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RESEARCH ARTICLE

Breast carcinoma in the Democratic Republic of the Congo: Characterization of hormone receptors

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Abstract: Purpose: Breast cancer is a heterogeneous disease, and understanding its characteristics is crucial for effective treatment. Therefore, this study aims to investigate breast carcinomas as a function of hormone receptors (estrogen and progesterone) in the Democratic Republic of the Congo (DRC), which can contribute to better management of breast cancer cases in the country. **Methods:** We conducted an analytical cross-sectional study from 2014 to 2016 in the cities of Kinshasa and Lubumbashi. Using non-random sampling, we collected 86 cases of breast carcinoma. **Results:** The study found that out of the 86 cases of breast carcinoma, 33 patients (38.3%) had both types of hormone receptors (ER+/PgR+), while 37 patients (43.0%) had negative results for both receptor types (ER-/PgR-). Additionally, 15 patients (17.4%) had only estrogen receptors. The study did not find any significant association between the presence of estrogen receptors and patient age, T stage, histological type, and Ki67 proliferation index. However, the study did observe that estrogen receptors were significantly more present in grade I and II tumors (74.4%) than in grade III tumors (40.4%) (OR = 4.3 [1.7-10.8]; p = 0.003). **Conclusion:** The findings of this study demonstrate a high prevalence of hormone receptors in breast cancer cases in the DRC. Additionally, the study revealed a significant association between the presence of estrogen receptors and tumor grade, underlining the relevance of these markers in the characterization and treatment of the disease.

Keywords: carcinoma, breast cancer, hormone receptors

Abbreviations

DRC: Democratic Republic of the Congo
ER: estrogen receptor
IHC: immunohistochemistry
NST: no specified type
PgR: progesterone receptor

1 Introduction

Breast cancer is a major public health concern worldwide, affecting millions of people each year [1]. As a complex and heterogeneous disease, it presents a varied range of forms, each with unique implications for diagnosis, prognosis, and treatment [2]. To date, there is no standard management plan that is effective for all forms of breast cancer. A majority of breast tumors (50-80%) are classified as invasive ductal carcinoma no specified type (NST) [3] due to their inability to be categorized into one of the other 20 subtypes [4]. Hormone receptors, such as estrogen receptors (ER) and progesterone receptors (PgR), play a critical role in the classification of breast cancer, influencing the decision-making process for treatment options. ER and PR are proteins that bind to hormones within cells, initiating changes within the cell. Hence, this classification is crucial in the management of the disease [5]. The presence or absence of hormone receptors such as ER and PgR can significantly affect the course of treatment of breast cancer, often determining the success or failure of hormone therapy. These receptors also provide critical information on the prognosis of the disease, including the aggressiveness of the cancer, the patient's survival rate, and the likelihood of recurrence [6]. Therefore, healthcare

professionals and patients must understand this classification to effectively manage breast cancer, which remains a significant public health challenge worldwide.

However, the presence of these hormone receptors varies from study to study. For instance, a Togolese study found 54.7% and 41% for estrogen and progesterone receptors respectively [6]. In the Democratic Republic of the Congo (DRC), a recent study by Sulu *et al.* [7] of 190 women with breast cancer reported that 85.26% and 77.37% of cases respectively. Despite the seriousness of this health problem, there is a notable lack of in-depth research and studies into the specific characteristics and nuances of this disease in the DRC, particularly with regard to the role and influence of hormone receptors [8]. As highlighted in the previous paragraph, hormone receptors play a crucial role in the categorization, prognosis and treatment of breast cancer, and understanding their role and prevalence in the DRC could lead to more effective treatment strategies and better patient outcomes.

The aim of this study is to describe the hormone receptors found in women with breast carcinoma in the DRC. The importance and potential impact of this study are underlined by its potential implications for the therapeutic approach and prognosis of breast cancer in the DRC.

2 Materials and methods

An analytical cross-sectional study was conducted between 2014 and 2016 in the cities of Kinshasa and Lubumbashi, including 86 patients with histologically confirmed localized breast cancer. We excluded patients with non-epithelial tumors, secondary tumors, metastatic forms from the outset, and localized breast carcinomas with synchronous tumors of digestive, hepatic, or other origin whose records could not be used.

Data was collected from medical records, focusing on variables such as patient age, TNM classification, treatment modalities, progression, and date of last news. Histological data were obtained from anatomopathological reports, including histological type, tumor size, lymph node status, Scarff-Bloom-Richardson (SBR) histopronostic grade modified by Elston and Ellis, and histological evaluation of chemotherapy from immunohistochemical reports (estrogen receptors, progesterone receptors, and Ki67 index).

Immunohistochemistry (IHC) was performed in Germany at Martin-Luther-University. Mouse monoclonal antibodies were used. For ER, clone 1D5 (Zytomed Systems, Berlin, Germany) was used. For PgR, clone 636 (Dako, Carpinteria, CA) was used. For HER2/neu, Hercep Test (Dako) was used. Clone MSK018 (Zytomed System GmBH BERLIN, Germany) was used for Ki67. These tests were performed using a semi-automated system (intelliPath; BiocareMedical, Pacheco, CA). ER and PgR were considered positive if nuclear impregnation was $>1\%$. A cut-off of 20% was used for Ki67.

The data were analyzed using SPSS23 software. Qualitative variables were presented in the form of frequencies. The Chi-square test was used to compare frequencies, and the odds ratio and its 95% confidence interval were calculated. The significance threshold was set at $p<0.05$.

3 Results

A total of 86 patients were included in the present study. The mean age of the patients was 48 years, with a range of 23 to 86 years. Of the patients, 36 (41.9%) were aged 50 years or older, and 2 (2.3%) were aged under 30 years. (see in Table 1)

According to T staging, the tumor was classified as T1 in 1.2% of cases, T2 in 24.4% and T3 in 54.7%. Histologically, invasive ductal carcinoma was the most common histological type (97.6%), associated with a lobular component in 1.2% of cases. The number of histological grade II and III tumors was high (40.7% and 54.7% respectively). We found that, immunohistochemically, ER were positive in 55.8% of patients and PgR were positive in 39.5%. The Ki67 proliferation index was >20 in 57.0% of cases.

Patients with both types of hormone receptor (ER+/PgR+) accounted for 38.3% (33/86), while patients with both types of hormone receptor negative (ER-/PgR-) accounted for 43.0% (37/86); 17.4% (15/86) of patients had only ERs (Figure 1).

Table 2 displays the correlations between patient characteristics and the presence of ER. We found no significant association between the presence of ER and patient age, T stage, histological type, and Ki67 proliferation index. However, we observed that ER were more present in grade I and II tumors (74.4%) than in grade III tumors (40.4%) (odds ratio = 4.3 [1.7-10.8]; p = 0.003).

Table 1 Age, clinical, and immunohistochemical characteristics of 86 patients

Variable	Number (n = 86)	Percentage (%)
Age		
<30 years	2	2.3
30-39 years	23	26.7
40-49 years	25	29.1
≥ 50 years	36	41.9
T Staging		
T1	1	1.2
T2	21	24.4
T3	64	74.4
Histological grade		
I	4	4.6
II	35	40.7
III	47	54.7
Histological type		
Invasive ductal carcinoma	84	97.6
Mixed invasive ductular and lobular carcinoma	1	1.2
Invasive papillary carcinoma	1	1.2
Estrogen receptors		
Present	48	55.8
Absent	38	44.2
Progesterone receptors		
Present	34	39.5
Absent	52	60.5
Ki67 proliferation index		
≤ 20	37	43.0
>20	49	57.0

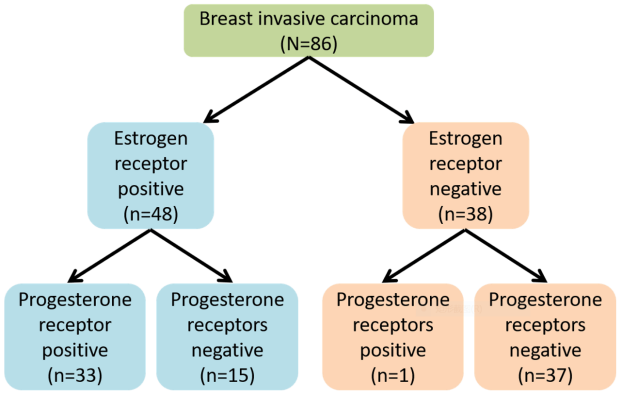

Figure 1 Distribution of patients with breast cancer according to estrogen and progesterone receptors

Table 2 Clinical-histological factors influencing the presence of estrogen receptors (ER)

Variable	ER positive (n = 48)		ER negative (n = 38)		OR [95% CI]	p-value
	n	%	n	%		
Age						
≤45 years	23	60.5	15	39.5	1.4 [0.6-3.3]	0.573
>45 years	25	52.1	23	47.9	1.0	
T Stage						
T1/T2	15	66.7	7	33.3	2.0 [0.7-5.6]	0.269
T3	33	51.6	31	48.4	1.0	
Histological grade						
I/II	29	74.4	10	25.6	4.3 [1.7-10.8]	0.003
III	19	40.4	28	59.6	1.0	
Histological type						
Invasive ductal carcinoma	46	54.8	38	45.2	1.0	
Mixed invasive ductular and lobular carcinoma	1	100	0	0	ind.	1.000
Invasive papillary carcinoma.	1	100	0	0	ind.	1.000
Ki67 proliferation index						
≤20	24	64.9	13	35.1	1.9 [0.8-4.6]	0.211
>20	24	49	25	51	1.0	

4 Discussion

Antihormonal treatments have significantly improved the treatment of breast cancer, reducing the need for surgery or radiotherapy [9]. The study used immunohistochemical techniques to determine the expression of nuclear hormone receptors in breast cancer patients in the DRC. The majority of patients (55.8%) had positive expression for at least one hormone receptor, indicating a significant representation of this characteristic. However, a high proportion of cases (43%) were without hormone receptors (ER-/PgR-), indicating the diversity of breast carcinoma subtypes and the high prevalence of triple-negative carcinoma subtypes in this population.

Hormone dependence is present in 38.3% of cases (ER+/PgR+), uncertain in 17.4% (ER+/PgR-), and absent in 43.0% (ER-/PgR-). PgR expression is crucial for prognosis, as it indicates a functional estrogenic pathway as PgR are induced by the ER [10]. The ER+/PgR- phenotype has a poorer prognosis due to transcriptional down-regulation of the ER, resulting in reduced efficacy with antiestrogen treatment [11]. The presence of ER-/PgR+ tumors is a topic of debate, as they represent only 1.1% of cases in this study and are considered an artefact. Some experts believe tamoxifen may be effective in treating ER-/PgR+ tumors [12, 13].

Hormone receptors were found in 55.8% of cases in this study, contrasting with studies conducted on white women, where hormone dependence is estimated to be over 70% [13, 14]. This is consistent with studies on African women, where hormone receptor negativity ranges from 22% to 35% in East Africa [15–17] and 44% to 80% in West Africa [18–20]. McCormack et al's [21] study in South Africa found that 35% of cases were hormone receptor negative. In the United States, 39% of black American women were hormone receptor negative, compared to 16% of Caucasian women [22]. In China, ER- tumors are estimated at 21.6% [23], while in India/Pakistan at 30.6% [24]. The study found similar results in West Africa and the United States for black American women, possibly due to shared hereditary heritage, eating habits, and reproductive habits among American women of African origin and patients from West and Central Africa, and the history of the slave trade.

The age at which someone is considered 'young' is not widely agreed upon, but studies have shown hormone receptors are more frequent in older individuals, while younger people tend to present non-hormone-dependent forms [25, 26]. This study found more ER+ tumors in individuals under 45, but no significant differences were found between age groups and hormone receptor presence or absence. The NST sub-group comprises heterogeneous tumors with variable phenotypes, including mixed ductular and lobular invasive carcinoma and papillary invasive carcinoma [27]. The study found a significant correlation between tumor grade and hormone receptor presence. Past research has demonstrated that less differentiated tumors are more likely to be non-hormone-dependent [11, 19, 28]. The histological grade, which incorporates the mitotic index, measures cell proliferation, and ER- tumors, often grade III and having a high mitotic index, are more proliferative [11].

Compared to stage T3, the study reveals that there are more ER+ tumors and fewer ER- tumors at stages T1 and T2. This difference is not statistically significant, but it could be due to factors such as non-accessibility to care, the high proliferative nature of ER- tumors, and the biological characteristics of the tumor, particularly the expression of hormone receptors. It is understandable that these tumors are often large and diagnosed at an advanced stage [29, 30]. Patients who delay consultation may experience changes in their tumor's biological characteristics [31]. Some authors argue that grade I and grade III tumors are different diseases with different activation pathways, and do not progress from grade I to grade III after a certain period [28]. The proportion of ER+ tumors decreases with increasing histological grade, possibly due to accelerated growth of ER- tumors due to loss of estrogen expression in advanced forms of the disease. ER- tumor status is most likely a false negative due to the failure to obtain a biopsy from the original ER+ tumor. African studies suggest the advanced stage of cancer at diagnosis and the predominance of ER- forms [28, 31]. Time can modify the characteristics of a tumor through the accumulation of genetic mutations, which can have repercussions on the phenotype.

5 Conclusion

The study reveals a wide range of hormone receptors, particularly estrogen and progesterone receptors, with almost half of cases being negative. The presence of estrogen receptors is significantly associated with tumor grade, with a predominance in grade I and II tumors. Accurate characterization of breast tumors is crucial for treatment decisions and patient outcomes.

Enhancing early breast cancer screening programs, improving tumor characterization techniques like immunohistochemistry, and improving access to targeted hormone therapy are also necessary. Further research is needed to understand the factors driving hormone receptor diversity and their impact on tumor progression, which could guide better breast cancer prevention and treatment strategies in the DRC.

Conflicts of interest

The authors declare that they have no conflict of interest.

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