

# Breast Cancer in Guinea: Molecular and Clinical-Pathological Characteristics

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## Abstract

**Introduction:** Breast cancer is the most common and deadly cancer among women worldwide. Immunohistochemistry techniques are routinely used to assess hormone receptor (HR) expression and the HER2 oncogene in breast cancer. The objective of this study was to describe the clinical, pathological, and molecular characteristics of breast cancer in Guinea. **Materials and Methods:** This was a retrospective observational study covering a period of 15 years and 8 months from April 11, 2007, to December 31, 2022, involving 144 patients with histologically confirmed breast cancer. Data from immunohistochemical studies conducted abroad were collected in each case, providing information on hormone receptor status (estrogen and progesterone), HER2 oncogene expression, and molecular subtype. **Results:** The average age was  $47.1 \pm 11.8$  years, ranging from 24 to 80 years. There were 142 (98.6%) women and 2 (1.4%) men, with a sex ratio of 1.4%. The average tumor size was  $13.1 \pm 11.1$  cm. Patients were in stage III and IV in 72 (50.3%) and 41 (28.6%) cases, respectively. The tumor was invasive ductal carcinoma in 127 (88.1%) cases and SBR grade III in 62 (43.1%) cases. Hormone receptors were positive in 75 (52.1%) cases. The HER2 oncogene was expressed in 47 (32.6%) cases. Among the molecular subtypes, there were 47 (32.6%) cases of Luminal A, 46 (31.9%) cases of triple negative, 26 (18.1%) cases of Luminal B, and 25 (17.4%) cases of HER2 overexpressed. **Conclusion:** Immunohistochemistry is unavailable in the country and, due to a lack of financial resources, very few patients have access to it. Despite this unavailability, the systematic use of this technique will make it possible to adapt and personalize treatment for each patient.

## Keywords

Cancer, Breast, Molecular Type, Her2 Oncogene

## 1. Introduction

Breast cancer is the most common and deadly cancer among women worldwide. Mass screening and improved treatments, particularly systemic treatments such as chemotherapy (CT), hormone therapy (HT), and targeted therapies, have reduced mortality [1].

In Guinea, the age-standardized incidence is 14.5 new cases per 100,000 and the mortality rate is 7.9 per 100,000. It is the leading cause of consultation at the oncology surgery unit (UCO) of the Donka National Hospital and accounts for 26% of all cancers [2].

Breast cancer is a heterogeneous disease, and current histological and clinical classifications do not allow its progression to be fully predicted. However, many genes and proteins have been studied in breast cancer [3]. Immunohistochemistry techniques are routinely used to assess the expression of hormone receptors (HR) and the HER2 oncogene in breast cancer. Currently, these are the only factors taken into account when choosing a treatment. Ki67 is a reliable prognostic marker, but its reliability is disputed due to low intra- and inter-observer and inter-laboratory reproducibility [4].

Breast cancer genomics is paving the way for increasingly personalized treatments. As the number of targeted therapies in development increases, the molecular segmentation of cancer into rare entities and the multitude of new molecules to be tested are leading to the implementation of therapeutic trials based on the molecular profile of tumors in order to direct patients towards the most suitable molecule [1].

*PEROU et al.* were the first to establish a classification system for breast tumors based on gene expression analysis and demonstrated the existence of four molecular classes of breast cancer: luminal-like, basal-like, normal-like, and HER2-enriched [5]. Later studies broadened the spectrum of analysis and showed the existence of five molecular classes in breast cancer: luminal A, luminal B, HER2-enriched, basal-like, and normal-like.

In current practice, so-called “triple-negative” (TNBC) or basal-like breast cancer is often associated with a poor prognosis, with a high risk of relapse and low survival rates [6]. A preliminary study conducted between 2007 and 2016 showed that immunohistochemistry for the molecular diagnosis of breast cancer is not widely available in our country [2] and, currently, in order to obtain this diagnosis, we have to send the sample to France (Cerba). The objective was to describe the clinical and anatomopathological characteristics of breast cancers and thus establish the distribution of breast cancers according to hormone receptor status and HER2 oncogene expression at the oncology department of the Donka National Hospital/Conakry University Hospital.

## 2. Materials and Methods

This was a retrospective observational study covering a period of 15 years and 8 months from April 11, 2007, to December 31, 2022, involving patients followed at

the oncology department of Donka National Hospital/Conakry University Hospital with histologically confirmed breast cancer using immunohistochemical analysis. The data collected included: sociodemographic data (gender, age at diagnosis); anatomic-clinical data (stage at diagnosis, tumor size, lymph node involvement, distant metastasis, histological type, histo-prognostic grade, laterality, macroscopic appearance). Data from the immunohistochemistry study conducted abroad were collected in each case, thus providing information on hormone receptor status (estrogen and progesterone), HER2 oncogene expression, molecular subtype, and Ki-67 proliferation index. Data analysis was performed using SPSS version 21.0 software. Fisher's exact test was used to compare patient characteristics according to molecular subtypes. The test was significant if the p-value was less than 0.05.

Anonymity and confidentiality of data were respected when recording the collection forms.

The authors declare no conflicts of interest.

### 3. Results

We collected 144 files of patients with histologically confirmed cancer using immunohistochemical analysis. The immunohistochemical examination completion rate was 17%.

The average age was  $47.1 \pm 11.8$  years, ranging from 24 to 80 years. There were 142 (98.6%) women and 2 (1.4%) men, with a sex ratio of 1.4%.

The right breast was affected in 65 (50.4%) cases, the left breast in 58 (44.9%) cases, and both breasts in 6 (4.7%) cases. The breast was ulcerated in 35 (32.4%) cases, with a breast mass in 144 (100%) cases; inflammatory in 32 (29.6%) cases, and permeation nodules were noted in 4 (3.5%) cases. The average tumor size was  $13.1 \pm 11.1$  cm.

At the time of diagnosis, the tumor was classified as T3 - T4 in 116 (80.5%) cases and N1 in 93 (66.0%) cases. It was an invasive ductal carcinoma in 131 (90.9%) cases, with SBR (Scarff-bloom-Richardson) grade III in 62 (43.1%) cases (**Table 1**).

At the molecular level, hormone receptors were positive in 75 (52.1%) cases, including estrogen receptors positive in 75 (52.1%) cases and progesterone receptors positive in 64 (44.4%) cases. HER2 status was expressed in 47 (33.3%) cases (**Table 1**).

For molecular subtypes, there were 47 (32.6%) cases of Luminal A, 46 (31.9%) cases of triple negative, 26 (18.1%) cases of Luminal B, and 25 (17.4%) cases of HER2 overexpressed. The characteristics of these molecular subtypes are shown in **Table 2**. There was no significant difference between subtypes in terms of age at diagnosis ( $p = 0.538$ ) or gender ( $p = 0.329$ ). Although the difference in mean tumor size between subtypes was not significant ( $p = 0.924$ ), the triple-negative subtype had a predominance of T3 - T4 lesions (39 cases), followed by luminal A (37 cases) ( $p = 0.527$ ). However, the subtypes were significantly different accord-

ing to lymph node status ( $p = 0.023$ ). The triple-negative subtype had the highest prevalence of regional lymph node involvement (13 cases), followed by luminal A (10 cases) (Table 2).

**Table 1.** Distribution according to basic characteristics of breast cancer.

Characteristics	Number	%
<b>Primary tumor (n = 144)</b>		
T1 - T2	22	15.3
T3 - T4	122	84.7
<b>Lymphadenopathy (n = 144)</b>		
N0	21	14.6
N+	121	84
NX	2	1.4
<b>Metastases (n = 114)</b>		
M0	103	71.5
M1	39	27.1
Mx	2	1.4
<b>Histology (n = 144)</b>		
CCI	131	90.9
CLI	6	4.1
Mucinous carcinoma	3	2.1
Other*	4	2.7
<b>SBR grade (n = 144)</b>		
SBR I	9	6.8
SBR II	61	42.4
SBR III	62	43.1
<b>Hormone receptors (n = 144)</b>		
Positive	75	52.1
Negative	69	47.9
<b>HER2 status (n = 141)</b>		
Expressed	47	33.3
Not expressed	94	66.7

**Table 2.** Characteristics of breast cancer subtypes.

Characteristics	Luminal A	Luminal B	HER2	Triple Negative	<i>P-value</i>
<b>Mean age ± standard deviation</b>	48.7 ± 11.9	47.2 ± 9.9	47.4 ± 10.9	45.1 ± 13.1	0.538
<b>Gender</b>					
Female	45	26	25	46	0.329
Men	2	-	-	-	

## Continued

Tumor size ± standard deviation	14.03 ± 11.03	11.4 ± 11.1	13.2 ± 10.3	12.7 ± 7.6	0.924
<b>Primary tumor</b>					
T1 - T2	7	4	6	5	0.527
T3 - T4	40	22	19	41	
<b>Lymphadenopathy</b>					
N0	7	8	4	2	0.023
N+	31	25	22	43	
<b>Metastases</b>					
M0	36	19	16	32	0.626
M1	10	7	9	13	
<b>Histological type</b>					
CCI	41	24	23	43	0.553
CLI	4	1	-	1	
Mucinous carcinoma	1		1	1	
Other*	2	1	2	2	
<b>Grade SBR</b>					
SBR I	5	2	1	1	0.262
SBR II	22	13	10	16	
SBR III	16	8	14	24	

Others\*: papillary carcinoma, neuroendocrine carcinoma, mixed carcinoma, mucinous carcinoma, sarcomatoid carcinoma.

**Table 3.** Distribution of cases according to Ki67%.

HR and HER2 status	Ki67 ≥ 0.2	Ki67 < 20%	P Value
Hormon Receptors n (%)			
Positive	19 (34.5%)	9 (16.4%)	0.1
Négative	23 (41.8%)	4 (7.3%)	
HER2 Oncogen n (%)			
Positive	12 (21.8%)	5 (9.1%)	0,5
Négative	30 (54.5%)	8 (14.6%)	

The Ki67 index was determined in 55 patients. It was less than 20% in 13 (23.7%) patients and greater than or equal to 20% in 42 (76.3%) patients in hormone receptors. The Ki67 index was greater than or equal to 20% in 12 (21.8%) HER2-positive breast cancers, compared to 30 (54.5%) HER2-negative breast cancers (**Table 3**).

#### 4. Discussion

The determination of the molecular profile of breast cancers was low in our series,

with only 20% of patients diagnosed during our study period undergoing immunohistochemical testing out of a total of 720 breast cancer cases. This result is consistent with that reported by Kingu *et al.* [7] but significantly lower than that observed by Dembélé *et al.* [8] in Mali, where immunohistochemistry was performed in 67.5% of diagnosed breast cancer cases. This difference could be explained by the unavailability of this test in our context, which is a consequence of its high cost, given that all samples are sent abroad for analysis. Regarding the study by Dembélé *et al.* [8], these results appear to be superior to our series due to the fact that this test was subsidized by the researchers.

Age at diagnosis is an important prognostic factor, as tumors diagnosed at a younger age are generally more aggressive and/or less responsive to treatment [9]-[11]. The average age of our patients was similar to that reported by Uyisenga *et al.* in Rwanda, who found an average age of  $49.9 \pm 7$  [12]. In France, Berman *et al.* reported an average age of 59.8 years [13]. This difference in age can be explained by higher life expectancy and the existence of more advanced technical facilities in developed countries. However, comparison of molecular subtypes in our study revealed no difference between them in terms of age at diagnosis ( $p = 0.538$ ).

In our study, right breast localization was more common. This result is similar to that of Darre *et al.* in Togo, who found more frequent involvement of the right breast in 46.2% of cases, but differs from that of Ghada *et al.* in Tunisia in 2017, who reported 58% in the left breast [14] [15].

Late diagnosis of breast cancer remains a current problem in our practice setting. The stage of breast cancer is considered a major determinant of breast cancer survival, with early-stage tumors associated with a better prognosis and higher survival rates than advanced tumors [16]. We observed a clear prevalence of T3 - T4 lesions, representing 84.7% of cases in our series, with regional lymphadenopathy noted in 84% of patients. Patient ignorance, poverty, recourse to traditional medicine, and a lack of knowledge about the disease among some healthcare professionals are all factors that contribute to delayed diagnosis in our context.

Invasive ductal carcinoma was by far the predominant histological type in our study, with 91 cases, or 80.0%. This predominance is evident in all African and global series [2].

The evaluation of the histo-prognostic grade in our series showed that SBR III and II grades accounted for 47% and 46.2% of cases, respectively, which is consistent with the findings of a Moroccan study [10].

In this study, histopathological grade SBR III was more associated with triple-negative breast cancer, which is a poor prognostic factor and consistent with the literature [16]. Tumor size was large in all subtypes but more pronounced in the Luminal A and triple-negative subtypes [5].

Hormone receptor testing and molecular subtyping are used as important predictive and prognostic factors in women with breast cancer. Hormone receptor positivity is correlated with a favorable prognosis [17]. In our series, we noted a high rate of HR positivity, as also reported in Algeria [18]. Similarly, although

HER2+ tumors were not predominant in our study, their proportion was similar to that reported in Morocco [10]. Regarding subtypes, Luminal A was the most common in our series (32.6%), followed by triple-negative (31.9%), Luminal B (18.1%), and HER2-overexpressing (17.4%). Our results are consistent with those of Khalil *et al.* [19] and confirm the preliminary study by Traore *et al.* [2]. Indeed, the luminal A phenotype is characterized by high expression of estrogen and progesterone receptors, while HER2 is negative, and it expresses cytokeratins 8, 18, and 19 and GATA3 [20] [21]. Luminal A phenotypes are associated with different clinical outcomes and therapeutic responses and a good prognosis [19]. Luminal A tumors are hormone-sensitive and benefit from hormone therapy [22] [23]. The luminal B phenotype has an immunohistochemical profile that is positive for estrogen receptors but less expressed than in luminal A, in addition to overexpression of Her2 and high expression of the ki-67 proliferation index [24] [25]. Luminal B phenotype tumors are also hormone-sensitive tumors, but will also benefit from chemotherapy [26]. HER2-enriched phenotypes are tumors characterized by high HER2 expression and the absence of hormone receptor expression. They have a poor prognosis but are associated with better responsiveness to trastuzumab-targeted therapy and anthracycline-based chemotherapy. The basal-like phenotype, commonly known as triple-negative, is defined by the absence of hormone receptors (ER-negative and PR-negative) but expresses high molecular weight cytokeratins (cytokeratins 5, 6, 13, and 14). Basal tumors have a poor prognosis [19] [27].

The molecular subtype distribution observed in our series, with a predominance of Luminal A followed by triple-negative breast cancer, is broadly consistent with reports from West Africa, particularly studies conducted in Guinea, Mali, and Senegal [2] [8] [19] [28]. This similarity may reflect shared genetic determinants among West African populations. Conversely, differences reported in other African series could be related to environmental or reproductive factors, as well as methodological variations, especially disparities in access to immunohistochemistry testing [10] [18].

No statistically significant differences were noted between molecular subtypes based on age, sex, tumor size at diagnosis, or metastasis status. We found that the triple-negative subtype was associated with a high frequency of T3 - T4 lesions, although the difference was not statistically significant. Gaye *et al.* [28] also found the same trend.

However, with regard to lymph node status, a significant difference was noted between molecular subtypes. The triple-negative subtype was associated with a high frequency of regional lymphadenopathy, as also reported by Gaye *et al.* [28].

However, these findings must be interpreted with caution due to a significant selection bias. Only about 20% of patients diagnosed during the study period were able to afford immunohistochemical analyses performed abroad. This may have resulted in a non-representative cohort with a potentially different sociodemographic and clinical profile, leading to an overestimation of hormone receptor-

positive tumors and an under-representation of more aggressive subtypes, particularly triple-negative cancers [2] [7] [8].

## 5. Conclusion

Breast cancer is the most common cancer in women in our unit, diagnosed at a locally advanced or metastatic stage. Invasive ductal carcinoma was the predominant histological type, and the dominant molecular subtype was luminal A, followed by triple negative, associated with a high histoprognostic grade. Immunohistochemistry is unavailable in the country and, due to a lack of financial resources, very few patients have access to it. Despite this unavailability, the systematic use of this technique will make it possible to adapt and personalize treatment for each patient.

## Authors' Contributions

All authors contributed to the design and implementation of the study. The preparation of materials, data collection, and analysis were carried out by [BAH Malick], [TOURE Alhassane Ismael], [SOUARE Mamadou Bobo], and [CISSE Kalil]. The first draft of the manuscript was written by [BAH Malick] and [CONDE Ibrahima Kalil], and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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