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Mammography in Nigeria: A Rigorous Retrospective Analysis of One-Year Utilization in a Tertiary Hospital

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Abstract

Background: Mammography screening is the most effective way to minimize breast cancer morbidity and mortality. Unfortunately, the uptake of mammography in Nigeria has been low. This study evaluated mammography studies in a Nigerian tertiary hospital to use insights from this study to proffer feasible solutions that can improve mammography services and uptake in Nigeria.

Methods: This is an IRB-approved retrospective analysis of all mammography studies done at a Nigerian tertiary hospital between March 2022 and February 2023. Anonymized patient data from the routinely filled risk-assessment questionnaires during mammography procedures and the mammography findings were entered into an Excel sheet. Data were analyzed using SPSS version 22, and a significant p was set at < 0.05.

Results: A total of 324 women with an average age of 51.06 ± 9.28 years (range 30 – 86 years) underwent mammography, 185 (57.1%) for screening, and 139 (42.9%) for diagnostic evaluation of breast symptoms. Half (49.7%) of the women had dense breasts (ACR-C and D). Community engagement (52%) and self-referral (20%) were the primary paths to mammography, with 20% of the women paying out of pocket for the procedure. Sixty-six ultrasound-guided core needle biopsies were recommended for further diagnostic workup, but 64 were performed, 4 of which were from screening. There was 30.8% and 100% concordance between radiology and pathology for BIRADS 4 and 5 lesions, respectively. Fifty-five cancers (55/324; 17.0%) were diagnosed, one with a size of 1.4 cm on screening (1/185; 0.5%) and 54 with an average size of 3.6 ± 1.9 cm (range 2.0 - 5.3) on diagnostic workup (54/139; 38.8%). Age at menopause and personal history of previous breast cancer independently predicted BIRADS 5 lesions on mammography, while age independently predicted malignancy at pathology.

Conclusions: Observations from this analysis show that more women attended mammography for screening rather than for diagnostic purposes; cancer detection rates in the screening and diagnostic population, a foundation for future studies that can inform public health policy in Nigeria; and significant risk factors that predict malignant lesions to guide recommendations for targeted risk-based systematic screening in Nigeria.

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Introduction

Breast cancer is a major public health challenge in Nigeria, with a three-fold higher incidence than four decades ago, late presentation, and a low 5-year survival rate [1-3].

By enabling early detection, mammography screening is the most effective way to minimize breast cancer morbidity and mortality [4]. There is considerable empirical evidence of the effectiveness of mammography in minimizing breast cancer morbidity and mortality worldwide, particularly in developed countries [4-5]. Unfortunately, like many other Low-Middle-Level Income Countries (LMICs), Nigeria has no breast cancer screening program [6]. Although there are other contributory factors, the absence of a well-coordinated national screening program plays a central role in the late presentation of most breast cancer patients in Nigeria [7].

Several nationwide studies auditing uptake in hospitals offering mammography services show meager patient uptake rates in Nigeria [8-21]. The poor mammography uptake in Nigeria contributes to the high mortality from the disease. The cost of mammography investigation is one of the reasons for the low uptake in Nigeria, as most Nigerians cannot afford annual mammography screening [7,10,11]. Moreover, even with the government contribution to cost reduction through the National Health Insurance Scheme (NHIS), a significant number of Nigerians in the urban and nearly all in the rural areas are not subscribed to NHIS [22]. In order to change the narrative, efforts have been made recently by non-governmental organizations (NGOs) like "Breast Without Spot (BWS)" and health professional bodies like the "Breast Imaging Society of Nigeria (BISON)" to create breast cancer awareness and improve the uptake of mammography screening in Nigeria, mainly by targeting the pink month of October annually to offer women free or subsidized breast cancer screening. However, the impacts of these efforts on mammography uptake vary across the regions and states in Nigeria depending on health system-related factors like infrastructure, and personnel, as well as patient-related factors like education, attitude towards screening medical examinations, and geographical access [9-11].

The challenges faced by health institutions in Nigeria to offer mammography services include but are not limited to the high cost of procurement of the imaging equipment and the add-on paddles required for diagnostic workup; shortage of trained personnel (Breast radiologists and technologists) per capita; the limited ability of the radiologists to biopsy mammographic findings, particularly the non-palpable screen-detected lesions, under image guidance due to lack of equipment and training; frequent downtimes of the machines as a result of the lack of purchased maintenance service contracts and the limited availability of qualified/trained biomedical engineering personnel to fix machines promptly; and lack of on-site physicist support when quality issues arise with the acquired images [23]. In addition, despite being in the era of digital technology and artificial intelligence, Nigerian health institutions are still struggling to keep up with the evolving technology. For example, 3D mammography, which has better sensitivity and specificity to detect breast cancer than 2D mammography, and Picture Archival and Communication Systems (PACS) for easy reference comparison to prior studies and archiving of older exams are only available in a few health institutions in Nigeria.

Previous authors have audited screening and diagnostic mammography in some tertiary hospitals across Nigeria [13-21], mainly reporting on breast densities and mammographic pathologies. However, those who reported on the study participants' risk factors reported on a few. Furthermore, none of these studies evaluated the concordance between radiologic and pathologic diagnoses, and the most recent audits were nearly a decade ago. Bearing in mind several efforts by NGOs and professional bodies in creating awareness for breast cancer screening in recent times, a recent audit evaluating the risk factors for breast cancer, referral pathways for mammography, radiologic-pathologic concordance of the breast pathologies and predictors of malignant lesions in women who undertake screening and diagnostic mammography will therefore be more representative of the current situation to provide pragmatic solutions to improve mammography services and uptake in Nigeria.

This study aimed to evaluate mammography studies in a Nigerian tertiary hospital, including the population profile, referral pathways, radiologic-pathologic concordance of the breast pathologies and the predictors of malignant lesions, to examine the present state of mammography uptake and findings in Southwest Nigeria. This rigorous evaluation can inform pragmatic solutions to improve mammography services and uptake in Nigeria.

Methods

Ethical considerations

The Ethics and Research Committee of the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC) approved the study (ERC/2023/03/21). The need for patient consent was waived for this retrospective study given all data were collected from the routinely filled questionnaires during mammography procedures in the department of Radiology.

Study design

This study is a retrospective analysis of mammography studies done between March 2022 and February 2023 at OAUTHC.

Study location

The index hospital (OAUTHC) is a tertiary hospital and a referral centre serving about 7.7 million people in the Southwest region of Nigeria and receiving patients from Osun State, where it is located, and adjacent neighbouring states like Ondo, Oyo, and Ekiti. The Osun state female population is 1,682,800, and those eligible for average-risk screening (40 years and above) are about 326,800 [24]. The hospital's Radiology department has a breast imaging and intervention unit with standard operating procedures (SOP) for the breast imaging investigations (digital 2D mammography and hand-held ultrasound) and interventions (ultrasound-guided core needle biopsy, clip placement, and wire localization) performed on eligible women referred for breast cancer screening and diagnostic evaluation. In addition, breast pathology services and physicians' with oncologic expertise are available in the hospital to treat breast cancer.

Mammography Standard Operating Procedure

The breast unit of the Radiology department has an established protocol for offering mammography services. Mammography is offered to patients thrice weekly, as well as ultrasound and ultrasound-guided core needle breast biopsies on these days. Patients are prepared for the procedure during booking by giving instructions not to use body creams and deodorant on the morning of the procedure and to avoid caffeinated drinks the night before.

A questionnaire **(Supplementary file)** about risk factors and indications for the study is completed by every woman before the imaging is done.

The mammography machine is a full-field digital Siemens Mammomat fusion machine, model number (240) 10762444; and serial number (21) 368, accompanied by two compression paddles (30 x 24 cm and 24 x 18cm). Standard full mediolateral oblique (MLO) and craniocaudal (CC) views are done routinely of each breast. However, when indicated, additional views like cleavage, axillary, exaggerated CC, rolled or tangential views are done. After the procedure, women with dense breasts (ACR-C and D) or a mass, irrespective of their breast density, also get a whole-breast or targeted breast ultrasound, respectively. For those with masses suspicious (BIRADS 4) or highly suggestive (BIRADS 5) of malignancy, an ultrasound-guided core needle biopsy is done by a trained breast radiologist on the same or the earliest convenient day for the patient, and samples are sent in formalin to the pathology department of the hospital for analyses. For lesions only visualized on mammography and are suspicious, a metallic skin marker is placed on the skin over the target lesion, and mammography is repeated before the biopsy procedure to ensure the proper location of the lesion on ultrasound. Once the marker is directly on the lesion on mammography, a mark is made on the skin at the exact location to guide biopsy on ultrasound, taking into consideration the distance of the lesion from the nipple and depth below the skin surface. If the target lesions are microcalcifications, specimen radiography is further done after the biopsy to confirm that the microcalcifications are in the specimen before being sent for pathology analysis.

A trained breast radiologist with 13 years' experience interpreting breast imaging and radiology residents in training reviews the images. A written report of results is made available for pick up by the patient within 48 hours of the study, except in situations where second opinions are required, and time is needed for a second read. Previous mammograms are compared with the index studies for women who had mammograms in previous years. Based on the risk profile and mammography images, appropriate recommendations are made in the results/reports.

Pathology results are retrieved within 2 weeks of the biopsy and communicated to the patients by the breast Radiologist during an in-person visit. Patients diagnosed with malignancy, symptomatic patients or any patient coming for breast imaging who is not already seeing a breast surgeon at OAUTHC is referred to the breast clinic for further management as warranted by biopsy results and/or symptoms.

Inclusion criteria

All mammography studies done on women at OAUTHC between March 2022 and February 2023 were included in the analysis.

Exclusion criteria

The post-neoadjuvant mammography studies of women on treatment for breast cancer were excluded from the analysis.

Data collection

De-identified patient data from the routinely filled risk-assessment questionnaires during mammography procedures in the department of Radiology and the mammography findings were entered into an Excel sheet . Participant data were identified with serial numbers.

Data analysis

Data were analyzed using Statistical Package for the Social Sciences Version 22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). Descriptive statistical analysis was done, and results are presented as frequencies/percentages on tables and charts as appropriate. Proportions were compared using chi-square or Fisher's exact test as appropriate. The relationship between suspicious imaging findings and clinical predictors was evaluated using univariate and multivariate logistic regression models. Similarly, the relationship between malignant histologic findings (following image-guided breast and/or axillary lymph node biopsies) and relevant clinical predictors was evaluated using univariate logistic regression. The alpha value was set at 0.05.

Results

Demography and risk factor profile of the study population

The demographic characteristics of the study participants are shown in supplementary table 1. More than half (170/324; 52.5%) were younger than 50 years. Almost all the women had their menarche at the age of 12 years and above (314/324; 96.9%) and were parous (313/324; 96.6%) **(See Table 1)**. Among the parous women, 69.0% (216/313) had their first confinement before the age of 30 and 95.8% (300/313) before the age of 35 **(See Table 1)**. About 95.2% (298/313) of the parous women were multiparous **(See Table 1)**, and 89.2% (266/298) of these multiparous (≥ 2 children) women had more than three years birth interval between their first and last confinement **(Supplementary table 2)**. About 96% (311/324) of the study population ever breastfed, with 97.4% (303/311) of those who ever breastfed having a total number of breastfeeding years of more than 12 months. See **Table 1**.

Half (162/324; 50%) of the study population was postmenopausal **(Table 1)**, 13.6% (22/162) of whom attained menopause at the age of 55 years or older **(See Supplementary Figure 1)**. One in six (55/324; 17%) women used oral contraceptive pills (OCPs), while only 1 in 100 (3/324; 0.9%) used Hormone Replacement Therapy (HRT). **See Table 1**

One in 10 (32/324; 9.9%) women had a family history of breast cancer. Family history of ovarian and colorectal cancers was seen in 1 in 100 (3/324; 0.9%) and 3 in 100 (9/324; 2.8%) women, respectively. All (324/324; 100%) women did not know their breast cancer gene (BRCA) status. About 11.4% (37/324) and 1.2% (4/324) have a personal history of breast cancer and previous high-risk lesions, respectively. None (0/324; 0%) of the women had a history of radiation therapy to the chest. Seven in 10 women (225/324; 70.8%) were overweight (body mass index ≥ 25kg/m2) and obese (body mass index ≥ 30 kg/m2), and less than a tenth (27/324; 8.3%) of the study population took alcohol. Half (160/324; 49.4%) of the women had dense (ACR- C and D) breasts on mammography **(See Table 1)**.

Referral pathways and presentations of the study population

Fifty-two percent (168/324) of the women presented for mammography through community engagement, while about 20% presented were self-referred **(See Figure 1)**. There were more screenings than diagnostic studies (about 3:2) **(See Table 2)**.

Overall, 1 in 5 women (64/ 324; 19.8%) paid out of pocket for their study **(Table 2)**. The ratio of screening to symptomatic population (8/185; 4.3% vs. 56/139; 40.3%) that paid out of pocket for their mammography was about 1:10 **(See Table 3)**. Seven (7/36; 19.4%) postmastectomy women presented for diagnostic studies of the non-mastectomy side, none (0/7; 0%) of whom paid out of pocket, while 29 (29/36; 80.6%) postmastectomy patients presented for screening studies of the non-mastectomy side, only 1 of whom (1/ 29; 3.4%) paid out of pocket **(See Table 3)**.

About half (71/139; 51.1%) of the symptomatic population presented with bilateral breast symptoms. Lumps (51/139; 36.7%) and pain (50/139; 35.9%) constituted the commonest symptoms, with over three-quarters (106/139; 76.3%) of women presenting for mammography after one month of onset of symptoms **(Table 4)**.

Mammographic findings with radiology-pathology concordance in the study population

Almost half (159/324; 49.1%) of the study population had a complementary/correlative ultrasound with their mammography studies **(Figure 2)**. Thirty-seven percent (120/324) had normal mammograms (BIRADS 1). BIRADS 2 and 3 lesions were more likely to be bilateral than unilateral (bilateral; 68/138 vs. right; 36/138 vs. left; 34/138: $p < 0.001$), while BIRADS 4 and 5 lesions were more likely to be unilateral than bilateral (right; 29/66 or left; 28/66 vs. bilateral; 9/66: $p < 0.001$) **(See Table 5)**.

Four women (4/185; 2.2%) of the screening population had findings for which biopsy was recommended. One of these lesions was malignant (ductal carcinoma-in-situ), while the remaining 3 were benign (hamartoma, phyllodes tumour, and fibrocystic disease) at pathology.

Vascular (16/77; 20.8%) and parasitic calcifications (12/77; 15.6%), as well as intramammary lymph nodes (12/77; 15.6%), were the commonest benign findings seen on mammography. **(See Table 6)**

The upper outer quadrant was the commonest location for benign and malignant lesions in both breasts (right breast: benign, 73/160 vs. malignant, 29/51 and left breast: benign, 66/167 vs. malignant, 25/49) **(See Table 7)**.

Morphologically abnormal axillary lymph nodes were seen in 9% of women with mammographically-detected axillary nodes (13/145; 9% on the right and 12/134; 9% on the left) **(See Figure 3)**.

About a fifth (69/324; 21.3%) of the study population had an ultrasound-guided breast and/or lymph node core needle biopsy **(Figure 2)**. A fifth (15/69; 21.7%) of those who had a biopsy had simultaneous breast and lymph node biopsies done **(Figure 2)**. The positive predictive value (PPV) of biopsy-proven breast cancer in BIRADS 4 (4/13) lesions was 30.8%. All BIRADS 5 lesions (51/51) were concordant with pathology (PPV of biopsy-proven breast cancer of 100%) **(See Table 8).**

Prevalent and incident cancer types in the study population

Fifty-five cancers (55/324; 17.0%) were diagnosed, one with a size of 1.4cm on screening (1/185; 0.5%) and 54 with an average size of 3.6 ± 1.9 cm (range 2.0 - 5.3) on diagnostic workup (54/139; 38.8%), all visualized on both mammography and ultrasound. Mammography cancer detection was 0.5% in the screening (1/185) and 38.8% (54/139) in diagnostic groups.

There were more postmenopausal cancers than pre/perimenopausal cancers in both the incident (postmenopausal 28/53; 52.8% vs. pre/perimenopausal 25/53; 47.2%) and prevalent (postmenopausal 5/6; 83.3% vs. pre/perimenopausal 1/6; 16.7%) cancers **(Table 9)**. However, this difference was not statistically significant ($p = 0.215$) **(See Supplementary table 3)**.

Three postmastectomy women had a recurrence in the ipsilateral (3/36; 8.3%) chest wall and another 3 in the contralateral breast (3/36; 8.3%). In addition, 2 (2/36; 5.6%) of these women also had morphologically abnormal lymph nodes in the axilla. The lesions in the symptomatic group in the postmastectomy women (5/5; 100%) were all concordant with pathology, while a third of the screening group (1/3; 33.3%) was concordant with pathology **(See Supplementary table 4)**.

Predictors of BIRADS 5 lesion and malignant pathology in the study population

The age of attaining menopause and personal history of breast cancer showed univariate associations with BIRADS 5 lesions on mammography in the study population. Attaining menopause at the age of 55 years or older increased the likelihood of a BIRADS 5 lesion by three times (OR=2.7; 95% CI 1.0 – 6.9; $p = 0.037$), while a woman with a personal history of breast cancer had an 87% (OR=0.13; 95% CI 0.02 – 0.96; $p = 0.019$) reduction in odds of having a BIRADS 5 lesion compared to a woman with no personal history of breast cancer **(Table 9)**. The likelihood of a BIRADS 5 lesion occurring in a woman who attained menopause at 55 years and above, however, doubled if she also had a personal history of breast cancer (OR=5.8; 95% CI 1.9 – 17.9, $p = 0.002$) **(See Table 9)**.

Only the age of 50 years and above showed univariate association with histologically-confirmed malignancy. The likelihood of a histologically-confirmed malignancy was five times (OR=5.1; 95% CI 1.0 – 26.7; $p = 0.037$) more in women aged 50 years and above than those below 50 **(See Table 10)**.

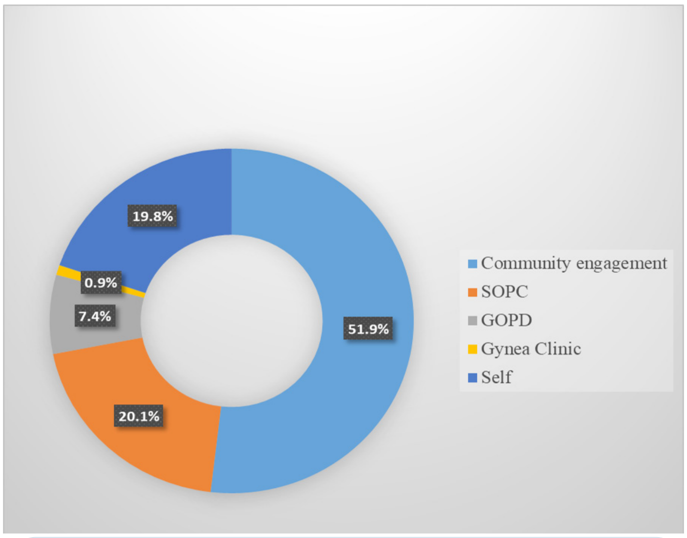


Figure 1: Pie chart showing referral pathway to mammography in the study participants.

Table 1: Risk factor profile of the study participants.

Characteristics	Freq. N=324	100%	Characteristics	Freq. N=324	100%
Age (years)			*Past history of breastfeeding*		
30-39	10	3.1	No	13	4
40-49	160	49.4	Yes	311	96
50-59	90	27.8	*Total breastfeeding duration (months)*		
60-69	48	14.8	0	13	4
≥70	16	4.9	01-Dec	8	2.5
Age at Menarche (years)			13-24	26	8
<12	10	3.1	25-36	55	17
Dec-14	138	42.6	37-48	70	21.6
15-17	138	42.6	>48	152	46.9
≥18	38	11.7	*Family history of breast cancer*		
Parity			No	292	90.1
0	11	3.4	Yes	32	9.9
1	15	4.6	*Family history of ovarian cancer*		
2	40	12.3	No	321	99.1
3	97	29.9	Yes	3	0.9
4	96	29.6	*Family history of colorectal ca*		
≥5	65	20.1	No	315	97.2
First confinement age (years)			Yes	9	2.8
<20	8	2.6	*BRCA 1 & 2*		
20-24	90	28.8	I don't know	324	100
25-29	118	37.8	*Personal history of breast cancer*		
30-34	84	26.9	No	287	88.6
≥35	12	3.8	Yes	37	11.4
Oral Contraceptives Pills			*Radiation therapy*		
No	269	83	No	324	100
Yes	55	17	*Previous high-risk lesion*		
Other contractive use			No	320	98.8
No	189	58.3	Yes	4	1.2
Yes (IUCD only)	96	29.6	*BMI Category*		
Yes (Injectable only)	12	3.7	Underweight	8	2.5
Yes (Implant only)	7	2.2	Normal weight	85	26.7
Yes (Condom only)	4	1.2	Overweight	115	36.2
Yes (IUCD + Others)	10	3.1	Obese	110	34.6
Yes (BTL)	6	1.9	*Waist:Hip category*		
Hormone replacement therapy			Low risk	22	7.4
No	321	99.1	Moderate risk	41	13.8
Yes	3	0.9	High risk	234	78.8
Alcohol intake			*Mammo ACR density*		
No	297	91.7	A	48	14.8
Yes	27	8.3	B	116	35.8
Menopausal status			C	146	45.1
Menopausal	162	50	D	14	4.3
Peri-menopausal	26	8			
Premenopausal	136	42			

Freq: Frequency; **IUCD:** Intrauterine contraceptive device; **BTL:** Bilateral tubal ligation

Table 2: Mode of presentation and means of payment in the study participants.

Characteristics		N	%
Mode of presentation among all subjects	Screening	185	57.1
	Symptomatic	139	42.9
	Total	324	100
Mode of presentation among menopausal subjects	Screening	93	57.4
	Symptomatic	69	42.6
	Total	162	100
Means of payment among all patients	NHIS	260	80.2
	OOP	64	19.8
	Total	324	100

NHIS: National Health Insurance Scheme, **OOP:** Out of pocket

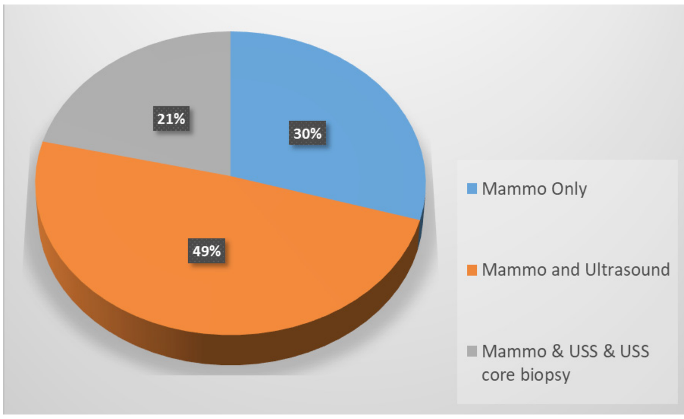


Figure 2: 3D pie chart showing the breast imaging studies done by the study participants.

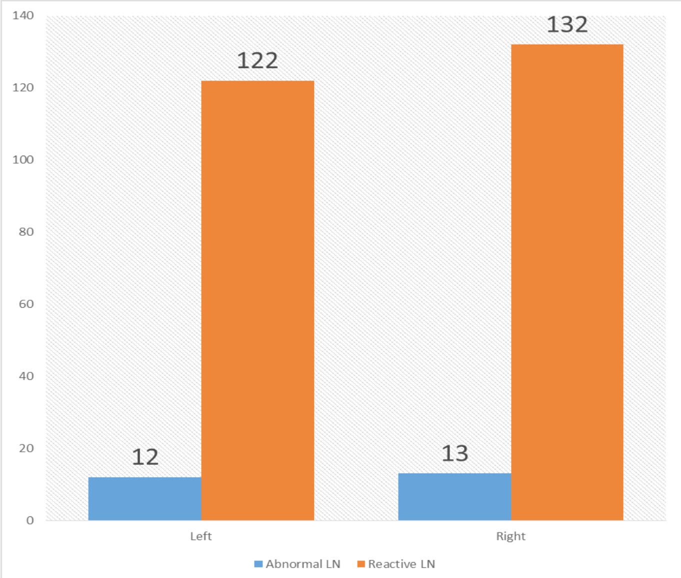


Figure 3: Bar chart showing the frequency of abnormal and reactive axillary lymph nodes in the study participants.

Table 3: Comparison of the mode of the presentation with means of payment in the study population.

Post-Mastectomy	Mode of presentation	Means of payment						p value
		NHIS		*OOP*		*Total*		
		n	%	N	%	N	%	
No	Screening	149	95.5	7	4.5	156	100	**< 0.001***
	Symptomatic	76	57.6	56	42.4	132	100	
Yes	Screening	28	96.6	1	3.4	29	100	1.000#
	Symptomatic	7	100	0	0	7	100	

*p-value is based on Chi square test; #p-value is based on Fischer's exact test; NHIS-National Health Insurance Scheme, OOP-Out of Pocket.

Table 4: Laterality of breast lesions, symptoms, and symptom duration in the study participants.

Characteristics		N	%
Laterality/ Breast affected	Left	34	23.8
	Right	38	26.6
	Right + Left	71	49.7
	Total	143	100
Symptoms	Lump	51	36.7
	Pain	50	35.9
	Nipple discharge	9	6.5
	Others	8	5.8
	Lump + Pain/Other symptoms	21	15.1
	Total	139	100
Duration of symptoms	<1 month	33	23.7
	1-6 months	57	41
	11-12 months	26	18.7
	>12 months	23	16.6
	Total	139	100

Table 5: Comparison of the positive breast findings with the laterality of the affected breast in the study participants.

	Laterality of the affected breast						*p*-values*		
	Left (L)		Right (R)		Left+Right (B)		LvsR	LvsB	RvsB
BIRADS Category	n	%	n	%	n	%			
2&3	34	54.8	36	55.4	68	88.3	0.951	**<0.001**	**<0.001**
4&5	28	45.2	29	44.6	9	11.7			
Total	62	100	65	100	77	100			

**p-values are based on Chi square test*

Table 8: Comparison of BIRADS 4 and 5 lesions with pathology findings for radiologic-pathologic concordance in the those who had ultrasound-guided core needle biopsy.

Pathology findings	BIRADS 4		BIRADS 5	
	N	%	n	%
Benign	9	69.2	0	0
Malignant	4	30.8	51	100
Total	13	100	51	100

Table 6: Types of benign breast lesions in the study participants.

Benign breast lesions	Left		Right	
	n	%	n	%
Vascular calcification	10	27.1	6	15
Parasitic calcification	8	21.6	4	10
Dermal calcifications	2	5.4	3	7.5
Round calcification	2	5.4	3	7.5
Rodlike calcification	1	2.7	3	7.5
Punctate calcification	0	0	1	2.5
Popcorn calcification	0	0	1	2.5
Intramammary LN	4	10.8	8	20
Breast cysts/abscess	3	8.1	1	2.5
Fibroadenomas	3	8.1	6	15
Others	4	10.8	4	10
Total	37	100	40	100

Table 7: Locations of benign and malignant breast lesions in the study participants.

	Left Breast			Right Breast		
Benign lesions	N	%	% of cases (N=127)	N	%	% of cases (N=124)
Upper outer quadrant	66	39.5	52	73	45.6	58.9
Upper inner quadrant	30	18	23.6	24	15	19.4
Lower outer quadrant	16	9.6	12.6	10	6.2	8.1
Lower inner quadrant	43	25.7	33.9	44	27.5	35.5
Subareolar/Retroareolar	12	7.2	9.4	9	5.6	7.3
Total	167	100	131.5	160	100	129
Malignant lesions	N	%	% of cases (N=37)	N	%	% of cases (N=39)
Upper outer quadrant	25	51	67.6	29	56.9	74.4
Upper inner quadrant	15	30.6	40.5	7	13.7	17.9
Lower outer quadrant	3	6.1	8.1	6	11.8	15.4
Lower inner quadrant	4	8.2	10.8	8	15.7	20.5
Subareolar/Retroareolar	2	4.1	5.4	1	2	2.6
Total	49	100	132.4	51	100	130.8

Table 9: Risk factors that predict BIRADS 5 lesions in the study population.

	Outcome: BIRADS 5 breast lesion					
Predictors	**Univariate**			**Multivariate#**		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Age ≥ 50 years	1.6	0.9-3.0	0.109	NI		
Age at Menarche <12 years	0.6	0.1-4.6	0.597	NI		
Nulliparity	1.9	0.2-15.5	0.522	NI		
Birth interval < 2 years*	-	-	-	NI		
First confinement age ≥ 25 years	0.8	0.4-1.5	0.453	NI		
Oral Contraceptives Pills	1	0.5-2.3	0.944	NI		
Alcohol intake	0.6	0.2-2.2	0.465	NI		
Age at Menopause ≥ 55 years	**2.7**	**1.0-6.9**	**0.037**	**5.8**	**1.9-17.9**	**0.002**
Breastfeeding	2.4	0.3-18.5	0.402	NI		
Breastfeeding duration < 1year	3.6	0.5-27.7	0.187	NI		
Family history of breast cancer	0.7	0.2-2.2	0.332	NI		
Family history ovarian cancer	0.8	0.8-0.9	0.447	NI		
Family history colorectal cancer	1.8	0.8-0.9	0.183	NI		
Personal history of breast cancer	**0.13**	**0.02-0.96**	**0.019**	**0.06**	**0.01-0.54**	**0.012**
Previous high-risk lesion	1.8	0.2-17.2	0.624	NI		
Obesity	0.6	0.3-1.2	0.601	NI		
ACR Breast Density C&D	1.1	0.3-4.5	0.907	NI		

R^2: Nagalkerke R square; **NI:** Not included; OR Odds ratio; * No statistics is computed because the predictor variable is a constant; #model **R^2 value:** 0.084

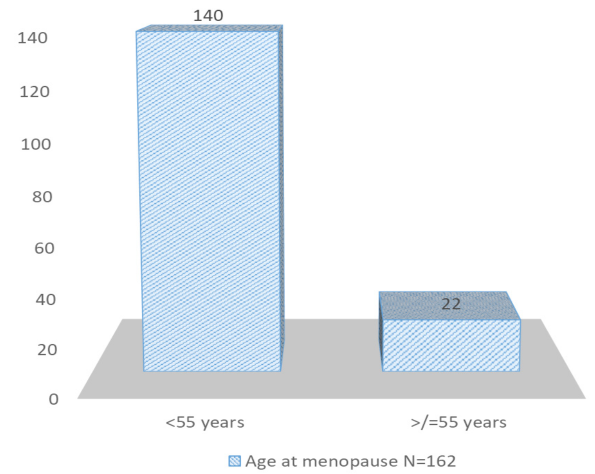
Table 10: Risk factors that predict Malignant pathology in the study population.

	Outcome: Malignant Pathology		
Predictors	**Univariate**		
	OR	95% CI	P value
Age ≥ 50 years	**5.1**	**1.0-26.7**	**0.037**
Age at Menarche <12 years	0.2	0.0-2.4	0.119
Nulliparity	1.2	1.1-1.3	0.575
Birth interval < 2 years*	-	-	-
First confinement age ≥ 25 years	1.3	0.3-5.2	0.755
Oral Contraceptives Pills	1.4	0.2-13.0	0.744
Alcohol intake	0.9	0.1-8.5	0.931
Age at Menopause ≥ 55 years	0.85	0.77-0.95	0.275
Breastfeeding	1.2	1.1-1.3	0.575
Breastfeeding duration < 1year	1.2	1.1-1.3	0.575
Family history of breast cancer	0.7	0.1-7.2	0.795
Family history ovarian cancer*	-	-	-
Family history colorectal cancer*	-	-	-
Personal history of breast cancer	0.9	0.1-8.5	0.931
Previous high-risk lesion	0.9	0.1-8.5	0.931
Obesity	0.6	0.1-2.8	0.68
ACR Breast Density C&D	1.1	0.3-4.5	0.907

OR: Odds ratio, * No statistics is computed because the predictor variable is a constant.

Sup table 1: Sociodemographic characteristics of the study population.

Characteristics		**Frequency N= 324**	**%**
Ethnicity	Yoruba	308	95.1
	Igbo	11	3.4
	Others	5	1.5
Marital status	Married	277	85.5
	Widowed	37	11.4
	Single/Separated	10	3.1
Level of education	None	11	3.4
	Postgraduate	71	21.9
	Primary	28	8.6
	Secondary	43	13.3
	Tertiary	171	52.8



Sup Figure 1: 3D bar chart showing age at menopause among the study participants.

Sup table 2: Length of birth interval between first and last confinement among multiparous study participants.

Birth interval (years)	**N**	**%**
<2	3	1
02-Mar	29	9.8
04-May	50	16.8
06-Jul	50	16.8
08-Sep	51	17.2
>/=10	114	38.4
Total	297	100

Sup table 3: Comparing breast cancer types with menopausal status in the study participants.

Menopausal status	Breast cancer (BC) type				*Total*		*p*-value
	Incident BC		Personal BC history				
	N	%	n	%	n	%	
Pre/Perimenopausal	25	47.2	1	16.7	26	44.1	0.215*
Menopausal	28	52.8	5	83.3	33	55.9	
Total	53	100	6	100	59	100	

*p-value is based on Fisher's exact test.

Sup table 4: Imaging and pathology findings in postmastectomy study participants.

	Mode of presentation					
	Screening		Symptomatic		*Total*	
	N= 29		N=7		N= 36	
	n	%	n	%	n	%
Postmastectomy breast USS						
Normal	28	96.6	5	71.4	33	91.7
Recurrent chest wall tumour	1	3.4	2	28.6	3	8.3
Postmastectomy Axilla USS						
No lymph node	26	89.7	6	85.7	32	88.9
Abnormal ALN	1	3.4	1	14.3	2	5.6
Reactive ALN	2	6.9	0	0	2	5.6
Contralateral breast Mammography/USS						
Normal/Benign lesion	28	96.6	5	71.4	33	91.7
Suspicious lesion	1	3.4	2	28.6	3	8.3
Pathology Findings						
Biopsy not indicated	27	93.1	2	28.6	0	0
Benign	1	3.4	0	0	1	14.3
Malignant	1	3.4	5	71.4	6	85.7

Sup table 5: Number of study participants who had core breast and lymph node biopsies.

Lymph node biopsy	Core breast biopsy					
	Yes		No		Total	
	n	%	N	%	N	%
Yes	15	22.4	2	0.8	17	5.2
No	52	77.6	255	99.2	307	94.8
Total	67	100	257	100	324	100

Discussion

This study is a retrospective analysis of mammography studies in a tertiary hospital in southwest Nigeria. It is the first study to comprehensively evaluate mammography uptake in Nigeria, elaborating the risk factor profile, mammographic findings with radiology-pathology concordance of findings that warranted biopsy, predictors of BIRADS 5 lesions on imaging and malignant pathology, and the referral path of the study population to mammography.

The analyses showed that more of the women who undertook mammography in the year under study had protective factors as they were younger than 50 years and multiparous; attained menarche at the age of 12 years and above, had a young age at their first confinement, a long birth interval between their first and last confinements and long years of breastfeeding. In addition, they attained menopause before 55 years of age, did not use OCP or HRT, did not take alcohol, had no family history of breast, ovarian, or colorectal cancer, did not have a personal history of breast cancer or high-risk lesion, and no history of radiation to the chest.

On the contrary, more of these women were overweight and obese. Obesity increases the risk of breast cancer, particularly postmenopausal cancer [25,26], as some studies found obesity to be protective against premenopausal cancer [25]. This paradoxical relationship between obesity and breast cancer depending on the menopausal status has been attributed to the difference in hormonal milieu between premenopausal (primary estrogen source is the ovary) and postmenopausal (primary estrogen source is the fat cells) women [25,26]. Observations from this analysis show that the prevalence of postmenopausal cancers was comparable to the premenopausal cancers, and obesity did not predict BIRADS 5 lesions or malignant pathology. Further research is recommended to understand the association between obesity and breast cancer in our population since the prevalence of obesity is increasing in Nigeria [27], with southwest Nigeria having the highest prevalence rates [27]. Curbing obesity with lifestyle modification may reduce the incidence of breast cancer cases in Nigeria.

Obesity has also been shown to be inversely related to breast density, and both breast density and obesity act as confounders to each other's effects [28]. The incidence of dense breast parenchyma patterns in this analysis is higher than expected for the high prevalence of obesity in the study participants. The relatively young age (40 – 49 years) of most participants (160/324 = 49.4%) could account for the high prevalence of dense breast parenchyma patterns in this analysis. The incidence of dense breast parenchyma patterns in this analysis is higher than in previous studies (49.3% in the index study vs. 16% by Akinola et al., vs. 29.8% by Obajimi et al., vs. 16.9% by Akande et al., vs. 29.7% by Adeyomoye et al.) [14,17-19]. While the study by Akinola et al. [14] had the majority (> 40.3%) of their study participants above 50 years, Akande et al., Obajimi et al., and Adeyomoye et al. had the majority (48.6%, > 50%, and 73.9% respectively) in their 40s and less [17-19]. However, these other studies did not report the BMI status of their study participants to be able to make further deductions on the reasons for the disparity in findings. There may be other determinants of breast density other than age and BMI status in our population. Also, breast density is usually a subjective assessment provided by the interpreting radiologist with reported inter and intra-observer variability, which limits comparison between studies. Nevertheless, the factors that influence breast density in Nigerian women require more study because this may hold the key to providing appropriate health education measures and better informing high-risk and supplementary screening for Nigerian women.

This analysis shows that mammography uptake was more for screening than diagnostic purposes, even in postmastectomy women. This finding contrasts previous sub-Saharan African studies that show mammography uptake is majorly for diagnostic workups [10,11,17, 29-36]. One of the reasons for the low mammography screening uptake in these previous studies is poor awareness of the disease and its screening methods [10, 11, 29-36]. The finding of the index analysis, therefore, suggests an improvement in breast cancer awareness in southwest Nigeria which is not unexpected as a result of some internationally funded breast cancer projects in this region of the country that are domiciled in OAUTHC, the hospital under study [37-39]. Furthermore, the contribution of these studies to increased mammography utilization for screening is seen in the present analysis, as community engagement was the commonest path to mammography, followed by self-referral. The significant contribution from self-referral seen in this study also suggests better education on the disease and its screening methods in the participants, which invariably leads to good health-seeking attitudes. The smaller size (1.4cm) of the cancer detected in the screening group compared to the cancers detected in the diagnostic group (3.6 ± 1.9 cm; range 2.0 - 5.3) further supports the benefit of mammography screening which is early detection of breast cancer.

In addition, a recent survey showed that 75% of the population in southwest Nigeria have access to mammography services within one hour of travel from their home [40]. Therefore, good geographical access may have also contributed to this outlook. Previous studies [10, 11, 29-36] also identified cost as a barrier to mammography screening in Nigeria and other Sub-Saharan countries. This present analysis further linked the screening attendance to cost reduction, as most of those who attended mammography for screening had their studies covered by NHIS rather than paying out of pocket. Despite only 5% of Nigerians having health insurance and 70% still financing their healthcare through the out-of-pocket payment method [41], the higher percentage of women utilizing NHIS for payment for their mammography tests compared to those paying out-of-pocket in this study was expected because of the education on NHIS given to women during community engagements which was the commonest pathway to mammography in this study. Despite the good population-level access to mammography in southwest Nigeria, the time-to-mammography from the onset of symptoms in most of the diagnostic population in this study was more than one month. The data also show that more of those who paid out of pocket for their study were in the diagnostic group. Therefore, cost and not necessarily access would have been the main contributor to the late presentation in the diagnostic group. Efforts to increase the number of Nigerians subscribed to NHIS may, therefore, contribute to the early presentation of women for diagnostic evaluation of breast symptoms in Nigeria, which is crucial in achieving the 60-day diagnostic interval from symptoms to tissue diagnosis recommended by the World Health Organization. Radiologists, therefore, play a key role in the gateway to evaluation (with screening and diagnostic evaluation) and getting tissue for a diagnosis (with image-guided biopsy) to move on to treatment promptly.

As increased awareness of the disease and its screening methods, good geographical access, and cost reduction from NHIS lead to increased mammography utilization for screening, attention should be given to potential challenges. For example, there is only one mammography machine in OAUTHC, the hospital under study, which may not cope with increased mammography uptake. Therefore, there is a need to provide more mammography machines to reduce the pressure on the only available machine in the hospital as the patient volume increases. In addition, mobile mammography vans can be alternatives to underserved, far-to-reach, and hard-to-reach Nigerian communities with locations far from the secondary and tertiary hospitals that provide specialized breast care. Collaboration between private multinational companies domiciled in Nigeria, and the government through public-private partnerships to provide more static mammography machines to hospitals and mobile vans to underserved communities will reduce the financial burden on hospitals and health institutions.

For the success of any screening program, there is a need for solid diagnostic support for further workup of screen-detected lesions, as evidenced in this analysis. The screen-detected lesions in this analysis could only get pathology diagnosis using ultrasound-guided core needle biopsy due to the lack of stereotactic biopsy equipment in the hospital under study, which may have caused under-sampling of the target lesions. Therefore, there is a need for the hospitals and health institutions' procurement departments to consult with breast radiologists in the radiology department to ensure the inclusion of all the required specialized paddles and stereotactic equipment for diagnostic workups during the purchase of mammography machines. There is also the need for the hospitals and health institutions' clinical services departments to provide an avenue for the training of the personnel that provides these screening and diagnostic services (radiologists and radiographers) to enhance the services provided in these hospitals/ health institutions.

The mammographic findings in women with BIRADS 2 and 3 lesions agree with the existing literature [14,17-19]. BIRADS 2 and 3 lesions were more likely to be bilateral than unilateral, with more of parasitic calcifications, vascular calcifications, and intramammary lymph nodes, and prevalent in the upper outer quadrant, similar to other Nigerian studies [14, 17]. On the contrary, BIRADS 4 and 5 lesions were more likely to be unilateral than bilateral in this study. The PPV of breast cancer in BIRADS 4 lesions was 30.8% in this study; therefore, almost 70% of BIRADS 4 lesions (9/13; 69.2%) yielding benign pathology, which included benign phylloides, hamartoma, fibrocystic disease, and fibroepithelial lesion. The high PPV in BIRADS 5 lesions in this study does not preclude the need for core needle biopsy in BIRADS 5 lesions, as preoperative tissue diagnosis is still recommended for definitive treatment.

While Nigeria has no formal national breast cancer screening program, a two- or even three-yearly population screening for average-risk women, known to reduce mortality [42] combined with a targeted risk-based annual invitation screening for high-risk women, may be considered for our resource-limited country. Understanding the predictors of malignancy on imaging and pathology in this study population may help provide a more informed approach to optimizing resources for breast cancer screening for high-risk women in Nigeria. Observations from this analysis show that women who attained menopause at age 55 and above were three times at risk of a BIRADS 5 lesion highly suggestive of malignancy compared to their counterparts who attained menopause younger than 55 years, with this risk doubling if they also had previous breast cancer. Also, women 50 years and above were five times more at risk of a malignant pathology than younger women. The invitation eligibility for targeted risk-based screening can build on the findings of this present study. Women who are 50 years and above, attained menopause after 55 years of age, and have had previous breast cancer for breast cancer screening can be targeted for risk-based screening. A recent retrospective review of cancer registries in Nigeria shows a sharp rise in female breast cancer at the age of 35 years, with a peak around 40 years of age [43]. Therefore, the age recommendation for population-wide screening in Nigeria should be a decade earlier than 40, the earliest age recommended for mammography screening in established breast cancer screening guidelines [43]. However, due to the implication of dense breasts in young women, other screening methods like ultrasound and MRI should be the way to go in young women. This is a wake-up call for members of BISON and the Association of Radiologists in Nigeria (ARIN) to develop national guidelines for routine and targeted high-risk breast cancer screening. In addition, there is a need for systematic auditing of results across all health institutions that provide mammography services to inform recommendations specific to Nigeria and benchmarks for individual and institutional performance.

In conclusion, this rigorous evaluation of the mammography studies in a Nigerian tertiary hospital shows that wider NHIS coverage, better geographical access, and increased awareness of the disease and its screening methods can increase mammography utilization for screening in asymptomatic women and prevent late presentation for diagnostic evaluation in symptomatic women. The cancer detection rates among the screening and diagnostic population in this analysis provide an important foundation for building future studies that can ultimately inform public health policy. In addition, the age of ≥ 50 years, the age of attaining menopause ≥ 55 years, and personal history of breast cancer are patient factors that should be considered in developing a systematic risk-based breast cancer screening program for Nigerian women. However, beyond mammography, any screening program needs a solid foundation of diagnostic imaging/biopsy capabilities, pathology collaboration, and surgical/oncology services for treatment. Collaborations between the government and multinational private companies in Nigeria will reduce the financial burden of procuring equipment required for this solid diagnostic imaging, pathology, and oncology capabilities. Also, a successful screening program should include patient navigation and assessment of the access/affordability of post-screening services. Therefore, a collaborative effort is required between BISON, ARIN, Surgical/Oncological societies, and the Nigerian government to build on observations from this study to develop an effective screening program for the country. Although this study provided some factors to guide targeted screening, the selection of breast cancer risk factors for targeted screening would have been better guided by the epidemiology of the disease within Nigeria. So, a multicenter epidemiologic study nationwide is recommended for more robust analyses. Nevertheless, the findings of this study provide evidence-based risk factors to drive risk-based breast cancer screening policies in Nigeria. Reducing cost, increasing awareness, and improving geographical access are pragmatic ways to increase mammography utilization for screening in Nigeria.

Study limitations

As a retrospective study, there are some limitations, given that the data reviewed from the records for this study depended on good recall of the women for long-term events when filling the risk-based questionnaires during their mammography studies. Errors in the timing of events could have occurred on the part of the women, which would have introduced information bias to the study. The researcher also depended on good record-keeping in the breast unit of the radiology department for data for this study which is another limitation of this retrospective study. However, the record staff of the breast unit regularly backs up patients' data on the hard copy questionnaires to the cloud weekly to prevent loss of information. Lack of long-term follow-up precludes an analysis of the true negative and false negative rates of normal mammography studies, and further study is warranted beyond this one-year analysis. Additionally, the small sample size limits a more robust assessment of screening cancer detection rates. Further studies are underway to provide a larger sample size analysis.

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