Breast Cancer in Togolese Women: Imaging and Clinicopathological Findings

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ABSTRACT

BACKGROUND: Breast cancer is the most common cancer in women, and its incidence and mortality rates are expected to increase significantly over the next few years, particularly in developing countries. The aim of this study was to describe the epidemiological, clinical, radiological, histopathological, and prognostic aspects of breast cancer in Togo.

MATERIALS AND METHODS: We retrospectively analyzed at our Department of Pathology of Lomé all cases of breast cancer in women confirmed by histology over a period of 20 years (2000-2019).

RESULTS: We collected 804 cases of breast cancer in women. The median age was 46.7 years (range, 12-86 years). Patients aged <40 years represented 48.38% of cases, and the left breast was more affected (51.24%). Most women were sexually active (71.52%) and resided in urban areas (66.29%). Carcinomas represented the predominant histological group (796 cases, 99.00%) with a predominance of invasive nonspecific type carcinoma (92.34%). These cancers were diagnosed at late stage III using Nottingham grading (55.10%). The TNM classification showed a predominance of grades T2NxMx (72.45%) and T4N1Mx (17.76%). The luminal B profile (40.85%) was found mostly, and the mutation of BRCA2 and BRCA1 genes was found in 2.61% of cases. Mastectomy was performed in 7.59%, radiotherapy in 3.61%, and chemotherapy in 18.66%.

CONCLUSION: Breast cancer is a frequent pathology in Togolese women, predominant in young adults, often diagnosed at a late stage with limited possibilities of treatment. The establishment of early care programs is essential.

KEYWORDS: Breast cancer, female, carcinoma, Togo, sub-Saharan Africa

Introduction

Breast cancer is the most frequently diagnosed cancer in women worldwide.[1,2] In 2018, more than 2 million new cases of breast cancer were diagnosed worldwide, representing 11.6% of all cancers.[1] In sub-Saharan Africa, diagnosis of breast cancer is often made at late stages, involving the life-threatening prognosis of patients.[3-6] Overall, in these countries, there are no structured breast cancer screening programs that have significantly reduced the incidence of breast cancer in developed countries.[7,8] The narrowness of the technical platform, in particular the means of exploration, screening, and diagnosis that are often concentrated in the capitals of its countries, complicates the problem of access to cancer care. Female breast cancer is expected to increase in incidence in its sub-Saharan countries, reaching more than 19.3 million women.[2] In addition, despite the immense progress in the treatment, the difficulty in the availability of anticancer molecules and their high costs compromise and darken the prognosis, leading to a high mortality linked to breast cancer in women.[9,10] The main risk factors linked to breast cancer are hormonal factors linked to premenopausal estrogen impregnation and genetic, behavioral, and environmental factors.[11,12] In Togo, a study carried out in 2016 on the epidemiology of cancers showed that breast cancer occupied the first rank.[13] In fact, breast cancer was reported in 21.2% of cancers in women and 10% of all cancers in Togo.[13] Therefore, breast cancer tends to become a major public health concern that requires special attention from the health ministry. The burden of diseases caused by breast cancer is significant. This study was carried out to reinforce the limited data available and to update epidemiological data on breast cancer,

given the absence of a cancer control plan and the absence of a support structure as well as of the national registry. The objective of this study was to examine the epidemiological, clinical, diagnostic, therapeutic, and prognostic aspects of breast cancer in Togolese women.

Materials and Methods

This is a retrospective analysis of all cases of breast cancer in women diagnosed histologically at the Pathological Anatomy and Imaging Laboratory of the Sylvanus Olympio University Hospital in Lomé, from January 1, 2000, to December 31, 2019 (20 years). Togo is a small country of 56 600 km², with an estimated population of 7 200 000, located between Ghana in the west and Benin in the east. The data were collected from the registers of the said laboratory. The data collected concerned sociodemographic data (frequency, age, location, marital status, family history, circumstances of discovery) and anatomopathological data (nature of the sample, histological group, histological type, Nottingham grade, TNM stage, molecular profile, and existence of mutations in the BRCA2 and BRCA1 genes).[14] Imaging data observed during ultrasound and mammography in patients with an imaging record were taken into account. Size, American College of Radiology (ACR) classification, and axillary lymphadenopathy have been studied.[15] We collected clinical, therapeutic, and prognostic data from patient medical records. Histological examination was performed on samples from the gynecological, surgical, and imaging departments. These samples are fixed with 10% formalin, embedded in paraffin, and stained with hematoxylin-eosin-saffron.

The immunohistochemical profile of the tumors was carried out based on anatomobiological results and based on the evaluation of estrogen and progesterone receptors, the overexpression of HER2, and the proliferation index Ki 67. The labeling of these receptors is considered positive when more than 10% of the cells are labeled, the HER2 receptor has a score of 3+, and when more than 14% of the cells are labeled in the proliferation index. According to the different phenotypes obtained, 5 immunohistochemical phenotype subtypes were defined: luminal A (ER+ and/or PR+, HER2− and Ki-67 <14); luminal B (ER+ and/or PR+, HER2− and Ki-67 >14 or ER+ and/or PR+, HER2+); HER2-positive (ER−, PR−, HER2+); triple-negative or basal-like (ER−, PR−, HER2−); and unclassified (the absence of overexpression of 1 of 3 molecules).[16,17]

Results

Sociodemographic data

Table 1 summarizes the epidemiological data. We collected 804 cases of breast cancer in women. The annual frequency was 40.20 cases. The median age was 46.7 (12-86) years. Patients aged less than 40 years represented 48.38% (n = 389), 307 (38.19%) were between the ages of 41 and 60 years, and 108 patients (13.43%) were aged >60 years. Regarding the location, the left breast was affected in 412 cases (51.24%), the

Table 1. Sociodemographic characteristics of women.

	NO. OF CASES	PERCENTAGE (%)
Age, y		
>40	389	48.38
40-60	307	38.19
<60	108	13.43
Minimum	12	
Maximum	86	
Median	40.20	
Occupation	518	
Employer	223	43.05
Housewife	201	38.30
Pupils and students	94	18.15
Economic status		
Poor	202	25.12
Moderate	344	42.79
Good	214	26.62
Excellent	44	5.47
Education level	603	
None	160	19.90
Primary	154	19.15
Secondary	184	22,89
University	105	13.06
Residence		
Urban	533	66.29
Rural	271	33.71
Marital status	714	
Unmarried	456	63.87
Married	208	29.13
Divorced	50	7.00
Parity		
≤1	275	34.20
>1	529	65.80
Menopausal		
No	575	71.52
Yes	229	28.48
Location		
Left breast	412	51.24
Right breast	369	45.90
Both breast	23	2.86

Table 2. Risk factors for women.

	NO. OF CASES	PERCENTAGE (%)
Family history	93	93/804
Breast cancer	69	69/93
Ovarian cancer	13	13/93
Associated breast and ovarian cancers	11	11/93
Oral or injectable contraceptives	88	88/804
Lack of physical activity	86	86/804
Obesity	56	56/804
Alcoholism	44	44/804
Smoking	38	38/804
Exposure to ionizing radiation	21	21/804

right in 369 cases (45.90%), and 23 cases (2.86%) were of bilateral location. The profession was known in 518 (64.43%) patients, of whom 223 (43.05%) were employees, 201 (38.80%) housewives, and 94 (18.15%) pupils and students. The socioeconomic level was low in 202 women and moderate in 344 women (Table 1). The level of education was mentioned in 603 cases. Women with primary (n = 154) and secondary (n = 184) education were the most represented. The rest were university level (105) and uneducated (160). Five hundred thirty-three (66.29%) women resided in towns and 271 (33.71%) in rural areas. Marital status was noted in 714 cases. They were single in 456 cases, married in 208 cases, and divorced in 50 cases. Most women (n = 575; 71.52%) were premenopausal and 529 (65.80) had at least 1 child. The family pathological history was known in 93 women (11.57%). There is a family history of breast cancer in 69 women, ovarian cancer in 13 women, and a combination of ovarian and breast cancer in 11 women. The other risk factors are summarized in Table 2.

Clinical data

The circumstances of discovery were dominated by the discovery of a palpable breast mass in 710 cases (88.31%). The mass was isolated in 547 cases, associated with clinical signs in 130 cases, and lymphadenopathy in 33 cases. The clinical signs observed were an "orange peel" appearance in 92 cases and skin ulceration in 38 cases. The other circumstances of discovery were clinical signs with an orange peel appearance (35 cases), ulcerations (8 cases), a bloody nipple discharge (21 cases), and fortuitously in 30 cases.

Imaging data

Breast imaging reports of only 670 (83.33%) patients were found. Overall, 155 (23.13%) patients performed a breast ultrasound only and 515 patients (76.87%) performed the ultrasound and mammography combination. From imaging examinations, lesions were classified as breast imaging reporting and data system (BI-RADS) 3 (probably benign) in 1.34%, as BI-RADS 4 (probably malignant) in 52.54% and as BI-RADS 5 (highly suspicious of malignity) in 46.12%. There were no BI-RADS 1 and 2.

Histopathological data

The samples received by the laboratory consisted of 209 biopsy fragments and 595 surgical specimens, including 534 nodulectomy pieces and 61 mastectomy specimens including axillary dissection. The nodulectomy pieces had a size varying between 1 and 12 cm, were poorly defined, were of firm consistency, and presented hemorrhagic foci. The mastectomy specimens often presented necrotic and hemorrhagic foci. Most of the dredging pieces had more than 3 lymph nodes (75%). Three histological groups were found: carcinomas (n = 796 cases, 99.00%), sarcomas (n = 6 cases, 0.75%), and lymphomas (n = 2 cases, 0.25%). The 6 sarcomas diagnosed consisted of 3 cases of primary angiosarcoma of the breast (3/6), Kaposi sarcoma (2/6) and fibrosarcoma (1/6). Nonspecific invasive carcinoma represented 92.34% (735 cases) of all carcinomas, followed by lobular carcinoma with 29 cases (3.64%) (Table 3). The other types of carcinoma were ductal-type carcinoma in situ in 22 cases (10%), neuroendocrine carcinoma (5 cases), papillary carcinoma (4 cases), and adenoid cystic carcinoma (1 case). Nonspecific invasive carcinoma was diagnosed in 556 surgical specimens, including 55 mastectomy specimens and 179 biopsy fragments. The Nottingham histopronostic classification of these invasive carcinomas corresponded to grade II in 405 cases (55.10%) and to grade III in 215 cases (29.25%). The TNM classification was made for 490 invasive carcinomas and showed the predominance of the T2NxMx (355 cases, 72.45%) and T4N1Mx (87 cases, 17.76%) grades (Table 3). The 6 cases of mammary sarcoma were diagnosed on nodulectomy specimens. The

Table 3. Histopathological characteristics of women.

	NUMBER OF CASES	PERCENTAGE (%)
Nature of the sample		
Nodulectomy	534	66.42
Biopsy	209	26.00
Mastectomy with axillary dissection	61	7.58
Histological types		
Invasive ductal carcinoma, NOS	735	91.42
Lobular carcinoma	29	3.60
Ductal intraepithelial neoplasia	22	2.74
Neuroendocrine carcinoma	5	0.62
Papillary Carcinoma	4	0.50
Cystic adenoid carcinoma	1	0.13
Angiosarcoma	3	0.37
Kaposi sarcoma	2	0.25
Fibrosarcoma	1	0.12
Lymphoma	2	0.25
Elston and Ellis classification (Nottingham)	620	
Grade I	00	00.00
Grade II	405	65.32
Grade III	215	34.68
TNM classification	490	
T2NxMx	355	72.45
T4N1Mx	87	17.76
T3NxMx	28	5.71
T2N2Mx	20	4.08
Molecular classification	71	
Luminal B	29	40.85
Her2 enriched	18	25.35
Luminal A	14	19.72
Triple-negative	10	14.08
BRCA gene mutations	21	
BRCA2	15	71.43
BRCA1	6	28.57

Abbreviation: NOS, not otherwise specified.

sarcomas were all grade 2 according to the French Federation of Cancer Centers Sarcoma Group (FNCLCC) classification.

Immunohistochemistry was performed in 78 cases of carcinoma, and 71 cases expressed hormone receptors. The molecular classification gives a predominance of the luminal B profile (29 cases, 40.85%) followed by the enriched her2 profile (18 cases, 25.35%). The others were luminal profile A (14 cases, 19.72%) and triple-negative (10 cases, 14.08%). The search for

mutations in the BRCA2 and BRCA1 genes was performed in 21 (2.61%) patients. The search for mutations in the BRCA2 and BRCA1 genes was carried out in 21 women. These were mutations in the BRCA2 gene in 15 cases (10.97%) and in the BRCA1 gene in 6 cases (3.66%). Table 3 summarizes the main histopathological data.

Therapeutic and prognostic data

Sixty-one patients (7.59%) underwent mastectomy with lymph node dissection. Radiotherapy was delivered to 29 patients (3.61%) at a dose of 50 Gy on the wall. Acute radiation therapy toxicity such as radiodermatitis was found in 20% of cases. Sequential chemotherapy was administered as a neoadjuvant in 88 patients (10.95%) and as an adjuvant in 62 patients (7.71%). The main side effects of chemotherapy were nausea and vomiting (79% of cases). Data after a median follow-up of 36 months reported 606 patients were lost to follow-up. For the other patients, the result was characterized by complete remission in 69 patients (8.59%), local relapse in 46 patients (7.12%), metastatic relapse in 38 patients (4.73%), and death in 45 patients (5.60%). The lungs were the main site of metastases in 60.53% of cases (23/38), followed by bone in 31.58% of cases (12/38) and liver in 7.89% (3/38). The 5- and 10-year overall survival was 45.96% and 20.20%, respectively.

Discussion

We collected a total of 804 cases of breast cancer diagnosed, with an average frequency of 40.20 new cases per year. This frequency is comparable to sub-Saharan African series, but remains significantly lower than that of Western studies.[4,18] The underestimation of frequencies in sub-Saharan Africa may be linked to an inefficient and limited health care system with few pathologists and oncologists, ignorance of patients, and lack of effective cancer registries.[12,19] These factors maintain the burden of this disease in African countries where the diagnosis of breast cancer is often made at a late stage.[2,20] Indeed, an increased awareness favors the early diagnosis of the pathology with a better prognosis.[20] In developed countries, the mortality rate of breast cancer follows an inverse trend with an average decrease of –1.3% per year between 1990 and 2018.[3] The average age of women in our series was 46.70 years, similar to the average age (48.13 years) reported in Cameroon.[21] In Europe and the United States, women with breast cancer are older than those in countries in sub-Saharan Africa.[22-24] In addition, 48.38% of women are aged ⩽40 years, which corresponds to the period of genital activity. The increase in the incidence of breast cancer in women under 40 in France has been low and steady for 20 years.[24] We observe in our series a decrease in breast cancer after 50 years, which may be linked, on the one hand, to the fact that certain habits such as breastfeeding are respected and, on the other hand, to the absence or low prevalence of certain risk factors such as hormonal treatments observed in this population.[7,25] Short life expectancy also reduces the onset

of cancer, so information and awareness about breast cancer screening are higher in this proportion of the population.[26,27] All these observations corroborate the hormonal character linked to breast cancer.

The radio-histological correlation in our series shows that more than half of the breast lesions classified as BI-RADS 4 (52.54%) by imaging were cancers on histology. This result is approximately identical to the 52.7% cancer rate found by Zonderland et al in their prospective series where they assessed the diagnostic performance of mammography and ultrasound for breast cancer diagnosis using the BI-RADS final assessment categories by 12-month follow-up and histocytopathology correlation in the Netherlands[12] Our results are superior to those of Guennoun et al[10] in Morocco who had found a proportion of 29% of cancer in lesions classified BI-RADS 4. This difference is precisely the origin of the clarifications made in the fourth editions of the BI-RADS classification of the ACR which specifies subtypes 4a, 4b, and 4c.[8,26]

We observed a predominance of invasive nonspecific carcinoma of 87.5%. Engbang et al and Edmund et al in Cameroon and Ghana, respectively, each found a predominance of invasive ductal carcinoma.[28,29] However, the low rate of carcinomas in situ could be justified by the unavailability of effective screening tools in all health structures. Most invasive carcinomas corresponded to grade III of the Nottingham classification (55.10%). Our results are similar to those of Lin et al.[30] Breast cancer is often diagnosed at a late stage in sub-Saharan countries, explaining the high rates of death from female breast cancer. Luminal molecular subtype B (51.6%) was the most frequent subtype in our study, corroborating with the results found in the literature.[31,32] The proportion of triple-negative in our series is similar to the series in Saharan Africa, varying from 13.3% to 38%.[33,34] The mastectomy with lymph node dissection is most often performed because most tumors are diagnosed at a stage with lymph node invasion. Surgery must necessarily be combined with other treatment methods, including chemotherapy, radiotherapy, and hormone therapy; this is for the control of cancerous disease in general.[33,35] Postoperative radiotherapy improves local control and progression-free survival but has no impact on overall survival.[29,36] Fifteen (18.3%) of our patients received radiotherapy. The molecular stratification of breast cancer has prognostic and therapeutic implications.[28-31] Patients with luminal A submolecular type cancer have a better prognosis and benefit from hormone therapy; those with luminal B submolecular type cancer have a better prognosis for chemotherapy.[36] Triple-negative molecular subtype cancers have a very poor prognosis according to the literature and are most often diagnosed in young women.[24,36] Given the young age of our patients, it is imperative to initiate other prospective studies to determine the risk factors associated with breast cancer to implement strategies to better manage and reduce the burden of this pathology in Togo. Togo has neither a radiotherapy center nor a subsidy policy for chemotherapy or hormone

therapy molecules, making the management of these cancers extremely complicated.

Conclusion

Breast cancer is a major public health concern and affects mainly young Togolese women. It is often diagnosed at advanced stages and poses a real problem of therapeutic management in most sub-Saharan countries. Invasive nonspecific carcinoma is the most diagnosed histological type. In Togo, there is not yet a real structured health policy for breast cancer screening to reduce breast cancer mortality, where resources to implement and maintain population-based screening programs are limited. It is therefore imperative that cancers are included in national health policies, by prioritizing health education for the early diagnosis of breast cancer and thus improving the prognosis. This requires the implementation of a real policy of capacity building for women in health care in Togo.

Author Contributions

T. Darré was responsible for the conception of the study; participated in the study design; undertook the field study; conducted the data collection, analysis, and interpretation; and wrote the manuscript. M.T., T. Djiwa, B.D., A.B., S.A.I., A.K.A., B.N., A.A., P.S., B.K.N., K.A., and A.S.B. were involved in the data collection, analysis, and interpretation. They wrote and finalized the manuscript. G.N.K. is responsible for the overall scientific management of the study, for analysis and interpretation, and for the preparation of the final manuscript. All authors have read and approved the final manuscript for submission for publication.

Availability of Data and Materials

Extracted data are with the authors and available for sharing on request.

Ethics Approval and Consent to Participate

This study received approval from the head of the laboratory department where the study was to be conducted. As it related to counting records, patient consent was not required. However, during the counting and data collection, patient names were not collected to preserve confidentiality. This study was approved by the "Comité de Bioéthique pour la Recherche en Santé (CBRS)" (Bioethics Committee for Health Research) from the Togo Ministry of Health, Ref No. 0101/2016/MS/CAB/DGS/DPLET/CBRS). The study has been carried out in accordance with relevant guidelines and regulations.

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