopausal and postmenopausal women and may be classified as increased ultrasonographic density. Therefore, the overall decrease in breast density with increasing age and the increase with breast cancer incident with age may appear somehow contradictory. However, many authors in their studies have tried to identify the factors that regulate density patterns and consequently affect breast cancer risk.[24-26] Further, Ginsburg *et al*. proposed that the reduction in mammographic density that occurs with increasing age, parity, and menopause reflects the involution of breast tissue.[25]

## CONCLUSION

This study revealed that the relationship between age and ultrasonographic breast density is inversely proportional and not absolute. Conversely, it concludes that ultrasonography is a reliable screening tool in the diagnostic process for mammary gland lesions. As an imaging tool, it is the preferred modality in dense breast as demonstrated in this study. The heterogeneous fibroglandular pattern appears to be the most common pattern in Southern Nigeria and also emerged as the high-risk group for breast cancer in this study, especially in middle-aged women. Our goal with this study is to provide an alternative imaging modality that is adequately efficacious and permits women of all ages, irrespective of lactation or pregnancy status to be screened for breast cancer.

### Ethical approval

Ethical approval was obtained at the Lagos University Teaching Hospital Health, Research and Ethics Committee.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

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