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Breast Cancer Characteristics and Immunohistochemical Profiles in Women Aged 41–69 Years.

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Abstract

Background:
Breast cancer remains a major global public health challenge, with a disproportionately high mortality burden in sub-Saharan Africa due to late-stage diagnosis and limited access to screening and treatment services. Understanding the biological heterogeneity of breast cancer in this region is essential to improve early detection and personalized management strategies. To describe the sociodemographic, clinical, radiological, and pathological characteristics of women aged 41–69 years with breast cancer and to identify factors associated with immunohistochemical marker expression (ER, PR, HER2/Neu, and Ki67).

Methodology:
A retrospective analytical multicenter study was conducted among 185 women with histologically confirmed breast cancer across five referral centers in Kinshasa and Matadi, Democratic Republic of the Congo, from January 2015 to December 2023. Data on sociodemographic, clinical, imaging, and pathological variables were collected. Associations with immunohistochemical markers were assessed using univariate and multivariate logistic regression analyses, and results were expressed as adjusted odds ratios (aOR) with 95% confidence intervals (CI).

Results:
The mean age was 51.9 ± 7.9 years, with a predominance of women aged 41–55 years (67%). Most tumors were invasive (90.3%) and predominantly invasive ductal carcinoma (64.9%). High Ki67 expression was observed in 70.3% of cases. Menopause, elevated BMI, advanced clinical stage, alcohol consumption, BI-RADS 5 lesions, and calcifications were significantly associated with aggressive immunohistochemical profiles. Multivariate analysis identified menopause and advanced stage as independent predictors of ER-negative expression, while BMI and alcohol consumption were strongly associated with HER2/Neu positivity.

Conclusion:
Breast cancer in this population is characterized by early onset and biologically aggressive tumor profiles. Clinical, radiological, and metabolic factors significantly influence immunohistochemical expression, underscoring the need for integrated screening strategies and individualized management approaches in resource-limited settings.

Keywords:
Breast Cancer, Immunohistochemistry, Sub-Saharan Africa, BI-RADS, Ki67, Tumor Heterogeneity

Introduction

Breast cancer is one of the leading causes of morbidity and mortality among women worldwide, representing a major public health concern. In 2022, approximately 2.3 million new cases were reported globally, with over 666,000 deaths, making it the most frequently diagnosed cancer in women [1,2]. Despite advances in screening, diagnosis, and treatment in high-income countries, substantial disparities persist across regions, particularly in low- and middle-income countries where healthcare infrastructure remains limited [3].

In Africa, breast cancer incidence is lower compared to high-income regions; however, mortality rates are disproportionately higher, reflecting late-stage presentation and inadequate access to diagnostic and therapeutic services [4,5]. Sub-Saharan Africa faces unique challenges, including insufficient screening programs, shortage of trained healthcare professionals, limited availability of diagnostic technologies, and sociocultural barriers that delay healthcare-seeking behavior [6].

The World Health Organization projects a significant rise in breast cancer-related mortality in the region, with estimates suggesting that nearly 135,000 women could die annually by 2040 if effective interventions are not implemented [7]. In the Democratic Republic of the Congo, these challenges are further compounded by fragile healthcare systems, financial constraints, and limited public awareness regarding early detection [8].

Consequently, a large proportion of patients are diagnosed at advanced stages, significantly reducing survival rates and increasing the burden on healthcare systems [9]. While organized screening programs such as mammography have significantly reduced mortality in developed countries [10], their implementation remains limited in resource-constrained settings due to infrastructural and economic limitations [11].

Beyond epidemiological concerns, breast cancer in women aged 41–69 years has significant socioeconomic implications. Women in this age group often play central roles within families and communities, contributing to economic stability and caregiving responsibilities. The diagnosis of cancer in this population can therefore lead to profound social and economic consequences, including loss of productivity and increased household financial burden [12].

Breast cancer is a biologically heterogeneous disease characterized by diverse histopathological and molecular subtypes, which influence prognosis and treatment response. Immunohistochemical markers, including estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2/Neu), and Ki67 proliferation index, are critical in defining tumor biology and guiding therapeutic decisions. However, the distribution and determinants of these markers vary across populations, particularly in under-researched regions such as sub-Saharan Africa.

In this context, understanding the interplay between sociodemographic, clinical, and radiological factors and immunohistochemical profiles is essential for improving breast cancer management. Therefore, this study aimed to describe the clinical and paraclinical characteristics of women aged 41–69 years with breast cancer in the Democratic Republic of the Congo and to identify factors associated with the expression of key immunohistochemical markers.

Methodology

Study Design

This study was designed as a retrospective analytical, multicenter investigation conducted over a nine-year period from January 2015 to December 2023. The retrospective nature allowed for the evaluation of existing clinical, radiological, histopathological, and immunohistochemical data to identify associations between patient characteristics and biological marker expression. The analytical approach focused on determining independent predictors of immunohistochemical profiles using multivariate statistical techniques.

Ethics

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki for research involving human subjects. Patient confidentiality was strictly maintained by anonymizing all collected data prior to analysis. No personally identifiable information was used during data processing or reporting. Verbal informed consent had been obtained at the time of clinical care, and only routinely collected clinical data were utilized for research purposes.

Setting

The study was carried out across five major hospitals and reference imaging centers in Kinshasa and Matadi, Democratic Republic of the Congo. These included Cliniques Universitaires de Kinshasa, Hôpital Général de Kinshasa, Centre Pilote d'Imagerie Médicale Kokolo (CEPIM), Centre d'Imagerie du Congo (CEIMEC), and Hôpital de Kinkanda. These centers function as key referral facilities for breast imaging, histopathological diagnosis, and oncological management, ensuring a representative and clinically relevant dataset.

Participants

The study population consisted of women aged 41–69 years with histologically confirmed breast cancer who had undergone comprehensive diagnostic evaluation, including mammography, ultrasound, and immunohistochemical profiling. Inclusion criteria comprised confirmed malignancy, availability of complete imaging and immunohistochemical data (ER, PR, HER2), and age within the defined range. Exclusion criteria included benign breast diseases, incomplete medical records, male patients, and individuals outside the specified age group. A non-probability consecutive sampling technique was employed, whereby all eligible patients during the study period were included.

Variables

The primary outcome variables were immunohistochemical markers, including estrogen receptor (ER-negative), progesterone receptor (PR-positive), HER2/Neu positivity, and Ki-67 proliferation index. Independent variables included sociodemographic characteristics (age, marital status, education, occupation), clinical parameters (tumor size, TNM stage, menopausal status, BMI, family history), radiological findings (BI-RADS classification, breast density, presence of calcifications), and histopathological features (tumor type, grade, invasive nature).

Data Sources and Measurement

Data were extracted from multiple sources, including medical records, imaging registries, and pathology reports. Mammographic and ultrasound examinations were performed using standardized imaging protocols at each center and interpreted by experienced radiologists, with collegial review in uncertain cases to improve

diagnostic consistency. Ultrasound-guided core biopsies were conducted by qualified radiologists. Histopathological and immunohistochemical analyses were performed at Cliniques Universitaires de Kinshasa, with additional academic support from international institutions (KU Leuven and Universiteit Gent) to ensure quality control and standardization of laboratory procedures.

Bias

Potential sources of bias included selection bias due to the use of non-probability sampling and inclusion of only patients with complete records, which may limit generalizability. Information bias was possible due to retrospective data collection and reliance on medical records. Additionally, certain variables such as alcohol consumption and self-breast examination were self-reported, introducing the possibility of recall bias. Efforts to minimize bias included standardized data extraction procedures and multivariate statistical adjustment for confounding variables.

Study Size

The study included a total of 185 patients who met the inclusion criteria over the defined study period. The sample size was determined based on the availability of eligible cases across participating centers rather than formal sample size calculation, which is consistent with retrospective observational study designs.

Statistical Methods

Data were entered into Microsoft Excel 2016 and analyzed using IBM SPSS Statistics version 26. Descriptive statistics were used to summarize patient characteristics. Normality of distribution was assessed to determine appropriate statistical tests. Quantitative variables were summarized using mean ± standard deviation for normally distributed data and median with interquartile range for skewed data. Group comparisons were performed using Student's t-test for normally distributed continuous variables and Mann–Whitney U test for non-parametric data. Categorical variables were analyzed using Pearson's chi-square test or Fisher's exact test when appropriate. Associations between independent variables and immunohistochemical markers were evaluated using logistic regression analysis. Initially, univariate analysis was conducted to identify significant predictors ($p < 0.05$), followed by multivariate logistic regression using a stepwise approach to determine independent associations. Results were reported as odds ratios (OR) and adjusted odds ratios (aOR) with 95% confidence intervals (CI). Multicollinearity was assessed using the variance inflation factor (VIF), and statistical significance was set at $p < 0.05$.

Results

Participants

A total of 185 women with histologically confirmed breast cancer were included in the final analysis after applying the eligibility criteria. All participants had complete clinical, radiological, histopathological, and immunohistochemical data available for evaluation. The study population was categorized into two age groups: 41–55 years (n = 124; 67%) and 56–69 years (n = 61; 33%). The mean age of the participants was 51.9 ± 7.9 years, with a statistically significant difference between the two age groups ($p < 0.001$). The participant selection process and baseline characteristics are summarized in Table 1.

Descriptive Data

Sociodemographic analysis revealed that the distribution of participants across provinces and districts did not differ significantly between age groups ($p > 0.05$). However, significant differences were observed in religion ($p = 0.031$) and marital status ($p < 0.001$), with a notably higher proportion of widowed women in the older age group (56–69 years). Educational status and occupational distribution showed no statistically significant variation, although the majority of participants were engaged in the informal sector (75.1%) (Table 1) . Clinical characteristics demonstrated that anthropometric parameters, including weight, height, and body mass index (BMI), were comparable between groups. The mean BMI of 25.6 ± 4.4 kg/m² indicated a tendency toward overweight status. Menopause was significantly more prevalent among women aged 56–69 years ($p = 0.007$), while parity showed a borderline significant increase in the older group ($p = 0.053$). The most common reason for consultation was a painful breast mass (61.1%), reflecting predominantly symptomatic presentation rather than screening-based detection. Most patients were diagnosed at advanced stages, with stage II (36.2%) and stage III (44.3%) being the most frequent, and no significant difference observed between age groups ($p = 0.963$) (Table 2). Radiological and histopathological findings indicated no significant association between age and BI-RADS classification on either ultrasound or mammography. However, breast density showed a significant variation with age ($p = 0.001$), with younger women more likely to exhibit higher density (ACR C–D), whereas older women predominantly had lower density patterns (ACR B). Histologically, invasive ductal carcinoma was the most common subtype (64.9%), and the majority of tumors were invasive (90.3%). Most tumors were moderately differentiated (61.1%), with no significant age-related differences. Immunohistochemical profiling demonstrated high frequencies of ER-negative (69.7%), PR-positive (71.9%), HER2/Neu-positive (18.5%), and high Ki67 expression (70.3%), indicating a predominance of biologically active tumors (Table 3) .

Outcome Data

The primary outcomes assessed were the expression patterns of immunohistochemical markers, including ER-negative status, PR-positive status, HER2/Neu positivity, and high Ki67 proliferation index. In univariate analyses, several clinical, radiological, and pathological variables were significantly associated with these outcomes. For ER-negative expression, significant factors included menopause, family history of cancer, advanced clinical stage (III–IV), BI-RADS 5 classification, presence of calcifications, and tumor necrosis. For PR-positive tumors, significant associations were observed with menopause, family history, alcohol consumption, drug use, self- breast examination, advanced clinical stage, BI-RADS 5 lesions, and calcifications. HER2/Neu positivity was significantly associated with BMI, menopause, alcohol consumption, drug use, higher BI-RADS categories, calcifications, and necrosis. Similarly, high Ki67 expression was associated with menopause, family history of cancer, alcohol consumption, BI-RADS 5 classification, calcifications, and necrosis (Tables 4–7) .

Main Results

Multivariate logistic regression analysis identified independent predictors for each immunohistochemical marker after adjusting for confounders. Menopause emerged as a consistent independent predictor of ER-negative expression (aOR = 2.18; 95% CI: 1.49–4.77; $p = 0.025$) and high Ki67 expression (aOR = 1.76; 95% CI: 1.19–4.53; $p = 0.024$). Advanced clinical stage was also independently associated with ER-negative tumors, particularly stage III (aOR = 2.26; $p = 0.048$) and stage IV (aOR = 3.75; $p = 0.030$). Radiological severity, particularly BI-RADS 5 classification, was consistently associated with aggressive tumor biology across multiple outcomes, including ER-negative (aOR = 2.57; $p = 0.032$), PR- positive (aOR = 2.83; $p = 0.028$), HER2-positive (aOR = 2.94; $p = 0.028$), and high

Ki67 expression (aOR = 3.54; p = 0.006). The presence of calcifications remained an independent predictor of ER- negative (aOR = 2.06; p = 0.046) and HER2-positive tumors (aOR = 2.80; p = 0.029). Family history of cancer was independently associated with PR- positive expression (aOR = 2.11; p = 0.037), while drug use (aOR = 1.96; p = 0.029) and self-breast examination (aOR = 2.27; p = 0.046) were also significant predictors. Additionally, higher BMI (aOR = 1.92; p = 0.001) and alcohol consumption (aOR = 3.42; p = 0.004) were identified as strong independent determinants of HER2/Neu positivity. The results demonstrate that clinical factors (menopause, stage), radiological features (BI-RADS classification, calcifications), and lifestyle/metabolic variables (BMI, alcohol use) significantly influence the biological behavior of breast cancer, reflecting substantial heterogeneity in tumor profiles within the studied population (Tables 4–7).

Table 1: Sociodemographic characteristics of patients.

Variables	Overall (n=185)	Age Group		p-value
		41–55 years (n=124)	56–69 years (n=61)	
Age (years); Mean ± SD	51.9 ± 7.9	47.3 ± 4.5	61.3 ± 4.1	<0.001*
Province of origin				
Kongo	98 (53.0)	62 (50.0)	36 (59.0)	0.257
Ngala	29 (15.7)	24 (19.4)	5 (8.2)	
Swahili	19 (10.3)	13 (10.5)	6 (9.8)	
Luba	39 (21.1)	25 (20.2)	14 (23.0)	
District				
Lukunga	59 (31.9)	42 (33.9)	17 (27.9)	0.872
Mont Amba	54 (29.2)	35 (28.2)	19 (31.1)	
Funa	42 (22.7)	27 (21.8)	15 (24.6)	
Tshangu	30 (16.2)	20 (16.1)	10 (16.4)	
Religion				
Catholic	80 (43.2)	49 (39.5)	31 (50.8)	0.031*
Protestant	30 (16.2)	19 (15.3)	11 (18.0)	
Revival Church	52 (28.1)	43 (34.7)	9 (14.8)	
Other churches	23 (12.4)	13 (10.5)	10 (16.4)	
Marital status				
Married	109 (58.9)	77 (62.1)	32 (52.5)	<0.001*
Single	38 (20.5)	32 (25.8)	6 (9.8)	
Divorced	5 (2.7)	5 (4.0)	0 (0.0)	
Widowed	33 (17.8)	10 (8.1)	23 (37.7)	
Education level				
Primary	20 (10.8)	10 (8.1)	10 (16.4)	0.095
Secondary	114 (61.6)	75 (60.5)	39 (63.9)	
Higher/University	51 (27.6)	39 (31.5)	12 (19.7)	
Profession				
Formal	46 (24.9)	32 (25.8)	14 (23.0)	0.409
Informal	139 (75.1)	92 (74.2)	47 (77.0)	

*p<0.05 is considered statistically significant

Table 2: Clinical characteristics of patients according to age.

Variables	Overall (n=185)	Age Group		p-value
		41–55 years (n=124)	56–69 years (n=61)	
Weight (kg)	69.7 ± 13.0	70.2 ± 13.8	68.6 ± 11.3	0.456
Height (cm)	164.8 ± 5.1	165.1 ± 5.3	164.1 ± 4.7	0.235
BMI (kg/m²)	25.6 ± 4.4	25.7 ± 4.6	25.4 ± 3.7	0.697
Age at menarche	13.1 ± 1.8	13.2 ± 1.5	13.1 ± 2.3	0.767
Number of pregnancies	2.0 (1.0-4.0)	2.0 (1.0-4.0)	3.0 (1.0-5.0)	0.053*
Menopause	58 (31.4)	21 (25.0)	27 (44.3)	0.007*
Family history of cancer	53 (28.6)	35 (28.2)	18 (29.5)	0.493
Reason for consultation				
Painless mass	64 (34.6)	40 (32.3)	24 (39.3)	0.354
Painful mass	113 (61.1)	77 (62.1)	36 (59.0)	
Check-up	8 (4.3)	7 (5.6)	1 (1.6)	
Alcohol consumption	45 (24.3)	33 (26.6)	12 (19.7)	0.198
Drug use	15 (8.1)	9 (7.3)	6 (9.8)	0.367
Self-breast examination	62 (33.9)	41 (33.6)	21 (34.4)	0.52
Attended awareness program	67 (36.2)	41 (33.1)	26 (42.6)	0.134
Side affected				
Right breast	48 (25.9)	33 (26.6)	15 (24.6)	0.457

Left breast	137 (74.1)	91 (73.4)	46 (75.4)	
Clinical stage				
Stage I	30 (16.2)	19 (15.3)	11 (18.0)	
Stage II	67 (36.2)	45 (36.3)	22 (36.1)	0.963
Stage III	82 (44.3)	56 (45.2)	26 (42.6)	
Stage IV	6 (3.2)	4 (3.2)	2 (3.3)	

*p<0.05 is considered statistically significant

Table 3: Paraclinical characteristics of breast cancer patients according to age.

Variables	Overall (n=185)	Age Group		p-value
		41–55 years (n=124)	56–69 years (n=61)	
Ultrasound				
BI-RADS 3	122 (65.9)	82 (66.1)	40 (65.6)	0.796
BI-RADS 4	23 (12.4)	14 (11.3)	9 (14.8)	
BI-RADS 5	40 (21.6)	28 (22.6)	12 (19.7)	
Mammography				
BI-RADS 3	15 (8.1)	12 (9.7)	3 (4.9)	0.603
BI-RADS 4	117 (63.2)	77 (62.1)	40 (65.6)	
BI-RADS 5	53 (28.6)	35 (28.2)	18 (29.5)	
Mammographic breast density				
ACR A	4 (2.2)	1 (0.8)	3 (4.9)	
ACR B	2 (1.1)	1 (0.8)	1 (1.6)	0.001*
ACR C	101 (54.6)	58 (46.8)	43 (70.5)	
ACR D	78 (42.1)	64 (51.6)	14 (23.0)	
Calcifications – Ultrasound	40 (21.7)	28 (22.6)	12 (20.0)	
Calcifications – Mammography	52 (28.1)	33 (26.6)	19 (31.1)	0.317
Histopathology				
Ductal carcinoma	120 (64.9)	78 (62.9)	42 (68.9)	
Adenocarcinoma	21 (11.4)	11 (8.9)	10 (16.4)	
Invasive carcinoma	23 (12.4)	18 (14.5)	5 (8.2)	
Lobular carcinoma	6 (3.2)	4 (3.2)	2 (3.3)	0.537
Mucinous adenocarcinoma	5 (2.7)	4 (3.2)	1 (1.6)	
Micro-papillary ductal carcinoma	4 (2.2)	3 (2.4)	1 (1.6)	
Lymph node carcinoma	3 (1.6)	3 (2.4)	0 (0.0)	
Malignant phyllodes tumor	3 (1.6)	3 (2.4)	0 (0.0)	
Invasive nature	167 (90.3)	113 (91.1)	54 (88.5)	0.375
Carcinoma in situ	14 (7.6)	8 (6.5)	6 (9.8)	0.294
Tumor with necrosis	9 (4.9)	7 (5.7)	2 (3.3)	0.373
Differentiation				
Well differentiated	13 (7.0)	9 (7.3)	4 (6.6)	
Moderately differentiated	113 (61.1)	74 (59.7)	39 (63.9)	0.879
Poorly differentiated	59 (31.9)	41 (33.1)	18 (29.5)	
Immunohistochemistry				
ER-negative	129 (69.7)	85 (68.5)	44 (72.1)	0.374
PR-positive	133 (71.9)	87 (70.2)	46 (75.4)	0.286
HER2/Neu-positive	34 (18.5)	21 (16.9)	13 (21.7)	0.28
High Ki67 expression	130 (70.3)	88 (71.0)	42 (68.9)	0.447

*p<0.05 is considered statistically significant

Table 4: Determinants of breast cancer immunohistochemical markers ER-negative.

Variables	Univariate analysis		Multivariate analysis	
	p-value	OR (95% CI)	p-value	OR (95% CI)
Menopause				
No		1		1
Yes	0.028*	2.10 (1.09-4.05)	0.025*	2.18 (1.49-4.77)
Family history of cancer				

No		1		1
Yes	0.047*	2.26(1.01-5.07)	0.744	1.10 (0.49-2.66)
Clinical stage				
Stage I		1		1
Stage II	0.246	1.33 (0.49-2.63)	0.845	0.79 (0.08-1.77)
Stage III	0.034	2.82 (1.55-6.08)	0.048	2.26 (1.23-6.22)
Stage IV	0.002*	3.81 (2.26-8.43)	0.030*	3.75 (2.29-7.41)
Ultrasound BI-RADS				
3		1		1
4	0.088	1.31 (0.84-3.10)	0.337	0.56 (0.17-1.82)
5	0.008	2.51 (1.27-4.98)	0.032*	2.57 (1.38-3.66)
Calcification				
No		1		1
Yes	0.001*	3.05 (1.55-5.99)	0.046*	2.06 (1.30-3.92)
Necrosis				
No		1		1
Yes	0.002*	2.98 (1.69-6.87)	0.023*	2.57 (1.54-5.62)

aOR : adjusted odds ratios ; CI : Confidence interval
*p<0.05 is considered statistically significant

Table 5: Determinants of breast cancer immunohistochemical markers PR-positive.

Variables	Univariate analysis		Multivariate analysis	
	p-value	OR (95% CI)	p-value	OR (95% CI)
Menopause				
No		1		1
Yes	0.048*	1.56 (1.07-3.64)	0.315	1.50 (0.68–3.32)
Family history of cancer				
No		1		1
Yes	0.019*	2.96 (1.53-5.18)	0.037*	2.11 (1.39–4.78)
Alcohol				
No		1		1
Yes	0.043*	1.89 (1.25-5.02)	0.801	1.13 (0.45–2.82)
Drugs				
No		1		1
Yes	0.014*	2.96 (1.67-7.56)	0.029*	1.96 (1.56–6.84)
Self-breast exam				
No		1		1
Yes	0.036*	2.69 (1.56-5.98)	0.046*	2.27 (1.95–5.40)
Clinical stage				
Stage I				1
Stage II	0.123	1.32 (0.58-2.39)	0.889	1.18 (0.12–3.02)
Stage III	0.002*	3.24 (1.98-7.26)	0.012*	2.14 (1.22–6.27)
Stage IV	0.001*	5.65 (2.59-9.28)	0.001*	5.58 (2.44–7.34)
Ultrasound BI-RADS				
3		1		1
4	0.158	0.68 (0.24-1.98)	0.484	0.65 (0.20–2.16)
5	0.002*	3.25 (1.58-6.27)	0.028*	2.83 (1.41–7.33)
Calcification				
No		1		1
Yes	0.045*	1.98 (1.06-3.25)	0.809	1.31 (0.14–1.94)

aOR : adjusted odds ratios ; CI : Confidence interval
*p<0.05 is considered statistically significant

Table 6: Determinants of breast cancer immunohistochemical markers HER2/Neu-positive.

Variables	Univariate analysis		Multivariate analysis	
	p-value	OR (95% CI)	p-value	p-value
BMI	0.001*	1.99 (1.24-3.37)	0.001*	1.92 (1.10–2.37)
Menopause				
No		1		1
Yes	0.035*	2.18 (1.24-5.01)	0.544	1.36 (0.50–3.71)
Alcohol				
No		1		1
Yes	0.002*	3.58 (1.98-6.99)	0.004*	3.42 (2.23–6.91)
Drugs				
No				1
Yes	0.044*	1.91 (1.02-4.96)	0.441	1.81 (0.39–3.23)
Ultrasound BI-RADS				
3		1		1
4	0.046*	2.11 (1.03-4.33)	0.086	1.29 (0.84–3.56)
5	0.001*	3.21 (1.98-6.91)	0.028*	2.94 (1.39–4.66)
Calcification				
No		1		1
Yes	0.011	3.06 (1.91-6.31)	0.029*	2.80 (1.30–3.96)
Necrosis				
No		1		1
Yes	0.039*	1.92 (1.09-3.58)	0.596	0.58 (0.08–4.39)

aOR : adjusted odds ratios ; CI : Confidence interval
*p<0.05 is considered statistically significant

Table 7: Determinants of breast cancer immunohistochemical markers high Ki67 expression.

Variables	p-value	Univariate analysis OR (95% CI)	p-value	Multivariate analysis OR (95% CI)
Menopause				
No		1		1
Yes	0.011*	3.12 (1.59-6.44)	0.024*	1.76 (1.19–4.53)
Family history of cancer				
No		1		1
Yes	0.038*	2.69 (1.51-5.36)	0.490	1.41 (0.53–3.79)
Alcohol				
No		1		1
Yes	0.047*	1.98 (1.03-2.99)	0.902	1.07 (0.38–1.32)
Mammography BI-RADS				
3		1		1
4	0.523	1.32 (0.59-4.36)	0.453	0.32 (0.02–1.56)
5	0.004*	3.92 (2.14-9.67)	0.006*	3.54 (1.94–8.24)
Calcification				
No		1		1
Yes	0.039*	2.12 (1.34-6.38)	0.907	1.18 (0.08–1.83)
Necrosis				
No		1		1
Yes	0.041*	1.89 (1.12-3.11)	0.158	0.13 (0.08–2.20)

aOR : adjusted odds ratios ; CI : Confidence interval
*p<0.05 is considered statistically significant

Discussion

This study provides important insights into the clinical, radiological, and biological heterogeneity of breast cancer among women aged 41– 69 years in the Democratic Republic of the Congo. The mean age of 51.9 years, with a predominance of women in the 41–55 age group, supports existing evidence that breast cancer in sub-Saharan Africa tends to occur at a younger age compared to high-income countries, where the median age at diagnosis typically exceeds 60 years [11,13]. This earlier onset may reflect demographic differences, genetic predispositions, environmental exposures, and reproductive patterns specific to African populations [14].

The significant association between older age and widowhood observed in this study likely reflects sociodemographic transitions rather than direct etiological relationships. However, marital status may indirectly influence disease outcomes through its impact on health-seeking behavior, social support, and adherence to treatment, as previously demonstrated in oncological studies [15]. The absence of significant differences in education level across age groups contrasts with findings from high-income countries, where lower socioeconomic status is often associated with delayed diagnosis and poorer outcomes [16]. In the present context, this may reflect uniformly limited access to organized screening programs, reducing disparities linked to educational attainment.

Clinically, the predominance of stage II and III disease at diagnosis confirms the persistent challenge of late presentation in sub-Saharan Africa [14]. The low proportion of cases identified through routine screening and the predominance of symptomatic presentation (painful breast masses) further highlight gaps in early detection strategies, consistent with WHO reports emphasizing limited screening uptake in low-resource settings [9]. These findings underscore the urgent need to strengthen population-based screening and awareness programs tailored to local healthcare realities.

Radiologically, while BI-RADS classification did not vary significantly with age, breast density demonstrated a clear age-related pattern, with younger women more likely to have dense breast tissue (ACR C–D). This finding aligns with established physiological changes related to hormonal status and supports evidence that higher breast density is associated with increased cancer risk and reduced sensitivity of mammographic detection [18–20]. These factors may contribute to delayed diagnosis in younger women and highlight the importance of complementary imaging modalities such as ultrasound in dense breast populations.

Histopathologically, the predominance of invasive ductal carcinoma is consistent with global patterns [21–23]. The high proportion of invasive tumors and elevated Ki67 expression observed in this study suggest a substantial burden of biologically aggressive disease. Although a majority of tumors expressed hormonal receptors (PR-positive), the high prevalence of ER-negative tumors and elevated proliferation index indicates a complex biological profile, potentially reflecting a higher frequency of luminal B or more aggressive subtypes in this population [24,25].

The multivariate analysis further elucidates the determinants of tumor biology. Menopause emerged as an independent predictor of ER- negative expression and high Ki67 levels, suggesting a shift toward more aggressive tumor phenotypes in postmenopausal women. While traditionally hormone receptor–positive tumors are more common in postmenopausal populations, studies in African settings have reported higher proportions of aggressive, hormone receptor–negative tumors, potentially linked to delayed diagnosis and underlying biological differences [7,11]. Similarly, advanced clinical stage was strongly associated with ER-negative expression, reinforcing the relationship between tumor progression and loss of hormonal differentiation [27]. The consistent association of BI-RADS 5 lesions with multiple aggressive immunohistochemical profiles highlights the strong correlation between radiological suspicion and tumor biology. This finding supports previous evidence indicating that highly suspicious imaging features are often predictive of high-grade and biologically active tumors [30]. The presence of calcifications and necrosis as significant predictors of aggressive tumor profiles further reflects underlying tumor hypoxia, rapid proliferation, and advanced disease progression [31,32].

Lifestyle and metabolic factors also played a significant role. Alcohol consumption was independently associated with HER2/Neu positivity, consistent with literature suggesting that alcohol may influence breast carcinogenesis through hormonal dysregulation and oxidative stress pathways [29]. Similarly, higher BMI was associated with HER2 positivity, supporting the growing body of evidence linking obesity to chronic inflammation, altered endocrine signaling, and tumor progression [33]. These findings emphasize the need to consider modifiable risk factors in breast cancer prevention and management strategies. This study highlights the multifactorial nature of breast cancer heterogeneity in a resource-limited

setting, where clinical, radiological, and metabolic determinants interact to influence tumor biology and disease progression.

Limitations

This study has several limitations that should be acknowledged. First, the retrospective analytical design limits the ability to establish causal relationships between identified determinants and immunohistochemical profiles. The reliance on existing medical records may have introduced information bias due to incomplete or inconsistently documented data. Second, certain variables, including alcohol consumption, drug use, and self-breast examination practices, were self-reported and therefore subject to recall and reporting bias. Additionally, the absence of detailed exposure assessment (e.g., duration, frequency, and intensity) limits the precision of these associations. Third, the use of non-probability consecutive sampling may affect the generalizability of the findings to the broader population. Patients included in the study were those who accessed tertiary care centers, potentially excluding individuals with limited healthcare access. Finally, the lack of advanced molecular and genetic profiling, including BRCA mutation status and genomic subtyping, restricts a deeper understanding of tumor biology and underlying mechanisms. Despite these limitations, the study provides valuable real-world data from a resource-limited context and contributes to the limited literature on breast cancer heterogeneity in sub-Saharan Africa.

Conclusion

This study demonstrates that breast cancer in women aged 41–69 years in the Democratic Republic of the Congo is characterized by early onset, late-stage presentation, and a high prevalence of biologically aggressive tumor profiles. Clinical factors such as menopause and disease stage, radiological features including BI- RADS classification and calcifications, and metabolic factors such as BMI and alcohol consumption were significantly associated with immunohistochemical marker expression.

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