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Breast Cancer: Clinical and Pathological Study at Lubumbashi and Kinshasa University Hospitals in the Democratic Republic of the Congo from 2014 to 2015

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Abstract: Often tumors in the African setting are described aggressive with high grading status. There is no national cancer registry nor suitable data on breast cancer in DRC. Better knowledge of this entity can improve its management. To demonstrate the clinical and pathological profile of breast cancer in Kinshasa and Lubumbashi (DR Congo). Cross-sectional study of 86 patients were included for clinical and pathological in the Cities of Lubumbashi and Kinshasa from 2014-2016. All cases were women with histological invasive breast carcinoma. Parameters studied were: age of patients at diagnosis, morphological type [33], grade [23] of tumor, tumor necrosis and Nottingham score. Statistical analysis used SPSS program and Pearson Khi-square test. From January 2014 to September 2016, 86 cases were reviewed. The average age of patients at diagnosis was 47.8 ± 12.1 years. In 74% of cases, patients were presented at stage T_3 or T_4. The average size of tumors was 6.6 ± 2.7 cm. Invasive Ductular carcinoma was found in 97.2% of cases. Grade 3 tumors were found in 54.7% and grade 1 in 4.7%. Tumor necrosis was present in 30.2% of biopsies. The Nottingham score higher than 5.4 was found in 62.8%. All the patients were treated by supra-radical mastectomy. Lymph nodes were numbered in each case. Prognosis of breast cancers is poor in Lubumbashi and Kinshasa University Hospitals for tumors are diagnosed later. To improve breast cancer management, tumor must be diagnosed earlier. Perception of this pathology and its correct assessment are important for better taking care in the Democratic Republic of the Congo.

Keywords: Breast Carcinoma, Clinico-Pathological Evaluation, Prognosis

1. Introduction

Breast cancer may be the most common cancer in women worldwide [21]. Early detection and several types of treatment has been shown able to reduce mortality in developed countries. However the prevalence remains still high in these countries [37]. This tumor appeared the most lethal cancer in women [20].

In Africa, the incidence of breast carcinoma is constantly growing [15, 56] and is the most prevalent among women in the South of the Sahara [42, 44]. About 324000 deaths are reported in low income countries in 2012 as due to breast

cancer [21].

Variations in the incidence of breast cancer through different populations, suggest the existence of different etiological factors in their biological expressions as well as their prognosis [38]. However, ethnicity and origin of patients are two major predictors in this variation [25]. Those may be inherited, environmental, hormonal (endogenous or exogenous) and socio-demographical factors [38].

In fact, studies have shown that the prognosis of breast cancer could be related to race and geography [18, 52]. In the United States, patients of African origin may have a worse prognosis more than white [40, 49].

Apart from the socio-economic aspect that can affect the prognosis and management, some reported that differences may be observed in the occurrence of pathology [26, 50].

This study was conducted to demonstrate clinical, histologic and prognosis of invasive breast carcinoma of women living in the Democratic Republic of the Congo.

2. Materials and Method

This cross-sectional study has been conducted in two cities of DRC (Lubumbashi and Kinshasa) from 2014-2016. A systematic sampling and collection of 86 cases have been made during this period.

2.1. Inclusion Criteria

All cases of sick women received during this period with breast carcinoma on the mean of a pathological diagnosis were reviewed after selection. Patients were informed and gave their agreements on the scientific study.

2.2. Exclusion Criteria

Every secondary or non-invasive lesion of the breast cancers were excluded.

2.3. Pathological Examination

Histopathologic analysis was made after embedding in paraffin and a coloring in haematoxylin and eosin according to a standard protocol.

The biopsies were prepared in the laboratories of pathological anatomy of Lubumbashi and Kinshasa. The diagnosis was confirmed in Germany (University of Halle) starting from the paraffin blocks sent.

The morphological analyses were performed according to the following procedure:

1. Embedding in paraffin blocks in Lubumbashi and Kinshasa Laboratories
2. Technique of usual coloring in Lubumbashi and in Germany
   a) Treatment of tissue

Biopsies were fixed in formalin, buffered 10%, dehydrated in ethanol and dipped in liquid paraffin after clarification in xylene. The paraffin blocks were formed and cut sections made on Rotary microtome to get slides.

b) Technics of normal coloring in Lubumbashi and Kinshasa (Universities Hospital) and in Germany (University of Halle).

The slides made were colored according to the technique common to haematoxylin and eosin according to the following procedure:

a. Dewaxing of slides in xylene
b. Rehydration in 100, 90 and 70° alcohol
c. Rinse in running water
d. Color in the haematoxylin of Mayer
e. Rinse in running water,
f. Bluing in the lithinee water
g. Rinse in running water
h. Color in the solution of eosin
i. Rinse in running water
j. Dehydration in alcohol of 70, 95 and 99°
k. Clarification in xylene
l. Mounting of the covers slides

Microscopic analysis and evaluation of prognosis

Histopathological lecture was made at the Departments of pathology in Universities of Lubumbashi and Kinshasa, confirmed at the Department of pathology in Germany (University of Halle).

The classification was based on the morphological criteria only. The carcinoma type was defined according to the classification of the WHO [33].

The grade of the tumor was determined taking account of the Elston and Ellis score [23]. The later assessment is based on the study of 3 parameters: tumor architecture, nuclear abnormalities and mitoses index. These 3 parameters are added together to get a total score, classifying the tumors in grade 1 (scores 3, 4 or 5), grade 2 (score 6 or 7) or grade 3 (scores 8 or 9).

The score of Nottingham is calculated by the following formula

$$NPI = G + L + (S \times 0.2)$$

NPI = Nottingham prognostic index; G = Tumor grade; L = number of involved lymph nodes (1= none, 2= one to 3 lymph nodes) and 3=more than 3 lymph nodes),; S = size of the tumor (in centimeters)

To deal with stage of tumor, UICC classification was used (58).

2.4. Treatment of Patients

All the patients were treated by radical mastectomy combined with ablation of detectable lymph nodes.

2.5. Parameters Studied

The parameters taken into account were clinical and histological: the age of the patient, the size of the tumor (measured in cm by taking the major axis), and the number of lymph nodes detectable during the surgery, the type of Carcinoma [33], the histological grade [23] and the presence or the lack of tumor necrosis.

2.6. Statistical Analysis

We used the program SPSS19. Quantitative data are

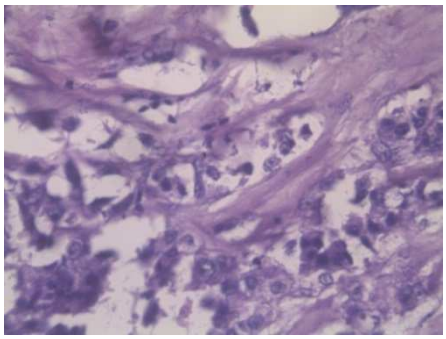
expressed as average with standard deviation. Qualitative data are presented in the form of frequency and proportion. We used the Pearson Chi-square to measure the factors association with a significance level less than 0.05 ($p<0.05$).

3. Results

From January 2014 to October 2016, 86 cases of mammary carcinoma were collected. Patients' age ranged from 27 to 86 years (Table 1). The average age was 47.8 ± 12.1 years. The average size of tumor was 6.6 ±2.7 cm (Table 2). The stages T1, T2, T3 and T4 respectively represented 1.2%, 24.4% and 74.4% (Table 2). The invasive ductular carcinoma, invasive lobular carcinoma and invasive papillary carcinoma respectively accounted for 97.7%, 1.2% and 1.2% (Table 3). Some image of invasive ductal carcinoma are shown in figures 1 and 2. Grade 1, grade 2 and grade 3 represented respectively 4.7%, 40.7% and 54.7% (Table 4). Tumor necrosis was observed in 30.2% of cases, thus 31.4% in grade 2 and 31.9% in grade 3 tumors. However the difference was not statistically significant (Table 5).

In younger patients aged of 45 or less, tumors of grade 3 accounted for 52.6% versus 7.9% of grade 1 tumors. Among those aged of more than 45 years, there was 56.3% of grade 3 tumors versus 2.1% grade 1 tumor. However the association (Table 6) was not statistically significant (P = 0.446).

Patients with a score of Nottingham between 2 and 2.4, between 2.4 and 3.4 between 3.4 and 5.4, and higher than 5.4 represented respectively 2.3%, 2.3%, 32.5% and 62.8% (Table 7).



HE x 40

Figure 1. *Invasive ductal carcinoma.*

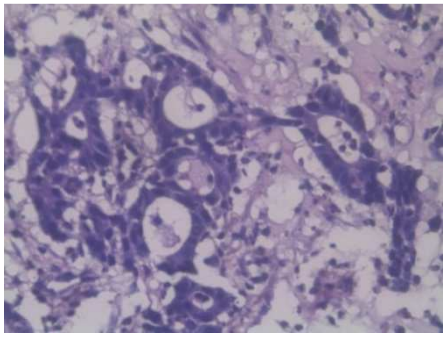


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Figure 2. *Invasive ductal carcinoma.*

Table 1. *Patients' age groups.*

Age	Number	Percentage	PC(*)
27-34	18	20.9	20.9
35-43	16	18.6	39.5
44-51	23	26.7	66.2
52-60	18	20.9	87.1
61-68	8	9.3	96.4
69-77	1	1.2	97
≥78	2	2.3	99.9
Total	86	100	

(*) PC: cumulative percentage

Table 1 shows that breast carcinoma has an occurrence in younger patients

Table 2. *Size of the tumor.*

Size of the mass (cm)	Number	Percentage
≤2 (T1)	1	1.2
> 2 to 5 (T2)	21	24.4
> 5 (T3) + T4	64	74.4
Total	86	100.0

Table 2 shows that the average tumor size was of 6.6 ±2, 7 cm. (Table 2). The stages T1, T2, T3 and T4 respectively accounted for 1.2%, 24.4% and 74.4%.

Table 3. *Tumor Histological types.*

Diagnosis	Number	Percentage
Invasive ductular carcinoma	84	97.7
Invasive lobular carcinoma	1	1.2
Invasive papillary carcinoma	1	1.2
Total	86	100.0

Table 3 shows that the invasive ductular carcinoma, and invasive lobular carcinoma and the papillary carcinoma respectively accounted for 97.7%, 1.2% and 1.2%.

Table 4. *Tumor histologic grade.*

Grade	Number	Percentage
1	4	4.7
2	35	40.7
3	47	54.7
Total	86	100.0

Table 4 shows that grade 1, grade 2 and grade 3 represented respectively 4.7%, 40.7% and 54.7%

Table 5. *Tumor necrosis and histologic grade.*

	Necrosis		P
	Yes	No	
Grade 1	0 (0.0%)	4 (100%)	0.402
Grade 2	11 (31.4%)	24 (68.6%)	
Grade 3	15 (31.9%)	32 (68.1%)	
Total	26 (30.2%)	60 (65.8%)	

Table 5 shows that the tumor necrosis is observed in 30.2% of cases. In grade 2, Necrosis was noticed in 31.4% and in 31.9 of grades 2 and 3 tumors. The difference was not statistically significant. (P = 0.402).

Table 6. *Grade Tumor and age of the patients.*

	Grade			P
	1	2	3	
≤ 45	3 (7.9%)	15 (39.5%)	20 (52.6%)	
> 45	1 (2.1%)	20 (41.7%)	27 (56.3%)	0.446
Total	4	35	47	

Table 6 shows that at patients aged 45 years or less we recorded 52.6% of grade 3 tumors versus 7.9% of grade 1. In elderly patients over 45 years there were 56.3% of grade 3 tumors versus 2.1% of grade 1. The association was not statistically significant (P = 0.446)

Table 7. *Score of Nottingham.*

Score of Nottingham	Number	Percentage
2 -2.4	1	2.3%
2.4-3.4	1	2.3%
3.4-5.4	14	32.5%
Sup 5.4	27	62.8%
Total	43	100.0

Table 7 shows that patients with a score of Nottingham between 2 and 2.4, 2.4 and 3.4, 3.4 and 5.4, and higher to 5.4 represented respectively 2.3%, 2.3%, 32.5% and 62.8%.

4. Discussion

The objective of this study was to evaluating the particularities of clinical and histologic features of the breast cancer in women in the Democratic Republic of the Congo in order to establish the prognosis.

4.1. Age of Patients

In this study, the average age is 47.8 years. This observation was made likely in others African publications as shown in the following table.

Table 8. *Comparison of age of the patients in some studies.*

Authors	Countries	Average Age
Kim M-J, 2006	South Corea	47.4 years
Bowen R. L, 2008	Great Britain	46 years (black), 67 years (whites)
Rambau P. F 2011	Africa	48 years
Adisa C A, 2012	Nigeria	47 years
Ohene-Yeboah et Adjei E, 2012	Ghana	49.1 years
El Fatemi, 2012	Morocco	46 years
Cong X, 2012	China	43 years
Ly M, 2012	Mali	46 years
Mohapatra M et Satijanarayana, 2013	India	48.7 years
Kantelhardt EJ, 2014	Ethiopia	43.0 years
Our study	DRC	47.8 years

These results on the average age in Africa are closer to Asian results. It is 47, 4 years in South Korea as observed by Kim et al. [32] and 43 years in China as shown in Xue et al. study [59]. Those observations are emphasized by comparative studies like those of Chalabi et al. [14], in Mediterranean countries (the age at diagnosis is 10 years less than that of the European women). In Britain, breast cancers are diagnosed at 46 years in black while they are found at 67 years in white women [12]. The same observation is reported in the United States by comparing blacks to white [19, 60]. For Bailes et al. [8], there may be the race and ethnic group factors in the variation in the onset of the tumor. Indeed, the factors responsible for this disparity on the age at diagnosis, are not completely understood. Some authors [6, 24, 54] thought that these may be related to the BRCA 1 and 2 genes and their variants. Abbas et al [1], Braverman [13] and Lin et al. [35] proposed a vitamin D deficiency pathway. And also, there is no study in our environment which has yet been conducted to determine the genetic forms of breast cancer even although it is well known that knowledge of hereditary tumors is important to in improving therapeutic approaches as proposed by Van der Groep [54] and Bogdanova [11]. For Key et al [31], SHBG (sex hormone binding globilin) may be associated with low incidence of breast cancer.

4.2. Stage of Presentation

Breast cancers have been diagnosed at stages T III or T IV in 74.4% in this study. The average size of our tumors was 6, 6 ± 2.7 cm. Many authors reported such observations in African women [10, 28]. For Rambau et al., in the East Africa [47], tumors were diagnosed at stage III or IV in 70% of cases. Table 9 is summarizing these findings in Africa and the world.

Table 9. *Comparison of stage of tumors in some studies.*

Authors	Countries	*STAGE OF PRESENTATION*		
		I	II	III or IV
Leong S. P. L, 2010	Canada	65%		
Leong S. P. L, 2010	USA	60-70%		
Leong S. P. L, 2010	Suede	56%		
Leong S. P. L, 2010	Japan		43%	
Leong S. P. L, 2010	South-Korea		40%	

Authors	Countries	*STAGE OF PRESENTATION*		
		I	II	III or IV
Leong S. P. L, 2010	India			29-59%(stage III)
Boder J M E, 2011; Ikpatt O F, 2002	Libya and Nigeria			+ de 50%
Raumbau P F, 2011	East of Africa			70%
Ohene. Yeboah M, Adjei E, 2012	Ghana			85%
Ly M, 2012	Mali			90%
Kantelhardt E J, 2014	Ethiopia			71% (stage III)
Amadori D, 2014	Tanzania			Most of
Our study	DRC			74%

The lack of awareness, women education of and women screening policy may be the major bases of late diagnosis in Africa. Coughlin [16] mentioned that misconception of cancer may be the cause of late diagnosis. He reported that African believed that cancers affect only white or older women. The proliferative power of tumors in black women was mentioned as one of the reasons that made the diagnosis of breast cancer at an advanced stage [3].

4.3. Histopathology of Cancer

The WHO classification of the breast cancers includes over 20 types [33]. This study reports 97.2% of ductular invasive carcinoma, 1, 2% of lobular invasive carcinoma and 1.2% and papillary invasive carcinoma. These findings are the same in Kantelhardt et al in Ethiopian women [30]. For Lakhani et al. [33], ductular invasive carcinoma represents 59%, and papillary invasive carcinoma and Lobular Invasive carcinoma record respectively for 5 and 4%. Many authors agreed that invasive ductular carcinoma is the most breast cancer in African and European women [24, 47]. These observations are well represented in Table 10.

Table 10. *Comparison of histologic type in some studies.*

Authors	Pays	% Ductal invasive carcinoma
Ihemelandu C. U (2007)	USA	79.8%
Kakarala M, 2010	India	69.1%
Kakarala M, 2010	Pakistan	65.7%
Pang J, 2012	Ghana	89%
Lakhani S, 2012 (O. M. S)		59¨%
Ly M, 2012	Mali	94%
Dowson S-J (2013)	-	70-80%
Reyal F (2013)	France	76%
Reyal F (2013)	South-Korea	87%
Kantelhardt EJ, 2014	Ethiopia	79.2%
Our study	DRC	97.2%

All the studies confirm that ductular carcinoma is the prevalent histological type of breast carcinoma anywhere in the world.

4.4. Grade of Tumors

The SBR (scarff bloom and richardson) grade modified by Elston and Ellis represents an important and independent histopronostic for metastatic risk factor and overall survival [46]. The majority of tumors in this study are of grade 3 (54.7%) as in most African series. But in European studies grade 3 tumors are less predominant [10]. Ganiy and Ganiyu [24] reported 15.8% of grade 3 tumors in Finland, and Reyal et al. [48] in France reported about 23% grade 3 tumors. These observations are represented in the following Table.

Table 11. *Comparison of tumor grade in some studies.*

Authors and year	Countries	Grade 3 Tumors
Ikpatt O. F, 2002	Nigeria	46.1%
Leong S. P. L, 2010	India	60%
P. F. Raumbau, 2011	Tanzania	56.4%
Ohene-Yeboah, Adjei E, 2012	Ghana	85.2%
Ly M, 2012	Mali	78%
Pang J, 2012	Ghana	52%
Ganiy, 2012	Finland	15.8%
Adisa C. A, 2012	Nigeria	100%
Reyal F, 2013	France	23%
Kantelhardt EJ, 2014	Ethiopia	57%
Present study	DRC	54.7%

Added to this table, study in the USA, women of African origins had more grade 3 tumors comparatively to white women [7, 39]. For many authors, difference between grade 1 and grade 3 tumors may have different pathogenesis and clinical expression and grade 3 tumors may not represent a long period of evolution of grade 1 tumors [33, 51]. It is also established that cancers in black women are more aggressive than in whites [12, 40, 45, 49, 55, 57] and there may be biologically different features between black and white women [57]. For Van der Groep et al. [54], this difference may be due to the BRCA1 gene mutation although the reason why this mutation is not well known [53].

4.5. The Relationship Between Tumor Necrosis and Grade of Tumor

Tumor necrosis is present in 30.2% in this study. Mohapatra and Satyanarayana [37], in India observed tumor necrotic in 8.9% of cases. In the USA, African women have presented more than necrosis [7, 39]. The presence of tumor necrosis is reported to be predominant in high grade [22, 23]. For Galant C. et al [23], tumor Necrosis is a bad prognosis factor because it shows a rapid growth rate, exceeding angiogenesis stimulated in the tumor. Indeed the mitotic index is among the components of the grade and is evidence of tumor proliferation. Van der Groep et al. [54] reported that BRCA1 tumors have a high frequency of necrotic areas in their study. In this study, tumor necrosis has been highlighted more in the grade 3 than in grade 2 even if the difference was not significant.

4.6. The Score from Nottingham

The Nottingham score takes into account the anatomy and tumor biology. It helps to establish the prognosis and survival times according to the score [23]. The majority of patients in this study (67.8%) have a bad score and an approximation of 50% of survival beyond 5 years according to this score. Bebenek et al. [9] in Poland, found a tumor diameter lower or equal to 5 cm. The Nottingham score showed a decrease from 1984 to 2003 for about 57 to 81%. Study on molecular gene expression by Yu et al. [61] may provide an explanation for the histological grade in breast cancer. Some studies in China [34] confirmed that there may be a decrease in the frequency of stage III tumor only by self-breast-examination and this can rise down the score from 40% in 1970 to 20 percent in 1990.

4.7. The Relationship Between Tumor Grade and the Patient Age

In the present study, there are patients with grade 3 tumors of over 45 years than those of younger age. However, the association was not significant. Several studies showed that young patients with breast cancer has a higher histologic grade [5].

5. Conclusion

Most breast carcinoma in the DRC are of bad prognosis because they are often diagnosed at stage T3 and T4. In many cases, patients are in actively age period. Most breast cancers are of the ductal invasive carcinoma type. To improve the prognosis, one must go through early diagnosis. A better evaluation of the perception of this pathology in our environment is very important because some designs contribute to a delay in breast cancer management. Perspectival, study of breast cancer biology in DRC may be useful for better management.

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