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Breast Cancer in Women: Epidemiological, Histological, Immunohistochemical and Molecular Sub-Types in the Republic of Congo

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ABSTRACT

Introduction: Breast cancer is a heterogeneous disease with a variety of morphological, molecular, treatment response and clinical outcome characteristics. The objective of this work was to assess the epidemiological, histological, immunohistochemical and molecular subtypes of breast cancer in women in the Republic of Congo.
Material and Methods: We carried out a cross-sectional descriptive study which took place from January 1, 2014 to December 31, 2020. The study focused on 150 cases of breast cancer in patients diagnosed at the University Hospital of Brazzaville (CHU-B). The epidemiological, clinical, histological, immunohistochemical and molecular subtypes were the variables studied.
Results: The mean age was 48.09 ± 13.87 years with the extremes of 22 years and 80 years. The study of the profession; the most represented in our study was that of the cultivator 20.67%. A predominance of breast cancer localization was observed in the left breast in 47.33%. The frequency of a family history was 7.33% or 11 cases. The most frequently represented histologic type was 62% invasive non-specific type carcinoma (CITNS). The most represented histological grade was Scarff Bloom Richardson grade II (51.33%), followed by grade III 24% and grade I in 12% of cases. Regarding the results of IHC; of the 150 cases, 102 (68%) had positive hormone receptors (HR +). The ORs were positive in 102 cases (68%) while the PRs were positive in 98 cases (65.33%). The Her2 oncogene was over expressed in 38 cases (25.3%). The Ki-67 proliferation index was known for the 150 cases, including 77 (51.33%) less than 15% and 73 (48.67%) greater than or equal to 15%. The distribution of molecular subtypes was 46% luminal A, 22% triple negative, 17% luminal B and 10% Her2 +. Tumors of unknown molecular profile were 5%. The correlation was found between molecular subtype and histological type. This result was statistically significant ($p < 0.05$). For the rest. There was no correlation between age and SBR grade ($p > 0.05$). The correlation was found between molecular subtype and histological type. This result was statistically significant ($p < 0.05$). For the rest. There was no correlation between age and SBR grade ($p > 0.05$). The correlation was found between molecular subtype and histological type. This result was statistically significant ($p < 0.05$). For the rest. There was no correlation between age and SBR grade ($p > 0.05$).
Conclusion: It should be noted that the association between histological and immunohistochemical diagnosis can help determine the phenotype of breast cancer, with the aim of guiding treatment and therefore improving response to treatment.

Keywords: Epidemiology, Histology, Immunohistochemistry, molecular subtypes, breast cancer, Republic of Congo.

INTRODUCTION

Breast cancer remains to this day a real public health problem in both developed and developing countries [1, 2, 3, 4]. Recently according to the latest estimates from Globacan 2020, it has become the first most common type of cancer in the world; thus surpassing lung cancer [5]. Breast cancer (BC) is the most commonly diagnosed cancer in women around the world. It is the leading cause of cancer death in most developing countries. With around 2.3 million new cases diagnosed in 2020, it accounts for 24.50% of female cancers and 11.7% of all human cancers worldwide. In Congo, it is the first of all cancers according to the latest estimates from GLOBOCAN 2020 [5]. There is a variable distribution from region to region of incidence rates around the world [6]. Breast cancer incidence rates are rising rapidly in the transition countries of South America, Africa and Asia as well as high-income Asian countries (Japan and the Republic of Korea) where rates are historically low [5].

Nowadays, the survival rate has improved in developed countries thanks to the practice of screening and the progress observed in the fields of diagnosis and treatment. But in developing countries, especially countries in sub-Saharan Africa, there is almost no appropriate structure for the good management of cancer patients and human resources are insufficient. We note the absence in most of these countries of sub-Saharan Africa of government programs in the fight against cancer. These reasons make it difficult to implement epidemiological surveillance for breast cancer in this part of the world [7].

In addition, these countries face difficulties in diagnosing and evaluating cancer and accessing cancer drugs at affordable prices and of good quality [7, 8]. Therefore, the therapeutic management of breast cancer represents a major issue in developing countries, particularly in Congo Brazzaville. HeIt is necessary to carefully evaluate the epidemiological and morphological aspects of breast cancer in order to avoid under treatment or overtreatment of patients, poor practices and inadequate allocation of financial resources, while increasing survival.

In countries with limited resources; in particular in Congo, the standard morphological examination remains the only recourse to the diagnosis of certainty and for the prediction of the prognosis. The use of immunohistochemical techniques in determining the molecular profile of breast cancer has greatly modified therapeutic strategies, which are not commonly used in our context.

In Congo Brazzaville, the anatomopathological features of breast cancer are poorly documented. To help fill this knowledge gap, we conducted a study to characterize the epidemiological, histological, immunohistochemical and molecular subtypes in the Department of Pathological Anatomy Cytology at the University Hospital Center of Brazzaville, Congo.

MATERIAL AND METHODS

Type and period of study: This was a descriptive and cross-sectional study covering the period from January 1, 2014 to December 31, 2020. The Pathological Cytology Anatomy Laboratory of the University Hospital of Brazzaville (CHUB) for the collection of cases and the immunohistochemical analysis (IHC) served as the study setting.

Study population: 150 paraffin blocks from breast cancer cases were identified and based on the selection criteria.

Inclusion criteria: were included in our study, all the samples of paraffin blocks from breast cancer tissues available at the Anatomy Cytology Pathology laboratory of the University Hospital of Brazzaville (CHUB) and having benefited from an

additional immunohistochemistry examination confirmed on histological basis after rereading by two pathologists.

Non-inclusion criteria: all degraded blocks for poor conservation or insufficient tissue; benign breast tumors and all paraffin blocks of breast cancer diagnosed in men.

Study methods

Collection of data: the patients with paraffin blocks of breast cancer tissues meeting the inclusion criteria were the subject of a three-fold investigation (socio-demographic, clinical and morphological).

Clinical, demographic and tumor characteristics were collected for each patient from medical records, anatomopathological examination requests sent to the laboratory and those indicated on the anatomopathological reports.

The demographic and clinical survey made it possible to find: age; marital status; the profession; family history of breast cancer; and tumor location.

The morphological investigation concerned the use of medical files and anatomopathological reports in search of: histological type; Scarff Bloom Richardson histo-prognostic grade; the positivity of ORs; the positivity of PR; HER2 expression and Ki-67 proliferation index.

Technical support for samples

Histopathology

Sections of 4 µm were microtome cut for each of the 40 paraffin blocks of breast cancer tissue. Tissue ribbons were spread on the slides for hematoxylin and eosin (H&E) staining. The obtained slides were dewaxed in three toluene baths for 5 minutes each. Then they were rehydrated with a series of decreasing alcohol baths (100%, 95% and 80%), each for 3 minutes. The sections were then stained with hematoxylin for 5 minutes, rinsed gently in tap water for 10 min, then stained with eosin for about 1 minute. The slides were subsequently dehydrated with an increasing series of alcohol (80%, 95% and 100% ethanol). After immersion for 5 min in a toluene bath,

The slides were re-read by the pathologist before immunohistochemical analysis to determine the histological type.

Breast cancer has been classified according to the World Health Organization 2012 (WHO 2012) [9]. Histological classification was performed using the Nottingham classification system and staging according to the 8th edition of the AJCC classification of 2017 [9, 10].

Immunohistochemistry

Immunohistochemistry procedures examining hormone receptor labeling (RO for estrogen receptor and RP for progesterone receptor) and expression of Her-2 were performed manually.

The technology used: Ultra vision quanto system using Horseradish Peroxidase (HRP) and Diaminobenzydine (DAB) with external control.

The following standard practices were performed: To analyze the labeling profile of hormone receptors and expression of Her-2 in super Frost plus slides, each was dewaxed in xylene, rehydrated in alcohol baths at degrees decreasing (100 °, 95 °, 70 °) and boiled for 45 minutes (in a water bath set to 96 °) in 10 mM citrate buffer (pH 6.0) for restoration of antigenic sites. Then the slides were incubated for 35 minutes at 37 ° C with primary monoclonal antibodies using the manual mode. Thermo Scientifique's manual Ultra vision detection system uses an indirect biotin-avidin system with a universal biotinylated immunoglobulin secondary antibody. The slides were incubated for 5 minutes with the 3, 3'-diaminobenzidine (DAB) until an appropriate brown color. Then the slides were counterstained with hematoxylin before mounting. Staining procedures were performed according to the manufacturer's recommendations. Negative controls were obtained by omitting the primary antibodies. After IHC, two pathologists examined all the slides.

The 150 blocks were analyzed for RO and RP labeling and HER2 expression in manual IHC.

Interpretation of the staining result Visual analysis under an optical microscope allowed the intensity of the staining and the percentage of tumor cells showing nuclear immunostaining for RO and RP (range: 0-100%) to be assessed.

Sections of breast tissue were considered positive for RO and RP if ≥ 1% of tumor cells showed positive nuclear staining according to the recommendations of the American Society of Clinical Oncology / College of American Pathologists [11]. The intensity of immunostaining and the percentages of cells stained for RO and RP were independently examined by two pathologists. The expression of HER2 was noted by scores of: 0, 1+, 2+ and 3+. The FISH technique was not used for equivocal HER2 results (2+) in the two groups (1 and 2) and only the 3+ score was considered positive for HER2 while the score ≤ 2+ was assumed negative for HER2.

The molecular breast cancer subtypes were defined using the combination of these IHC markers, namely:

Table I : Classification adopted for breast cancer subtypes [7, 12, 13].

Molecular subtype	Markers expressed
Luminal A	OR + / RP +, HER2 -, Ki - 67 ≤ 14%
Luninal B	RO + / RP +, HER2 + or RO + / RP +, HER2 -, Ki - 67> 14%
Her2 +	RO-, RP-, HER2 +
Triple negative	RO-, RP-, HER2-

Statistical analysis

The following software was used: Microsoft Excel version 2016 for the creation of the database and Graph Pad Prism version 5.0.0.3 for data processing. The results were expressed as mean ± standard deviations for the quantitative variables and in number and / or percentage for the qualitative variables. The comparison of the qualitative variables was made by the chi2 test and that of the quantitative variables by the student test (t-test).

The p-values indicated a statistically significant difference when its value was less than or equal to 0.05 (p≤0.05) at a 95% confidence interval.

Ethical considerations

The present work was carried out within the framework of scientific research. As a result, it was approved by the Health Science Research Ethics Committee (CERSSA) according to opinion No. 061 and the related investigation guaranteed the confidentiality of the data.

RESULTS

Table II: Socio-demographic characteristics

Age groups	*NOT*	*%*
20—29	*14*	*9.33*
30—39	*32*	*21.33*
40—49	***38***	***25.33***
50—59	*31*	*20.67*
60—81	*35*	*23.33*
Total	*150*	*100*
Profession		
Shopkeeper (2)	*17*	*11.33*
cultivator (4)	***31***	***20.67***
unemployed graduate (1)	*23*	*15.33*
Student (7)	*13*	*8.67*
Civil servant (6)	*30*	*20.00*
unknown (5)	*23*	*15.33*
Retired (3)	*13*	*8.67*
Total	*150*	*100*
Marital status		
Single	*42*	*28*
Married	*37*	*24.67*
free Union	*71*	*47.33*
Total	*150*	*100*

Table III : Clinical, histological and SBR grade parameters

Type of sample	*NOT*	*%*
Biopsies	***79***	***52.67***
Nodulectomy	*34*	*22.67*
Mastectomy	*37*	*24.67*
Total	*150*	*100*
Location		
Law	*60*	*40*
Left	***71***	***47.33***
Bilateral	*4*	*2.67*
Unknown	*15*	*10*
Total	*150*	*100*
Family history		
Yes	***11***	***7.33***
No	*139*	*91.67*
Total	*150*	
Histological type		
Non-specific invasive carcinoma	***93***	***62***
Invasive lobular carcinoma	*41*	*27.34*
Mixed carcinoma	*9*	*6*
Muciparous carcinoma	*2*	*1.33*
Medullary carcinoma	*2*	*1.33*
Total	*150*	*100*
SBR		
I	*18*	*12*
II	***77***	***51.33***
III	*36*	*24*
Unknown	*19*	*12.67*
Total	*150*	*100*

From 2014 to 2020, we collected 1201 cases or 36.66% of breast cancers out of 3276 cancers recorded during this period and 150 (12.49%) met the inclusion criteria for our study. The mean age of the patients was 48.09 ± 13.87 years with the extremes of 22 years and 80 years; and a median of 47 years. The most represented age group was the 40 to 49 age group with 38 cases or 25.33% (Table 2).

The study of the profession; the most represented in our study was that of farmers 20.67%, followed by civil servants 20% and unemployed graduates 15.33% (Table 2).

The marital status; the common-law group was the most represented with 47.33% (Table 2).

The most frequent type of sample was breast biopsies in 79 cases, or 52.67% of cases. The rest of the nature of the samples has been shown in Table 2.

A predominance of breast cancer localization was observed in the left breast in 47.33% (Table 3).

The frequency of a family history was 7.33% or 11 cases (Table 3).

The most frequently represented histologic type was 62% invasive non-specific type carcinoma (CITNS). The most represented histological grade was Scarff Bloom Richardson grade II (51.33%), followed by grade III 24% and grade I in 12% of cases (Table 3).

Table IV : Correlation of molecular subtypes with age, histological type and SBR grade

Settings	***Luminal A***	***Luminal B***	***HER2 +***	***Triple negative***	***p-value***
Ages (years)					***0.36***
20—29	*7 (10.00)*	*3 (12.00)*	*1 (6.67)*	*1 (3.04)*	
30—39	*15 (21.43)*	*7 (28.00)*	*1 (6.67)*	*4 (12.12)*	
40—49	***18 (25.71)***	***11 (44.00)***	***5 (33.33)***	***7 (21.21)***	
50—59	*14 (20.00)*	*2 (8.00)*	*5 (33.33)*	*10 (30.30)*	
60—81	*16 (22.86)*	*2 (8.00)*	*3 (20)*	*11 (33.33)*	
Histological type					***0.02***
Non-specific invasive carcinoma	***47 (67.14)***	***14 (56.00)***	***8 (53.33)***	***24 (72.73)***	
Invasive lobular carcinoma	*16 (22.86)*	*9 (36.00)*	*5 (33.33)*	*7 (21.21)*	
Mixed carcinoma	*5 (7.14)*	*1 (4.00)*	*2 (13.33)*	*1 (3.03)*	
Muciparous carcinoma	*1 (1.43)*	*0 (0)*	*0 (0)*	*1 (3..03)*	
Medular carcinoma	*1 (1.43)*	*1 (4.00)*	*0 (0)*	*0 (0)*	
SBR grade					***0.72***
Grade I	*7 (10.00)*	*3 (12.00)*	*2 (13.33)*	*3 (9.10)*	
Grade II	***36 (51.43)***	***14 (56.00)***	***10 (66.67)***	***15 (45.45)***	
Grade III	*21 (30.00)*	*6 (24.00)*	*2 (13.33)*	*7 (21.21)*	
Unknown	*6 (8.57)*	*2 (8.00)*	*1 (6.67)*	*8 (24.24)*	

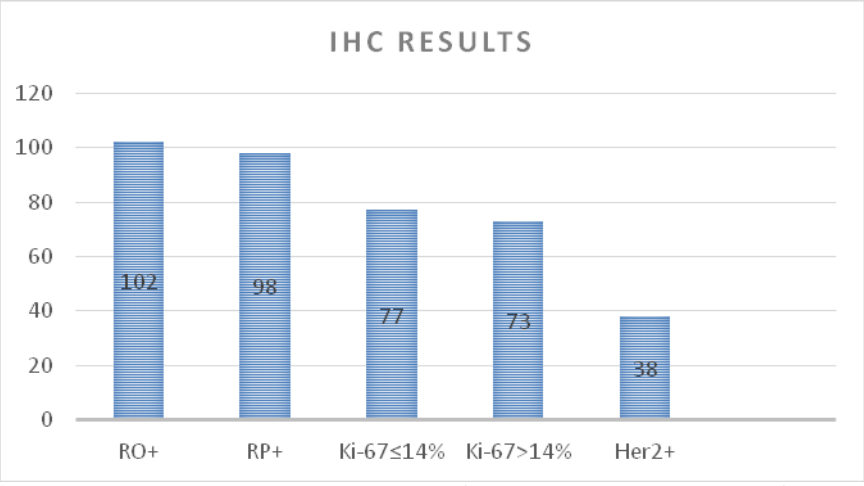

Figure 1 : Hormone receptor IHC results, the Ki-67 proliferation index and the expression of Her2 score 3+.

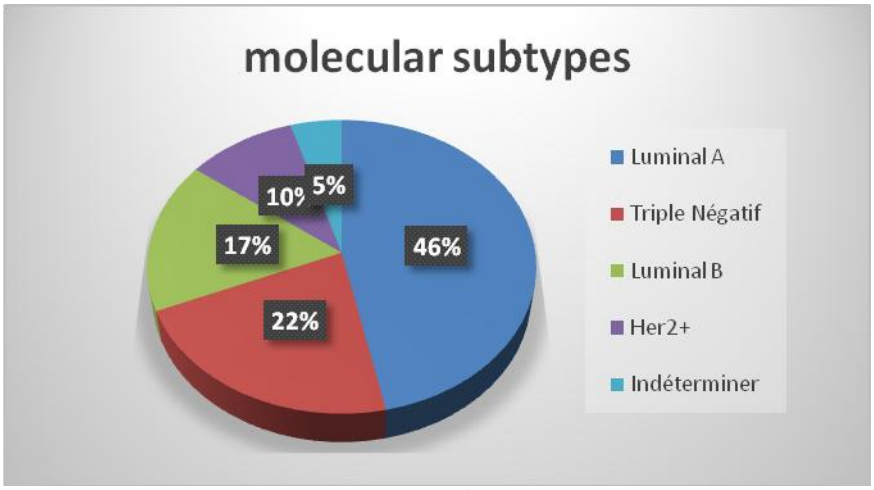

Figure 2: the distribution of molecular subtypes.

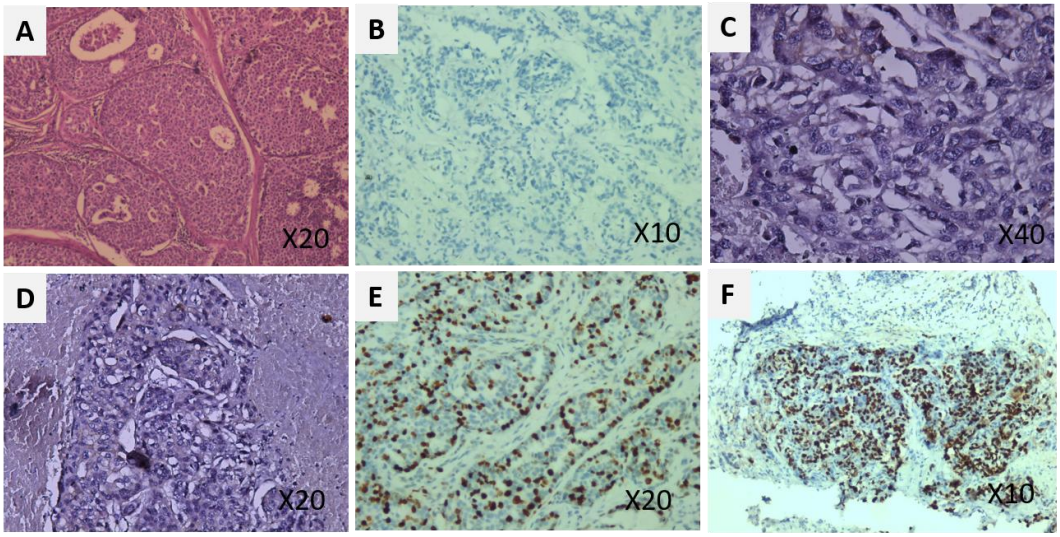

Figure 3: Representative histological and immunohistochemical figures illustrating: an invasive nonspecific type carcinoma (A), malignant breast tissue without nuclear staining; RO negative (B), malignant breast tissue without nuclear staining; PR negative (C), malignant breast tissue without membrane labeling of Her2; (D), breast malignant tissue with nuclear staining at the limit of 14% Ki-67 (E) and breast malignant tissue with nuclear staining greater than 14% of Ki-67.

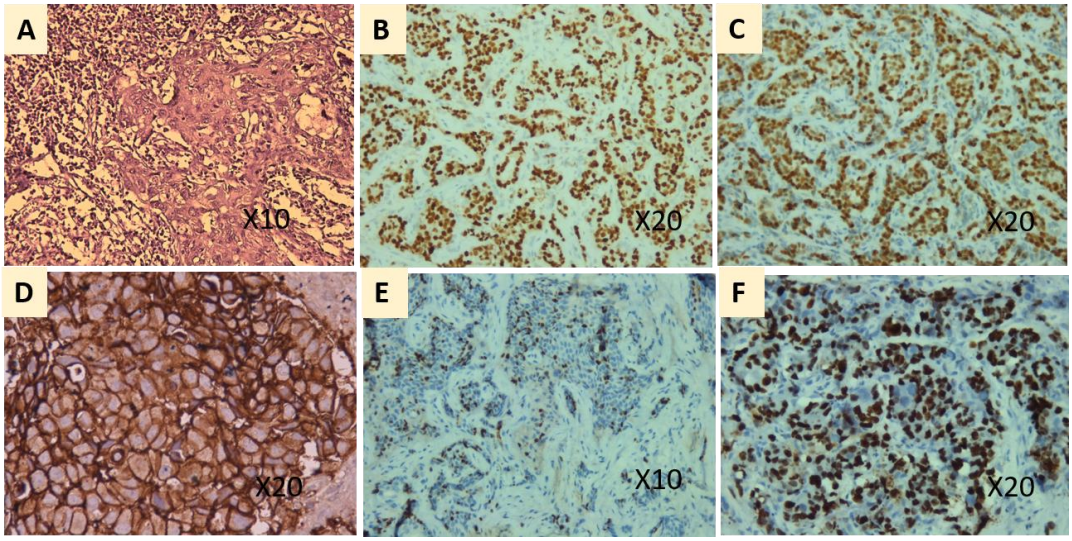

Figure 4: Representative histological and immunohistochemical figures illustrating: medullary carcinoma (A), malignant breast tissue with nuclear staining; RO positive (B), malignant breast tissue with nuclear staining; PR positive (C), malignant breast tissue with cell membrane staining (score 3+) demonstrating the complete "ring" pattern of Her2; (D), malignant breast tissue with nuclear staining≤14% of Ki-67 (E) and breast malignant tissue with nuclear labeling>14% of Ki-67.

Regarding the results of IHC (Figure 1); of the 150 cases, 102 (68%) had positive hormone receptors (HR +). The ORs were positive in 102 cases (68%) while the PRs were positive in 98 cases (65.33%). The Her2 oncogene was over expressed in 38 cases (25.3%). The Ki67 proliferation index was known for the 150 cases, including 77 (51.33%) less than 15% and 73 (48.67%) greater than or equal to 15%. The distribution of molecular subtypes was 46% luminal A, 22% triple negative, 17% luminal B and 10% Her2 +. Tumors of unknown molecular profile were 5% (Figure 2).

The correlation was found between molecular subtype and histological type. This result was statistically significant ($p < 0.05$) (Table 4).

For the rest. There was no correlation between age and SBR grade ($p > 0.05$) (Table 4).

DISCUSSION

Nowadays, the incidence of breast cancer in Africa is increasing exponentially according to the data recently published by Globocan 2020 [5]. The epidemiology and morphological aspects of breast cancer in African women, especially sub-Saharan, in terms of current knowledge, remain insufficient and poorly documented. It is evident that in the future, the current data will undergo modifications due to a foreseeable evolution of the risk factors of the disease, in particular the evolution towards an increasingly urban way of life [14]. Sub-Saharan African (SSA) countries are currently undergoing an epidemiological transition and are facing the so-called "double burden" of being simultaneously affected by major infectious and chronic diseases, including malignant tumors. [15].

In this study, we were able to establish a frequency of 36.66% of breast cancer cases among all cancers diagnosed in the Anatomy, Cytology and Pathology department of the CHU-B during the period 2014-2020. This frequency to confirm that breast cancer remains to this day a real major public health problem in our country. It is important that politicians can take urgent measures to curb the incidence of this pathology through screening campaigns and the equipment of technical platforms in diagnostic support services. In addition, the 150 cases retained in the framework of this study are related to the selection criteria, especially plus the presence of an additional report of the patients' IHC. In this study, IHC was only performed in the 150 (12.49%) breast cancers diagnosed during this period due to the unavailability and high cost of receptor testing. This very limited access to the IHC, as evidenced by the frequency (12.49%) in our country, has also been observed in most countries of sub-Saharan Africa [9,16, 17, 18]. These results reflect difficulties in the regular assessment of tumor subtypes and poor access to radiation therapy and targeted agents in Mozambique, which impede the adequacy of care based on patient stage and subtype. breast tumor. Ultimately, they reflect the underfunding of breast cancer care on the "treatment" side in this low income setting.

In our study, the selection criteria were established in order to avoid bias in the interpretation of the results. These criteria were also used by Ablayi et al., [9] in 2020 in Togo; as well asMiguel et al., [7] in 2017 in Angola in a study aimed at providing a first look at the molecular subtypes of breast cancer in this country.

The sampling strategy was to obtain a number of cases necessary for statistical significance of the results. The size of our sample of 150 cases is closer to several studies [9, 10, 19, 20] and significantly superior to other studies [21, 22].

According to WHO (Globocan 2012) [23], breast cancer is the prerogative of women under 65. Age at diagnosis of breast cancer is a very important prognostic factor [24]. In this study, the mean age was 48.7 ± 13.7 years and there was a peak incidence in the 40-49 age group with 25.33%. This finding is similar to several studies carried out in Africa [25, 26, 27] and the Middle East [28]; but different from the relatively younger

age of women with breast cancer reported in several studies in other African countries [7, 29, 30].

The most represented profession (20.67%) was that of farmers, followed by civil servants or State agents with 20%. As the number of cases and the costs of new breast cancer treatment options increase around the world [31], its financial burden will increase worldwide. It is therefore important that the recent program to fight cancer, which has just been set up this year by our government, can already estimate the cost of health care linked to cancer, in order to design public policies for the allocation of resources. Indeed, in low / middle income countries, the cost of cancer care is poorly defined [32].

It has been shown by research that the young age groups of breast cancer patients were associated with a family history of breast cancer [33]. In our study, only a few cases (7.33%) had a family history of breast cancer. Our result is slightly higher than that of Mihret et al. in Ethiopia recently in 2021 which had found a proportion of 5.2% of family history of breast cancer [34] and significantly lower than that reported in Benin by Gnangnon et al. 2020 with a frequency of 11.8% [35]. This proportion of 7.33% of cases of family history discovered in this study will certainly constitute the future fields of research to be treated in the future; otherwise, there is currently no evidence to link the etiology of this family history to our breast cancer cases. In other words, in our series, the family history of breast cancer did not appear to be significantly related to the occurrence of breast cancer; almost all (92.67%) of the study population had no family history of breast cancer.

In this study, the location of the malignant tumor of the breast more affected the left breast at 47.33% against 40% for the right breast, this difference can be explained by the practice of breastfeeding. Bilateral localization concerned 2.67% of our patients. Our results were corroborated with those of Traoré et al. [36] who reported 62.9% of breast cancers located on the left and Engbang et al. [27] who reported 52% of left-seated breast cancers. On the other hand, they were different from those of the other authors, like Darré et al. [37] in 2013 in Togo, which reported 46.22% right location and 44.89% left location and 8.89% both breasts.

The diagnosis of certainty was made by histology in all cases. Thus in our series, we identified 62 % of invasive carcinoma of the nonspecific type and 27.34% of infiltrating lobular carcinoma of all the invasive carcinomas in our work. This is in agreement with the histological investigations of breast cancer in many countries. [22, 38; 39;40].

In our series, the most represented histological grade was grade II SBR (51.33%), followed by grade III 24% and grade I in 12% of cases. This ranking was also those of: Fouhi et al. [41] reported 55.90% grade II, 32.60% grade III and 11.50% grade I breast cancers, Traoré et al. [16] found grades SBR II in 31 cases (53.4%), SBR III in 21 cases (36.2%) and SBR I in 6 cases (10.3%) while Stierer et al. [42] out of 299 breast carcinomas reported 163 grade II carcinomas, i.e. 54.51%. These observations are contrary to those reported in Libreville by Meye et al. according to which, grade II occupied the last position after grades III and I [43] and in Tunisia where Sahraoui et al. have reported a predominance of histological grade III representing 41% of cases; grades II and I represented 38% and 21% respectively.[44]

In contrast, the histological type and tumor grade have insufficient prognostic and predictive implications and limited clinical utility [20]. Therefore, it is useful to determine the RO, RP, Her2 and Ki-67 status by the immunohistochemical technique to choose their treatment and assess patient survival.

Tumor differentiation in breast cancer cases is of great importance in the management of malignant disease of the breast. Hormonal estrogen receptors are markers of tumor differentiation. In this

study, the hormonal receptors were studied in 150 patients, these receptors were positive in 68% of the assessments carried out.

In this study, 68% of patients expressed estrogen receptors. This result is identical to that obtained in a French study carried out by Vincent et al. [45] which reported 68% positive RO.

In this series of 98 cases, 65.67% of patients expressed PR. This result corresponded to that of Fouad A. et al. [46] obtained 64.5% of patients expressing PR. Andthe positivity of the progesterone receptors testifies to the functionality of the estrogen receptors. The hormonal progesterone receptors are positive in 40 to 50% of cases, they are prognostic factors since the expression of these receptors is an element of good prognosis and especially predictive of the response to hormonal treatment [47].

In our study, we obtained 25.3% of HER2 positive patients. Our results corroborate those of the literature [46, 48]. Affane et al. [49] had found rates higher at 53%.

The molecular classification of breast cancers has been highlighted thanks to advances in molecular research on gene expression using cDNA chips, in other words RNA seq technology. [50, 51]. The latter is almost difficult to implement in hospitals, especially because of its high cost and its technical complexity. Thus, a scientific consensus was found to supplicate this cDNA chip technology by another more practical and less expensive; that of Immunohistochemistry which makes it possible to demonstrate the Antibody-Antigen reaction on a paraffin section of the tissue of an organ such as the breast. IHC enables molecular subtyping of breast cancer [52].

The molecular profile was obtained from the results of hormone receptors, HER2 and the Ki-67 proliferation index. According to the so-called Sorlie and Peru molecular classification, several breast cancer subgroups can be distinguished: Luminal A, Luminal B, HER2, triple negative (basal-like).

Thus, in our series, we obtained 46% of the cancers which are of the Luminal A group, 22% for the Triple negative group, 17% Luminal B and 10% HER2 positive. Luminal A tumors have a good response to hormone therapy, and Luminal B tumors have a variable response to hormone therapy but respond quite well to chemotherapy. [53, 54]. In sub-Saharan Africa, luminal A is more common in some countries [55, 56], while in others the triple negative is most common [57, 58]. The distribution of the molecular classification in our study is comparable to that of other studies published in Africa [59] and the West. [60].

HER2: Overexpression of HER2 appears to be associated with a higher risk of recurrence and is a predictive factor of response to treatment with anti-HER2 (traztuzumab) [61]. Thus, the overexpression in our study of 10% of HER2 (HER2 +), presents a statically significant difference with that of Rharrassi I et al in Morocco [62] who reported 23.52% of overexpression of HER2 in a number of 85 patients.

Triple negative: It is characterized by the absence of hormone receptors and the absence of expression of growth factor HER2. We recorded 22% of triple negatives which differs greatly from the multicenter study (Nigeria and Senegal) by Huo D et al [58], which found 55% of triple negatives in a number of 507 cases.

Breast cancer subtypes correlated with histologic type ($p = 0.02$). A significant association between histological type and breast cancer has also been reported in Moroccan [63], in Sudanese and Eritrean women [64].

In this study, we found no correlation between molecular subtype and age, SBR grade. While in several studies, some authors have reported a significant association between molecular subtype and age [51, 65].

Finally, it is reasonable to mention certain methodological limitations of the present study. Indeed, in view of the cases

diagnosed during the study period and the size of the sample, the results presented may not be representative of the Congolese female population with breast cancer. Indeed, the present study includes a selection bias which is due to the recruitment of participants with an IHC result available; but also, the lack of clinico-pathological information; all of this led to a small sample size. And our results should be limited only to women treated in Brazzaville. Larger population sample studies are needed to help guide the nation's newest cancer control program. Another aspect to note concerns the fact that we were not able to evaluate the cases of equivocal results of HER2 for lack of tools allowing to carry out the fluorescence in situ (FIS), and the absence of cytokeratin 5/6 to identify the different subsets of triple negative cancer. Despite its stated limitations, our study reinforces the notion that the association between histological diagnosis and immunohistochemistry can help determine the phenotype of breast cancer, with the aim of guiding treatment and therefore improving response to treatment.

CONCLUSION

Through this study, we have identified the epidemiological, morphological and distribution aspects of molecular breast cancer subtypes and their associations with certain clinico-pathological characteristics in women in Congo Brazzaville. The women with breast cancer at Brazzaville University Hospital were diagnosed at an early and advanced stage with regard to the SBR grade. The two predominant molecular subtypes were Luminal A and Triple negative. The IHC markers have very great therapeutic and prognostic implications in the overall management of patients with breast cancer. Thus, the availability of receptor tests should be a priority, in order to propose the best modalities for the treatment of breast cancer.

Thanks

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Conflicts of interest

The authors declare no conflict of interest.

Contributions from the authors

Dimitry Moudiongui: conception and writing of the article; **Anicet Boumba:** data analysis and interpretation; **Gervillien Malonga:** critical review of the article; Fabien Mouamba: critical review of the article; **Fidèle Mambouene:** critical review of the article; **Donatien Moukassa:** critical review of the article; **Jean Félix Peko:** final approval of the version to be published. All authors have read and approved the final version of the manuscript.

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