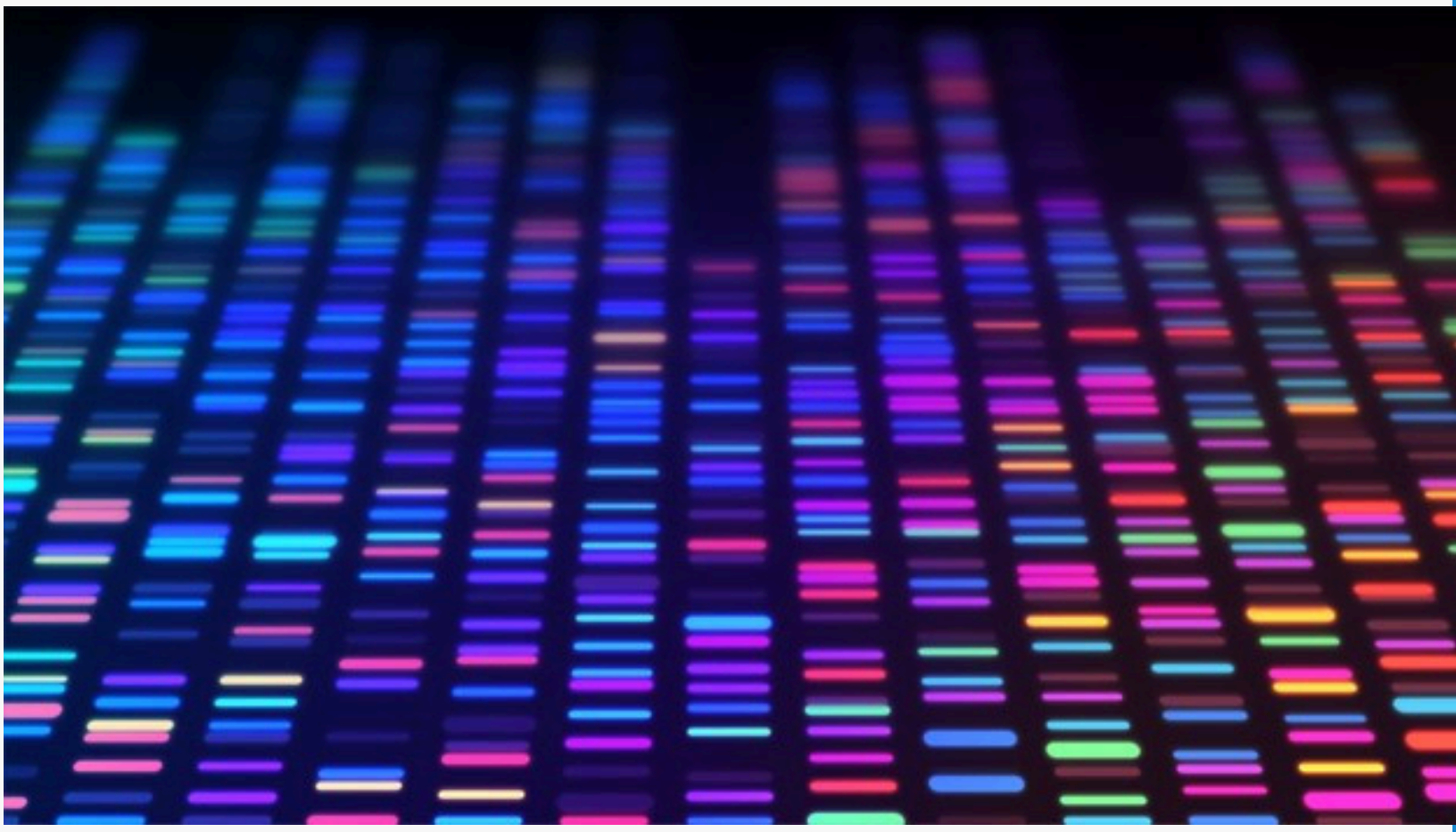
Evaluation of the biological characteristics of breast cancer in women from Nigeria: A non-interventional pilot study

VOLUME 1



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Abstract

Breast cancer remains a major cause of cancer-related deaths globally, with distinct characteristics among African populations. This study delves into the biological features of breast cancer in Nigerian women to bridge knowledge gaps in this area. By examining 30 treatment-naïve patients across various cancer centers, the study focused on key factors like hormone receptor status, HER2 expression, tumor grade, and molecular subtypes.

The majority of cases (96.67%) were invasive ductal carcinomas, with half classified as high-grade tumors. A notable finding was the high prevalence of triple-negative breast cancer (40%), while HR-positive subtypes were less common (ER-positive: 43.33%; PR-positive: 10%). Additionally, 20% of cases were HER2-positive. These results highlight the aggressive nature of breast cancer in this population, characterized by a higher proportion of high-grade and hormone receptor-negative tumors.

The study emphasizes the urgent need for tailored diagnostic and treatment approaches, increased access to targeted therapies, and further research into genetic and environmental factors that contribute to breast cancer in Nigerian women. Future studies with larger sample sizes and advanced molecular profiling are essential to inform effective interventions and improve outcomes for this vulnerable population.

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1. Introduction

Globally, breast cancer is the most frequently diagnosed cancer and currently accounts for the highest number of cancer-related deaths among women. African countries, including Nigeria, face unique challenges in managing breast cancer due to limited healthcare resources, cultural perceptions and delayed diagnosis (1, 2).

Studies have shown that breast cancer in African women, particularly in Nigeria, often presents at a more advanced stage and with more aggressive characteristics than in Western populations (3,4,5). While subtypes generally differ in prevalence globally, recent studies focusing on Nigerian women have observed a high prevalence of aggressive subtypes—especially in breast cancer cases which are devoid of HER2, progesterone, and estrogen receptors, also known as triple-negative breast cancers (TNBC) (6,7,8).

Hormone receptor (HR) status is a significant factor in breast cancer treatment, as HR-positive cancers are generally more responsive to hormone-based therapies. However, several studies have highlighted a low prevalence of HR-positive tumors in African women compared to their Western counterparts (9, 10).

TNBC is more difficult to treat, as targeted hormone therapies are ineffective, making it an area of active research. Additionally, Luminal B tumors, which tend to be more aggressive than Luminal A, are commonly observed in Nigerian women; these subtypes often correlate with younger age. at diagnosis and larger tumor sizes (11). Although Luminal B is more aggressive than Luminal A, they are both susceptible to endocrine therapy like tamoxifen and typically offer a more favorable prognosis than other molecular subtypes.

The HER2-positive subtype has also been identified, though with variation in prevalence. While there are targeted therapies for this subtype that make it more manageable than TNBC, researchers have identified new genes with significant mutations enriched in HER2-positive breast cancer among Nigerian women. Therefore, aggressive characteristics are prevalent in breast tumors among Nigerian women, irrespective of the subtype (12).

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This aggressiveness is due to tumor heterogeneity which is intertumoral (observed in breast cancers from different individuals) and/or intertumoral (illustrated by histological and bio-molecular variability, chromosomal,

1. Introduction cont'd

genomic, metabolic and epigenetic changes, in addition to cellular plasticity and the tumor microenvironment). All of which makes accurate diagnosis and prognosis more challenging.

Understanding the biological characteristics specific to this population is crucial to developing effective treatments and improving patient outcomes. This has prompted researchers to consider potential genetic and environmental factors that influence these findings. By looking at the prevalence of hormone receptor (HR) positivity and HER2 expression, this study aims to investigate breast cancer subtypes and characteristics that are common among Nigerian women.

2. Methodology

The objective of this prospective, observational, non-interventional pilot study is to investigate the biological characteristics of breast cancer in women from Nigeria. In order to assess data collection methods, spot possible logistical problems, and produce preliminary data that might guide effect size estimates and variance calculations for larger future studies, pilot studies usually use smaller sample sizes, usually between 10 and 30 participants (13,14).

This study used a sample size of 30 participants to gather foundational data for the design of larger studies. The study was conducted across various Cancer centers in Nigeria, including Lagos, Abuja, Ibadan, Benue, and Ogun state from February 2024 to August 2024. These locations serve a large and diverse population, ensuring representative sampling for the pilot study.

Participants were recruited through outpatient departments at the study locations. Informed consent was obtained from each participant after explaining the study's purpose, procedures, benefits and risks. The participants were assured of confidentiality and their right to withdraw at any point without any impact on their medical care.
Relevant data including age, ethnicity, family history of breast cancer and reproductive history were collected from patients, while the tumor characteristics (size, grade, and stage),

2. Methodology cont'd

lymph node involvement, metastasis status and other relevant clinicopathological details were collected from the pathological analysis of the breast tissues. All data was recorded in a secure, anonymized database for further analysis.

Haematoxylin and eosin (H&E) stained slides and immunohistochemistry slides stained for ER, PR, and HER-2 were created from tumor specimens that had been preserved as formalin-fixed, paraffin-embedded (FFPE) tissue blocks. These slides were reviewed by the pathologist to evaluate their microscopic features, including tumor grade, stage and molecular subtypes.

The Nottingham modification of the Scarff-Bloom-Richardson grading system was used to assess histological grade. This system evaluates three key factors: the formation of tubules, the size and variation of nuclei and the rate of cell division. Each factor is assigned a score of 1 to 3, and the total score determines the tumor's differentiation level. Tumors with scores of 3-5 are well-differentiated (grade 1), 6-7 are moderately differentiated (grade 2), and 8-9 are poorly differentiated (grade 3). Tumor sizes were categorized as small (less than 2 cm), medium (2-5 cm) and large (over 5 cm). Immunohistochemical analysis was employed to evaluate the presence and activity of specific biomarkers associated with breast cancer, including Ki-67, which indicates the rate of cell proliferation.

Additionally, the hormonal receptor status—estrogen receptor (ER) and progesterone receptor (PR)—as well as the human epidermal growth factor receptor-2 (HER2) were assessed to determine the tumour's molecular profile. Based on the receptor expression patterns, tumours were classified into subtypes such as triple- negative breast cancer (TNBC), ER-positive, PR-positive or HER2-positive. To ensure accuracy and consistency, scoring was conducted using established methodologies: the Allred scoring system was applied for ER and PR evaluations, while HER2 expression levels were determined through the HER2 immunohistochemistry assay.

2. Methodology cont'd

2.1 Inclusion Criteria

The study included women aged 18 years and older who were recently diagnosed with breast cancer and who were treatment-naïve—meaning they had not received chemotherapy, radiation therapy, or surgical procedures prior to the commencement of the study. All study participants were of Nigerian heritage to focus specifically on local genetic and environmental factors.

2.2 Exclusion Criteria

Patients with prior breast cancer treatment, patients with other concurrent cancers and patients currently undergoing treatment.

2.3 Data Analysis

IBM SPSS version 24.0 was used to analyze the data. Frequencies and percentages were used to summarize the distribution of breast cancer subtypes and other molecular characteristics within the research population.

2.4 Ethical Considerations

Institutional Review Board (IRB) approval and participant informed consent were obtained. Study coordinators handed information packets and explained study protocol in detail including the rights to withdraw at any time and well as right to confidentiality. Additionally, the study did not cause harm to any human subject and was conducted in compliance with the World Medical Association's 2000 Declaration of Helsinki's ethical principles.

3. Results

30 research participants with breast malignancies from mastectomy specimens from different cancer institutions in Nigeria were used in this investigation. Patients ranged in age from 35 to 63, with a mean age of 48.73 years. 43.33% of the study population, or the 40–50 age range, (5th decade) had the highest number of cases (Table 1).

Age groups	Frequency, (n)	Percentage (%)
<40	5	16.6
40-50	13	43.33
51-60	9	30
>60	3	10

Table 1: Distribution of study cases by age

3. Results cont'd

29 (96.67%) out of 30 participants had invasive ductal carcinoma of no special type (NST) (Figure 1). According to the Nottingham grading scheme, 10% (3) of cases had grade I breast cancer, whereas 40% (12) and 50% (15) of cases had grade II and grade III disease, respectively (Figure 2).

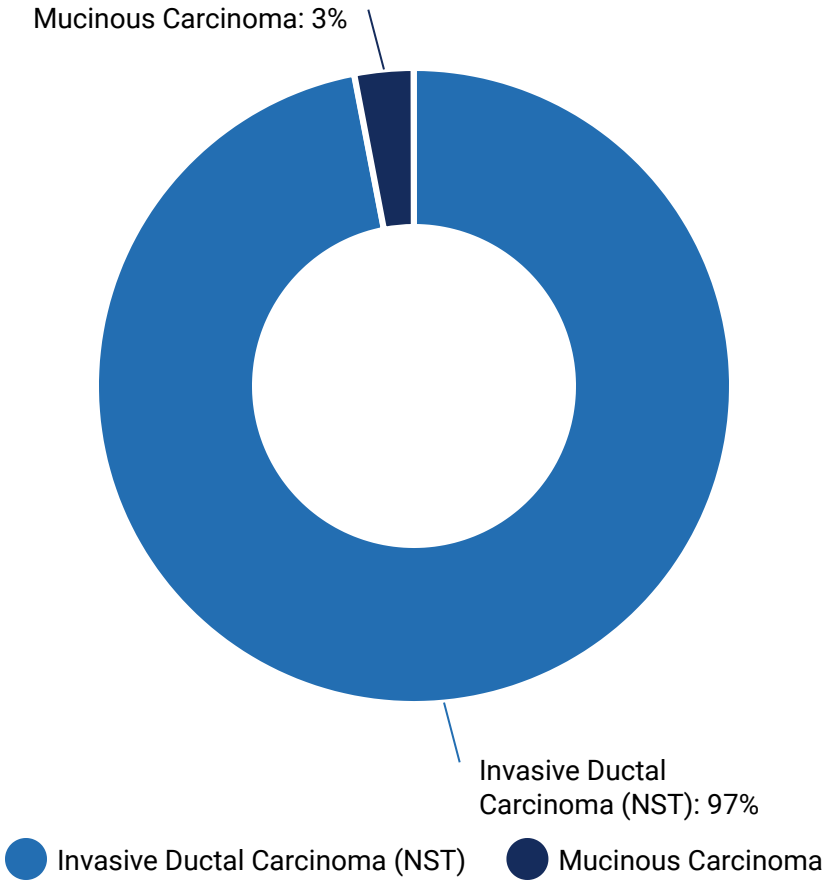


Figure 1: Distribution by histological subtype

3. Results cont'd

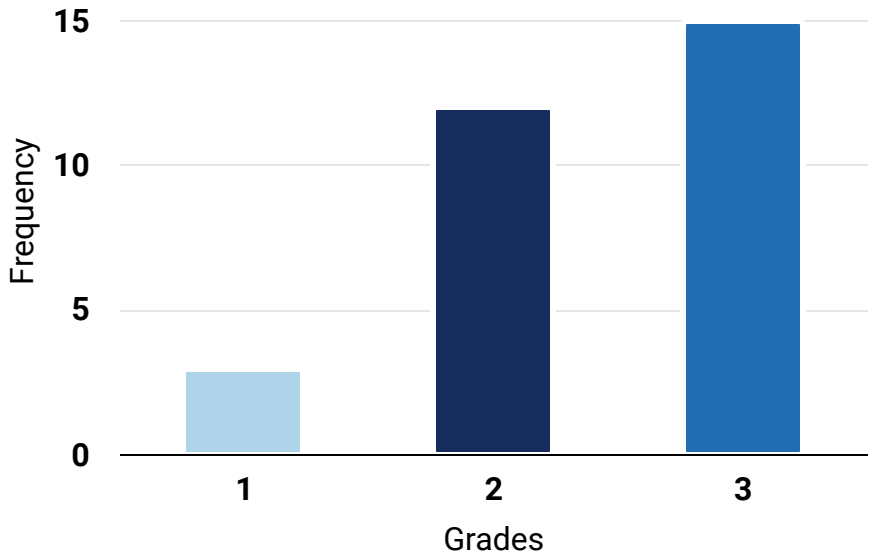


Figure 2: Distribution of cases by grade

Monoclonal ER, PR, and HER-2 antibodies were used for immunohistochemical analysis of each case. Some of the tumour cells (43.33%) were ER-positive, while the majority (56.67%) were ER-negative. Conversely, 10% were PR-positive and 90% were PR-negative. Just 20% of the tumour cells tested positive for HER-2 (Table 2 and Figure 3).

Hormone Receptor	Positive	Negative
ER	13 (43.33%)	17 (56.67%)
PR	3 (10%)	27 (90%)
HER-2	6 (20%)	24 (80%)

Table 2: Hormone receptor status of breast cancer cases

Furthermore, triple-negative (ER-/PR-/HER-2-) patients made up 40% of all cases, whereas luminal A and luminal B cases made up roughly 27% and 16% of all cases, respectively. Of all the cases, about 17% were HER-2 enriched (ER-/PR-/HER-2+). (Fig. 4).

3. Results cont'd

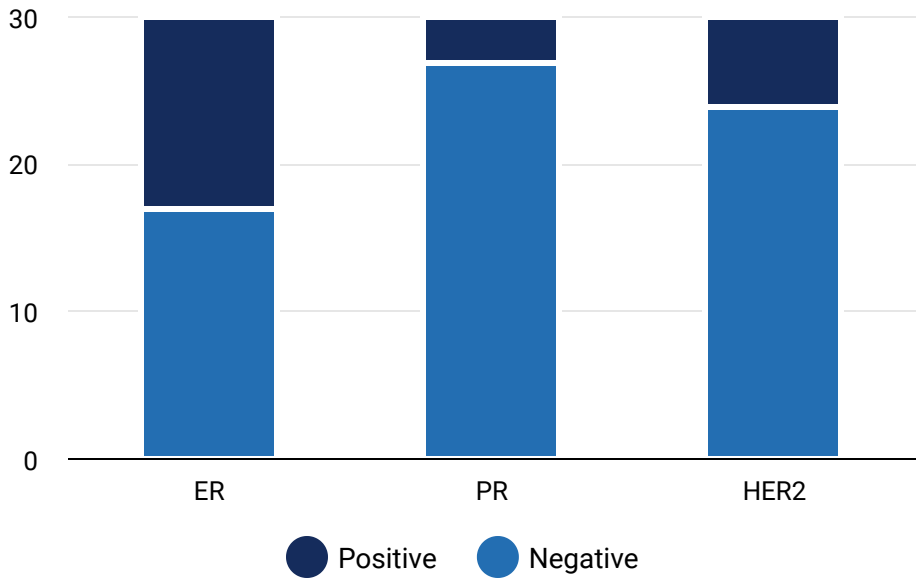


Figure 3: Comparison of positivity vs negativity of hormone receptors across cases

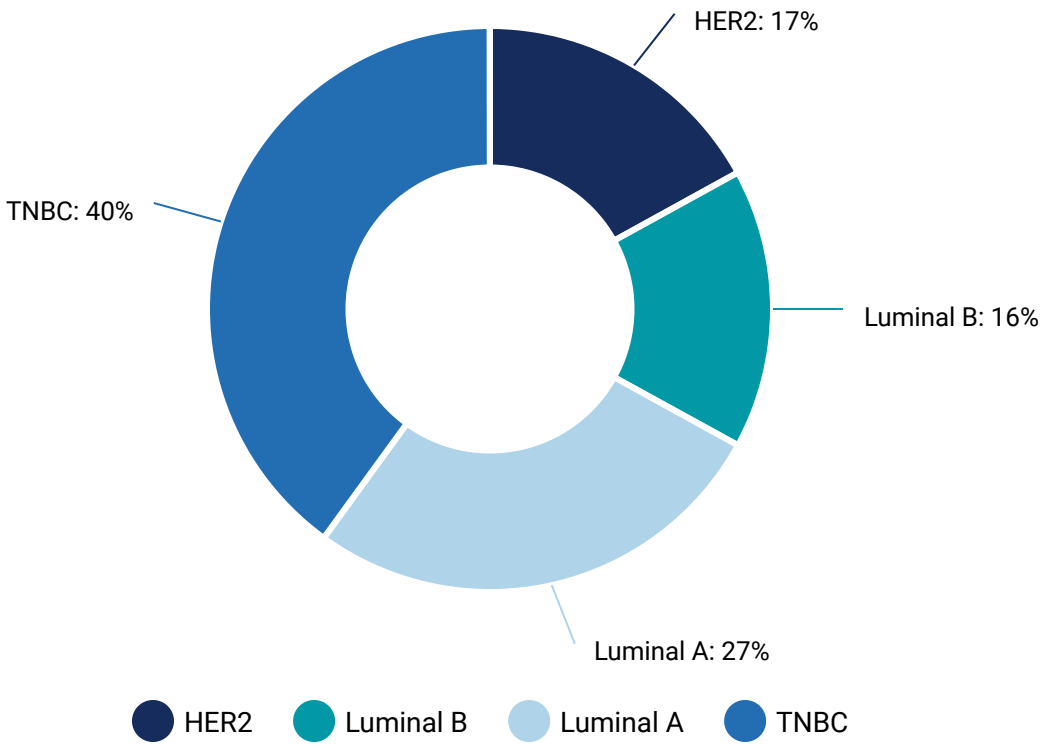


Figure 4: Distribution of molecular subtypes across cases

3. Results cont'd

	<40	40-50	51-60	>60	Total
Nottingham Histological Grades	*n*	*n*	*n*	*n*	*n*
Grade 1	0	2	1	0	3(10%)
Grade 2	2	5	5	0	12(40%)
Grade 3	3	6	3	3	15(50%)
Grand total	5	13	9	3	30(100%)
Molecular subtypes	*n*	*n*	*n*	*n*	*n*
Luminal A	2	4	2	0	8(26.66%)
Luminal B	0	3	2	0	5(16.67%)
HER-2	1	1	2	1	5(16.67%)
TNBC	2	5	3	2	12(40%)
Grand total	5	13	9	3	30(100%)

Table 3: Age distribution of breast cancer grades and molecular subtypes

4. Discussion

This preliminary study offers important information about the underlying biological characteristics of breast cancer specifically observed in women from Nigeria. It contributes to a deeper understanding of the disease in this population, with particular attention on molecular subtypes, HER2 expression, and hormone receptor (HR) status. These results add to the existing knowledge of breast cancer among African populations, emphasizing unique patterns that may influence clinical management and outcomes in Nigeria. The average age of participants in this study was 48.73 years, and the 40–50 age group had the highest incidence (43.33%). This aligns with findings two decades apart, reporting a similar age range for breast cancer occurrence among Nigerian women (1, 5). Studies from sub-Saharan Africa, including Nigeria suggest that breast cancer tends to manifest at a younger age in African women compared to Western populations, where the median age is around 60 years (1, 4). The relatively young age of onset in African women is thought to be influenced by genetic predispositions, environmental factors, and possibly the under-diagnosis of breast cancer among older women (11).

Our study found that invasive ductal carcinoma of no special type (NST) was the most prevalent histologic group, accounting for 96.67% of cases. This is consistent with previous research showing that invasive ductal carcinoma is the

4. Discussion cont'd

most common histological type in Nigerian women (8, 11). In terms of tumourgrading, Grade III tumors constituted 50% of cases, followed by Grade II (40%) and Grade I (10%). This distribution indicates a high frequency of aggressive, high-grade tumors, aligning with studies suggesting that African women are more likely to present with high-grade breast tumors (10, 12). The high proportion of aggressive, high-grade tumors highlights a significant concern, as they are associated with poorer prognosis and reduced responsiveness to standard hormone therapies. This aggressiveness has been linked to delayed diagnosis, limited access to early screening, and potential differences in tumour biology among African populations (7, 12).

Our findings indicate that 56.67% of tumours were ER-negative, while PR positivity was observed in only 10% of cases. Additionally, HER2 positivity was found in 20% of cases, which is within the range reported in other African studies. The low prevalence of hormone receptor-positive tumours in Nigerian women is consistent with previous research, which reported lower rates of HR positivity in African populations (7, 8, 9). HR-negative tumors tend to be more aggressive and have fewer treatment options, posing a significant challenge to effective management. HER2- positive tumors are also known for their aggressive nature but can be treated effectively with HER2-targeted therapies such as trastuzumab. However, due to the high cost and limited availability of targeted treatments in Nigeria, HER2-positive patients may not receive optimal care, contributing to poorer outcomes in this group(6).

According to our research, the prevalence of molecular subtypes was as follows: HER2-enriched was 16.67%, Luminal A was 26.67%, Luminal B was 16.67%, and triple-negative breast cancer (TNBC) was 40%. The significant TNBC rate in this group is consistent with prior studies that have reported similar rates of 35-50% in Nigerian and African American women. In comparison, Western studies report lower rates of prevalence, typically around 10-15%, highlighting a stark contrast that may be driven by genetic, environmental, or sociodemographic factors (6, 9).

TNBC is often associated with a younger age of onset and worse prognosis compared to other subtypes, which reflects the patterns observed in our study population. Chemotherapy is the primary therapeutic

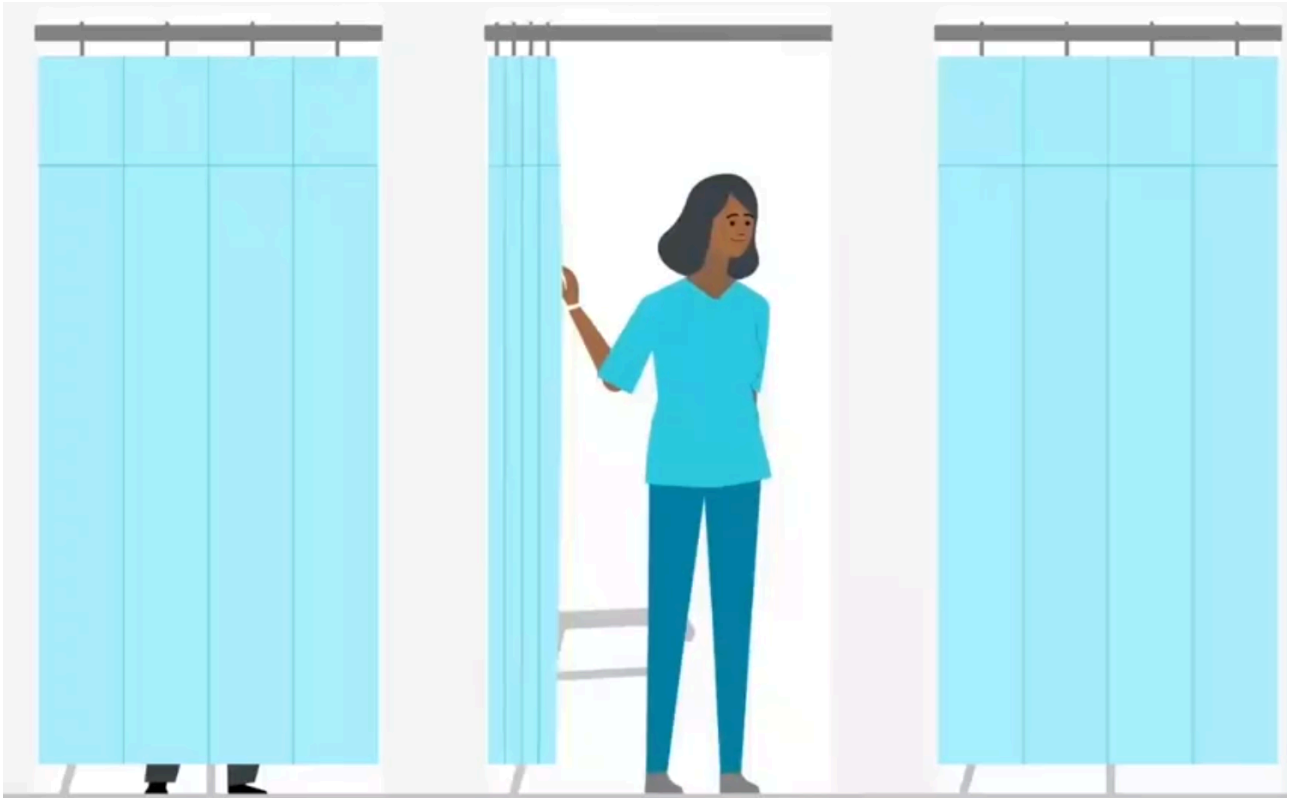
4. Discussion cont'd

option for TNBC because there are no specific medications for this condition. The disproportionately high prevalence in African women underscores the importance of research into alternative treatment options and interventions tailored to this aggressive subtype. The predominance of aggressive subtypes and high-grade tumors among Nigerian women suggests a need for more accessible and affordable treatment options, particularly targeted therapies. Studies have indicated that African populations may benefit from personalized therapeutic approaches, but limited access to diagnostic and molecular profiling tools constrains clinical management. Our results support the argument that molecular profiling and targeted treatment accessibility are essential for improving breast cancer outcomes in Nigeria (11, 12).

The lower incidence of HR-positive tumors implies limited efficacy for hormone- based therapies, such as tamoxifen or aromatase inhibitors, that are commonly used in Western populations. For Nigerian women with HER2-positive or TNBC subtypes, targeted therapies and immunotherapy, which have shown success in Western populations, are less accessible due to cost and healthcare infrastructure limitations (8).

Genetic factors may contribute to the aggressive nature of breast cancer in African women. Research suggests that breast cancer cases in Nigeria often exhibit a higher frequency of gene mutations, including those in BRCA1, BRCA2, and TP53, which are linked to aggressive tumour phenotypes and early onset (12). Genetic counseling and testing are necessary for high-risk individuals in this demographic, since the high frequency of TNBC among Nigerian women may indicate a distinct genetic susceptibility. The aggressive breast cancer phenotypes seen in Nigerian women may also be influenced by environmental factors, such as lifestyle, reproductive history, and potential exposure to carcinogens (11)

5. Limitations and future directions



This pilot study provides initial insights into the molecular features of breast cancer in Nigerian women, although certain limitations must be noted. One limitation was our small sample size of 30 individuals, which limits the generalizability of our findings to the larger Nigerian population. However, our multicenter approach across ethnic zones supports diverse representation in our data

Furthermore, the cross-sectional design of the study only records data at one time, making it difficult to evaluate how tumor features or patient outcomes have changed over time. The study also did not take into consideration possible confounding variables that could affect the features and outcomes of breast cancer, such as socioeconomic position, access to healthcare, and lifestyle factors.

To further understand the burden of breast cancer in this population, larger, longitudinal studies that take socioeconomic determinants of health and thorough molecular investigations into account are necessary.

6. Conclusion

According to this study, breast cancer in Nigerian women is unique and aggressive, with a higher frequency of triple-negative and high-grade tumors and a lower incidence of hormone receptor-positive subtypes. These findings underscore the need for tailored public health strategies, including enhanced screening programs, early detection initiatives and the development of affordable, accessible treatment options that address the unique tumor biology observed in this population.

Addressing these challenges is crucial for improving breast cancer outcomes and reducing prognostic disparities between African and Western populations. Future research should focus on large-scale, longitudinal studies that incorporate advanced molecular profiling and consider the impact of genetic, environmental and sociodemographic factors on breast cancer characteristics and patient outcomes in Nigeria.

7. Financial support/sponsorhip

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8. Conflict of Interest

No conflict of interest exists

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