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Epidemiological, Diagnostic, Therapeutic and Evolutionary Profile of Inflammatory Breast Cancer (IBC) in the Oncology-Hematology Service, Burkina Faso

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Abstract: *Introduction*: Inflammatory breast cancer (IBC) represents a particular clinical entity characterized by its rarity, rapid evolutionary pace and pejorative prognosis. This was a retrospective descriptive study from January 01, 2020 to June 30, 2022 in the clinical oncology-hematology service of CHU B. This study included 62 patients with inflammatory breast cancer. The diagnosis of IBC was clinical as defined by the American Joint Cancer Committee (AJCC) with a diagnosis of anatomopathological confirmation. IBC accounted for 37.57% of breast cancers reported during our study period. The average age of patients was 47 years. The age range of [40 years-50] represented 37.09% followed by those of [50 years-60 years] and [60 years-70] with each 19.35%. The average consultation time was 12 months. Signs of inflammation were found in all patients followed by the presence of nodules during clinical examination. Infiltrating ductal carcinoma accounted for 95% of cases followed by infiltrating lobular carcinoma in 3%. Modified Scarff Bloom Richardson grade II (mSBR) was encountered in 93.5% of cases followed by mSBR grade III with 6.5%. Only 11 patients (17.74%) were able to perform immunohistochemistry. Thus, the results found 43% and 23% respectively of type luminal A and luminal B and 23% classified type Triple negative. Chemotherapy was performed in 51 patients (82.25%) and was palliative in 32 patients (62.74%). Ten (10) patients underwent surgery including 9 mastectomies with axillary dissection (90%). Radiotherapy was performed in 02 patients (3.22%). Median survival was 05 months and overall survival at 12 months was 23%. Finally, IBC is a fairly common pathology according to this study and affects especially young women under 50 years. Its management is complex by the fact that specific examinations and anti-cancer are difficult to access.

Keyword: Inflammatory Breast Cancer, Profile, Burkina Faso

1. Introduction

Breast cancer is the most common cancer in women in the world, and Africa is no exception, where it is the first cancer with an incidence [1].

In addition, there are features of breast cancer including

inflammatory breast cancer (IBC) whose definition by the American Joint Committee of Cancer (AJCC), is described as a clinicopathological entity characterized by diffuse erythema associated with edema, often without underlying palpable mass [2, 3]. It represents the most aggressive entity, most often diagnosed at an advanced stage with rapid evolution, which makes it very poor prognosis [4, 5]. Inflammatory breast cancer (IBC) is divided into two entities which are primary inflammatory breast cancer and secondary inflammatory breast cancer. These two clinical entities are individualized within breast cancers by epidemiology, pathogenesis, diagnostic criteria and a specific prognosis [2, 6]. However, the presence of inflammatory signs is not necessarily related to tumor infiltration by inflammatory cells, and the inflammatory phenotype is mainly due to blockage of the lymphatic vessels of the dermis by tumor emboli [5]. According to several studies, IBCs produce low amounts of most inflammation cytokines such as IFN alpha, IL-1 and IL-2, however, some gene expression studies have shown the activation of "inflammation pathways". Significant angiogenesis has been demonstrated in IBC: an increase in intratumoral density in microvessels, or percentage of endothelial cells and, in several studies, high levels of angiogenic factors (VEGF, VEGFR1, VEGF2, Ang-1, Ang-2, etc.) [5]. There is also in the IBC a lymphangiogenesis that contributes to tumor dissemination and can be highlighted "morphologically" and by high levels of lymphangiogenic factors: VEGF-C VEGF-D, FCF2 etc. [6, 7].

Primary inflammatory breast cancer is relatively rare with an incidence of 1 -5% of all breast cancers but aggressive, marked by a rapid pejorative course [3, 5]. In the United States, in 2017 a study found an incidence of 1.25% with a particle distribution in the American black population [8]. In 2015 in France, a study found an incidence of 1.88%, just as the ROGE study found a similar incidence for 369 patients with IBC [9].

Inflammatory breast cancer is characterized by a particular geographic distribution. In the North African region, the incidence was 5-7% [10]. Several studies conducted in North Africa found 8% incidence in Morocco [2], in Tunisia in 2018 an incidence that varied between 5-7% [3] and in Algeria an incidence of 9.4% [11].

On the other hand, sub-Saharan Africa seems to have high prevalence of inflammatory breast cancer because the black population has a greater susceptibility. In Congo in 2013, a study found an incidence of 37.6% [12], in Côte d'Ivoire in 2013, 54% [13] and in 2018, a frequency of 17.9% [14]. These frequencies were quite high compared to North Africa [10].

Inflammatory breast cancer remains little explored in Burkina Faso, a study conducted on inflammatory breast cancer in the city of Ouagadougou in 2012 revealed a prevalence of 6.7% with an average age of 46.31 years at diagnosis [15].

Since 2018 with the creation of the University Hospital of Bogodogo (CHU-B), it was set up the first clinical hematology oncology service in all of Burkina Faso. The latter quickly became the reference service in oncology. The aim of this study was to study the epidemiological, diagnostic and therapeutic profiles of inflammatory breast cancer in the clinical hematology oncology department of the CHU-B.

2. Methods

2.1. Type, Period and Setting of Study

This was a retrospective descriptive study conducted from 01 January 2020 to 30 June 2022, in the clinical hematology oncology department of the Bogodogo University Hospital (CHU-B) in Ouagadougou, Burkina Faso.

2.2. Study Population and Sampling

This was an exhaustive sample that included all patients with inflammatory breast cancer with confirmed anatomopathological diagnosis in medical oncology and/or hospitalized in the clinical hematological oncology service. However, patients whose clinical record is incomplete is less than 70%.

2.3. Data Collection and Data Sources

Data were collected from patient clinical records and consultation records. A data sheet was used to collect socio-demographic data such as age, sex, occupation and place of residence; risk factors including nulliparity, late menopause, personal history of breast cancer, family history of breast cancer, hormone replacement therapy; interrogation and physical examination data: pain, heat, redness, swelling, orange peel appearance, nipple retraction, nodules, ulceration; paraclinical data: hemogram, blood ionogram, renal function, liver function, markers of breast cancer, anatomopathological examination, thoraco-abdominopelvic scan; and data on medical treatment.

2.4. Data Entry and Analysis

Microsoft Word office software in its 2010 version was used for text entry.

Data was captured and analyzed using Epi info software version 7.2.2.6. The survival curve was plotted according to the Kaplan Meier model.

2.5. Ethical Considerations

The information was collected in accordance with confidentiality and medical confidentiality. They were used only for scientific purposes.

3. Results

3.1. Socio-Epidemiological Data and Risk Factors

The study enrolled 165 breast cancer patients between 2020 and 2022 in the clinical hematology oncology

department of the CHU-B, 62 of whom had a IBC or 37.57% of all breast cancer patients. The average age of our patients was 47 years +/- 12 with extremes of 23 years and 79 years. The most affected age group was 40 to 50 (37%). The patients were mostly (64.5%) unemployed women, followed by women traders (6.5%). Fifty-two patients or 83.87% resided in urban areas and ten patients or 16.13% in rural areas.

More than the majority (90.3%) of patients were multiparous and had breastfed (Table 1).

Table 1. *Distribution of patients by risk factors.*

Risk Factors	Effective (n=62)	Percentage (%)
Parity	56	90,3
Breastfeeding	56	90,3
Late menopause	28	45,2
Nulliparity	6	6,5
History of breast cancer in the family	4	9,7
Alcohol	3	4,8
Oestroprogestative contraception	3	4,8
Personal history of breast cancer	2	3,2
Chewing tobacco	2	3,2

3.2. Reasons and Time for Consultation

The most common reasons for consultation were nodules in all patients (100%) associated with pain (100%), heat (100%) and redness (100%) in the affected breast (Table 2).

Unfortunately, the average consultation time was 12 months +/- 15.17 with extremes ranging from 01 months to 72 months.

Table 2. *Distribution of patients by reason of consultation.*

Reasons for consultation	Effective	Percentage (%)
Nodules	62	100
Ulceration	7	11,3
Orange peel skin	5	8
Serohematic breast discharge	2	3,2
Breast retraction	1	1,6
Left axillary adenopathy	1	1,6

3.3. Physical Signs and Paraclinical Examinations

Physical examination showed that the right breast was the most affected 56.5% and that all patients (100%) had skin inflammation. In addition other signs such as orange skin appearance (85%), lymphadenopathy (82.1%), nodules (67.7%), ulcerative necrotic lesion (19.3%), nipple retraction (8%), hepatomegaly and cholestasis syndrome (4.8% each), a mastectomy scar and serobloody breast discharge (3.2% each), splenomegaly and lymphedema of the left arm (3.2% each) were observed in all patients.

As for paraclinical examinations, all patients (100%) performed a thoraco-abdomino-pelvic CT, against 3.2% (2 patients) having benefited from bone scan and Cerebral CT, finally one (01) patient benefited from Hepatic MRI (1.6%). As for the biological assessment 82.3% were able to carry out the blood count, blood ionogram and liver transaminase against 17.7% and 11.9% who carried out respectively the markers CA15-3 and ACE.

3.4. Histology, Immunohistochimistry, Modified Scraff-Bloom and Richardson Grade (mSBR)

All patients (100%) were able to perform a confirmatory anatomopathological examination. Anatomopathological examination of the breast biopsy parts found invasive carcinoma of non-specific type of breast in 95% followed by invasive lobular carcinoma in 3%. The most recovered SBR grade was that of grade II with 93.5% followed by grade III with 6,5%. Immunohistochemistry was performed by 17.7% (11 patients) of which 7 patients had positive receptors (ER+PR) and 3 patients were triple negative and 1 was HER2 positive (Table 3).

Table 3. *The distribution of patients according to immunohistochemistry.*

Molecular type	Effective	Percentage (%)
Luminal type A	4	43
Luminal type B	3	23
Triple negative	3	23
HER-2+	1	11
Total	11	100

3.5. Secondary Location

In this study, metastases were found in 37 of our patients (59.6%). The most represented metastatic sites were lungs (27%), liver (21%) and bones (24%), pleura (10%), contralateral breast (7%), brain (5%), mediastinum (4%) and heart (2%).

3.6. Therapeutic Aspects, Evolutions, Duration of Follow-up and Latest News

Chemotherapy was performed in 51 patients or 82.3%. Chemotherapy was palliative in 32 patients (51.6%) and curative in 19 patients (30.7%).

The average cure was 5 +/- 2 with extremes ranging from 1 cure to 12 cures. Docetaxel monotherapy (100 mg/m², 21-day cycle) was the most commonly used (50.98%); followed by AC60 (doxorubicin 60 mg/m² and cyclophosphamide 600 mg/m², 21-day cycle) (47.06%).

The FAC60 protocols (5-fluorouracil 600 mg/m²; doxorubicin 60 mg/m², cyclophosphamide 600 mg/m², 21-day cycle), and AC60-Zometa (4 mg zoledronic acid was administered every 28 days) represented 23.53% and 19.60% respectively. The carboplatin-paclitaxel protocols (carboplatin AUC 6, paclitaxel 175 mg/m², 21-day cycle); FEC100 (5-fluorouracil 500 mg/m², epirubicin 100 mg/m², cyclophosphamide 500 mg/m², 21-day cycle), and compressed endoxan 50 mg/m² (21-day cycle) each represented 5.88%. Capecitabine protocol (2000 mg/m² for two weeks, 21-day cycle) represented 33.92%. Weekly AC60-Taxol protocols (weekly paclitaxel was administered at 80 mg/m²), FAC50 (5-fluorouracil 500 mg/m², doxorubicin 50 mg/m², cyclophosphamide 500 mg/m², 21-day cycle) and EC75 (epirubicin 75 mg/m², cyclophosphamide 600mg/m², 21-day cycle) each accounted for 1.96%.

Surgery was performed in 10 patients. There were 9 (90%) who underwent mastectomies associated with axillary

dissection. Clean mastectomy was performed in one patient (10%).

A total of 11 patients underwent immunohistochemistry, including 05 patients (45.45%) who received hormone therapy whose molecules were dependent on the age and menopausal status of Goseline 3.6 mg, Tamoxifen 20 mg tablet or Letrozole 2.5 mg. None of the patients performed targeted therapy. Adjuvant radiotherapy was performed by 02 patients (3.22%).

The average duration of follow-up of patients was 06 months +/- 6.07 with extremes ranging from 1 month and 31 months. Over the period of our study 73% of patients had died. Median survival was 5 months, overall survival at 12 months was 23% (Figure 1).

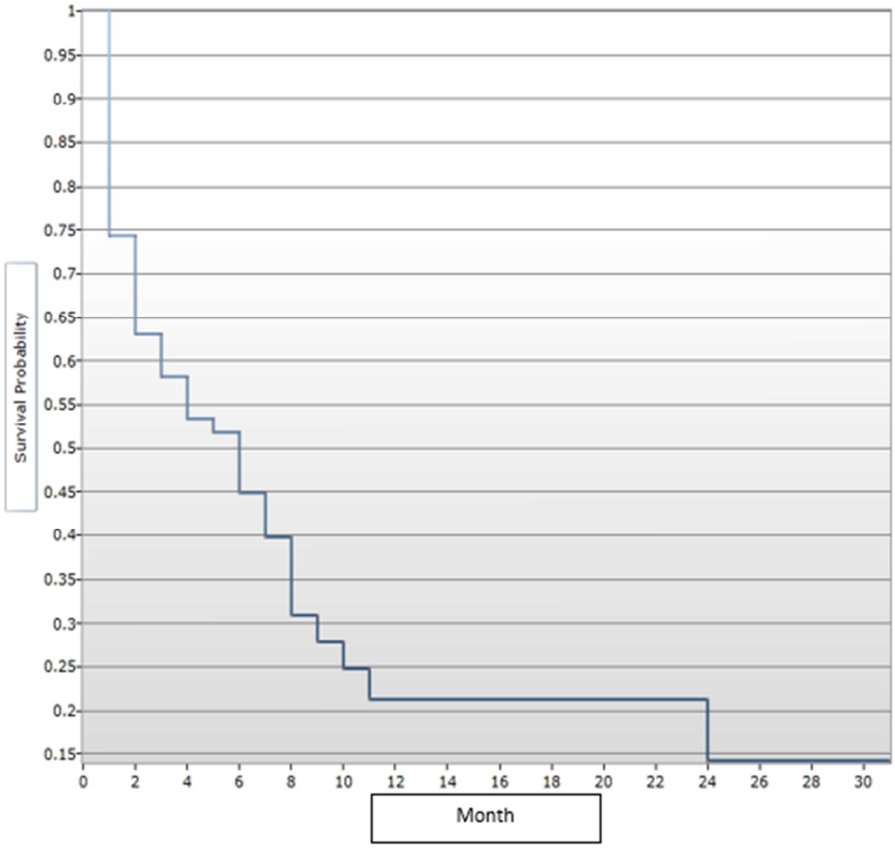

Figure 1. *Patient survival curve representation (n=62).*

4. Discussion

4.1. Limits and Constraints

The limitations and constraints of our study were related to its retrospective nature. Some data from our collection sheet has not been entered for some patients. This is due to the fact that some practitioners have not provided certain information in the medical records of patients. Despite this, we were able to obtain results that we compared with data from the literature and conduct the following discussion.

4.2. Socio-Epidemiological Data and Risk Factors

Inflammatory breast cancer (IBC) accounted for 37.57% of breast cancers in our study. These results are significantly higher than those of a previous study in Burkina Faso that reported 6.7% [15], those of another study in Morocco that found 4.05% [2] and the study conducted in Côte d'Ivoire that found 17.9% [14]. In France, one study estimated the prevalence of IBC at 2.17% [16, 17], well below that of our study. This would be explained by the fact that IBC has a higher frequency in black subjects than in others.

The average age of patients in our study was 47 years, which is similar to those found in Côte d'Ivoire [14] and Morocco [18] who reported 46.5 and 47 years respectively. In the United States of America, a study reported the average age of patients of 57.3 years [19], which is higher than the average age of our patients.

In our study, patients had a low socio-economic level (unemployed 64.5%). This was found in previous studies (57.8%) in Burkina Faso [15], as well as the one (52.3%) conducted in Côte d'Ivoire [14]. This would be explained by the fact that the employability rate of women in Burkina Faso according to the World Bank in 2018 was 35%. Most patients (83.87%) in the study were from an urban area, as was a previous study that reported 53.3% [15]. This may be justified for urban patients who have easy access to health services.

This study allowed us to note that 90.3% of patients were multiparous as in the previous study conducted in Burkina Faso with 62.1% [15]. In Morocco, the results were also similar, with 69.59% of IBC patients being multiparous [18].

Multiparity and breastfeeding would not be a protective factor for breast cancer.

4.3. Reasons for Consultation and Consultation Period

During our study, all of our patients showed signs of inflammation and nodules. The study in Morocco found 93% of patients with inflammatory signs and 61% of nodules [2]. This is in line with the AJCC definition of IBC. During our study, the average consultation time was 12 months. In Morocco, the average consultation period was 9 months [20] compared to 10 months in Côte d'Ivoire [14]. These long consultation periods are explained by the lack of financial means, socio-cultural habits (traditional treatment), the lack of oncology centers and the insufficiency of therapeutic management.

4.4. Physical Signs and Paraclinical Examinations

In this study, both breasts were affected whose right breast (56.5%) as in Côte d'Ivoire the right breast was found in 52.3% [14]. This could mean that there is no preferential site for the IBC.

On clinical examination, inflammatory signs such as increased breast size (100%), the presence of orange skin appearance (100%) and heat (100%) are most common, as in the study in Morocco [4].

Tests such as CA15-3 assays, ACE assays, immunohistochemistry were performed very little by patients. This is due to the high cost of these examinations, the reduced number of health facilities that carry them out and also their unavailability.

4.5. Histological Aspects and Grade mSBR

The most common histological type in the study was non-invasive breast-specific infiltrating carcinoma (95%) This was the same finding (71.4%) in the previous study in Burkina Faso [15] and in the study conducted (93.23%) in Morocco [2] and Côte d'Ivoire (81.8%) [14]. This means that the fact that non-specific breast type infiltrating carcinoma is the most common histological type found in IBC.

Grade II of MSBR (92.3%) was the most found in our study, which was also found in Morocco in nearly 53.65% [2], and also another study found grade II as dominant in its study with 63.7% [20]. SBR is a major histoprognostic indicator correlated with tumor aggressiveness, metastatic potential and survival.

Since the 2000, authors [21] had proposed a molecular classification based on the genomic profile of breast cancers. This classification has improved the understanding of the disease, and defined distinct prognostic breast cancer groups that can benefit from more individualized treatment. Pathology is the cornerstone of therapeutic decision-making. Only 11 patients realized it, among them: 4 were of luminal subtype A, 3 of luminal subtype B, 3 others were triple negative and 1 had HER-2 +. In the literature the CSI are of triple negative type against 03 in this study. This could be explained by the fact that very few patients in the study performed IHC because of its accessibility.

4.6. Secondary Location

The preferred sites of IBC metastasis are similar to those of breast cancer: bones, lungs and liver. In this study it was also the sites of metastases most encountered. This could be explained by the fact that breast cancer is an osteophilic and lymphophilic cancer [5].

4.7. Therapeutic and Evolutionary Aspects and Lifespan

The treatment of IBC is multimodal in our study we noticed that the most followed treatment regimen by patients was first chemotherapy followed by locoregional treatment and then according to the immunohistochemistry of hormonal therapy, (associated or not with chemotherapy) as in the study conducted in Morocco [2] and in France [17], which also followed the same treatment regimen, during the international consensus on the management of IBC in Texas-United States this same treatment regimen was adopted [22]. Chemotherapy was not performed by all our patients because of the excessive prices of anticancers. Surgery was performed in 90% of the patients in our study, in Cameroon by Binyom et *al*., 2020 [23], reported 95% of their patients. In the study in France [16], it was also the most performed surgery in 92.85% of patients. In conditions of late diagnosis with advanced stage, the use of mastectomy according to Patey with axillary curage remains the technique of choice if surgery was indicated. Surgery improves local control of the disease.

It was performed by only 02 patients. External beam radiation therapy after Patey is a standard of treatment. Hormone therapy was induced in 05 patients (45.45%) in the study who had positive hormone receptors. This low proportion of patients who were indicated for hormone therapy in the study may be due to the high cost of immunohistochemistry and the lack of universal health coverage in Burkina Faso. HER-2 was overexpressed in 1 patient. She could not benefit from a specific treatment with trastuzumab because of the high cost of this molecule. The overall survival at 12 months of the patients in our study was 23% against more than 80% in France [16], this would be explained by the fact that in our study 59% patients were metastatic. The prognosis of IBC remains poor despite the use of multimodal treatment.

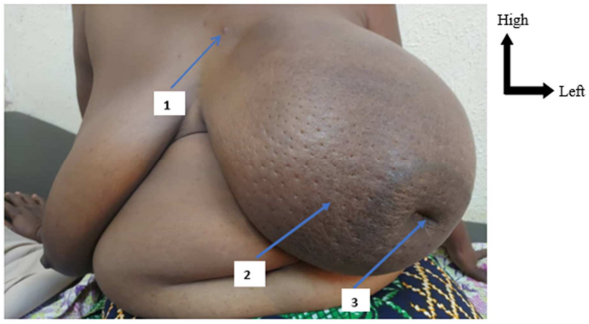

Figure 2. *Image of a woman with inflammatory breast cancer in the right breast showing a permeation nodule in the upper-inner quadrant (1), orange skin appearance (2), and nipple retraction (3).*

5. Conclusion

Breast cancer is one of the first reasons for consultation in the clinical oncology-hematology department of CHU-B. This study revealed that IBC is relatively common. It mainly affects young women under 50, usually metastatic when diagnosed. The diagnosis of IBC is late in most cases, some examinations of the diagnostic, extension and pre-therapeutic assessment are often inaccessible with long delay. The management of IBC is made difficult with the high cost of anticancers. The prognosis of IBC is poor due to its high metastatic potential. Hence the interest of defining a screening strategy to increase awareness and early detection.

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Conflicts of Interest

The authors declare no conflicts of interest.

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