

Epidemiological, Clinical, Paraclinical and Therapeutic Characteristics of Pregnancy-Associated Breast Cancer: Experience of the Medical Oncology Department of Hassan II University Hospital, Fez

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Abstract

Introduction: Breast cancer represents a major public health problem and is the most common cancer among women worldwide. Its occurrence during pregnancy is rare and is defined as breast cancer diagnosed during gestation or within one year postpartum. Pregnancy-associated breast cancer (PABC) is often described as more aggressive, mainly due to delayed diagnosis compared to breast cancer occurring outside pregnancy. The coexistence of these two clinical conditions poses significant diagnostic, therapeutic, and prognostic challenges. The aim of this study was to describe the epidemiological, clinical, paraclinical, and therapeutic characteristics of breast cancer diagnosed during pregnancy in patients managed at Hassan II University Hospital in Fez. **Methods:** This was a retrospective descriptive study including pregnant patients diagnosed with breast cancer and treated at the Medical Oncology Department of Hassan II University Hospital, Fez, between January 1, 2021, and December 31, 2024. Epidemiological, clinical, radiological, histopathological, and therapeutic data were collected and analyzed descriptively. **Results:** Twelve patients were included, representing 3.1% of all breast cancer cases. The mean age was 35 years, and 57% of patients were multiparous. Breast cancer was diagnosed during pregnancy in all cases, with a mean gestational age of 20 weeks. The main presenting symptom was self-detection of a breast lump (70%), with a

mean consultation delay of 4 months. The mean tumor size was 30 mm. Local inflammatory signs were observed in 50% of cases, and suspicious axillary lymphadenopathy in 33%. Metastatic disease at diagnosis was present in 16.7% of cases, mainly involving bone metastases. Invasive carcinoma of no special type accounted for 95% of cases, with SBR grade II - III tumors in 85%. Hormone receptors were negative in 50% of patients, HER2 overexpression was observed in 25%, and the triple-negative subtype in 16.7%. All patients received chemotherapy, and surgery was performed in 83% of cases. Disease evolution was marked by recurrence in 50% of patients. **Conclusion:** Pregnancy-associated breast cancer remains a complex clinical entity, often characterized by delayed diagnosis and aggressive histopathological features. Through this monocentric series, one of the few reported in our setting, our study highlights the epidemiological, clinical, paraclinical, and therapeutic characteristics of PABC within a Moroccan university hospital. It emphasizes the importance of early, guideline-based multidisciplinary management to allow appropriate oncological treatment during pregnancy and underlines the need to strengthen awareness and early diagnosis in order to improve maternal outcomes.

Keywords

Breast Cancer, Pregnancy, Pregnancy-Associated Breast Cancer, Chemotherapy, Multidisciplinary Management, Gestational Cancer, Hormone Receptor Status, HER2-Positive, Oncologic Outcomes, Maternal-Fetal Health

1. Introduction

Breast cancer is the most common malignant tumor among women worldwide and represents a major public health issue due to its high prevalence and significant impact on female mortality. When breast cancer occurs during pregnancy or within one year after delivery, it is defined as pregnancy-associated breast cancer (PABC) [1]. This clinical entity remains rare, with an estimated incidence ranging from 1 in 3000 to 1 in 10,000 pregnancies, but its frequency is increasing as a result of delayed childbearing and the rising incidence of breast cancer among young women [2] [3]. The diagnosis of PABC is often delayed, mainly due to the physiological changes of the breast during pregnancy and lactation, which may mask typical clinical and radiological signs. This diagnostic delay frequently leads to presentation at a more advanced stage and is associated with more aggressive histopathological features [4] [5]. In addition, pregnancy-related constraints require specific diagnostic and therapeutic adaptations, particularly by limiting certain investigations or treatments that may pose teratogenic risks [6]. The management of PABC represents a major clinical challenge and requires a multidisciplinary approach involving obstetricians, medical oncologists, surgeons, and radiologists, with the aim of optimizing maternal prognosis while minimizing fetal risks

[1] [6]. Despite these complexities, appropriately adapted therapeutic strategies—including surgery and chemotherapy administered at suitable stages of pregnancy—have demonstrated that effective oncological treatment can be achieved without significantly compromising maternal or fetal outcomes [1] [6]. In this context, the present retrospective study aims to describe the epidemiological, clinical, paraclinical, and therapeutic characteristics of pregnancy-associated breast cancer at Hassan II University Hospital in Fez, providing original data from an African setting where published evidence remains limited but essential for improving both local and international management strategies.

2. Materials and Methods

2.1. Study Design and Period

This was a retrospective descriptive study conducted over a four-year period, from January 1, 2021, to December 31, 2024, at the Department of Medical Oncology, Hassan II University Hospital, Fez, Morocco.

2.2. Study Population

All patients diagnosed with breast cancer during pregnancy or within one year postpartum and managed at Hassan II University Hospital between January 2021 and December 2024 were eligible for inclusion. Breast cancer cases diagnosed during the postpartum period were systematically searched in the department records. No cases diagnosed within one year after delivery were identified during the study period, explaining their absence from the final series.

2.3. Inclusion Criteria

- Confirmed pregnancy at the time of breast cancer diagnosis.
- Histologically confirmed diagnosis of breast cancer.
- Availability of a complete medical record.

2.4. Exclusion Criteria

- Patients diagnosed with breast cancer prior to pregnancy.
- Incomplete or non-exploitable medical records.

2.5. Data Collection

Data were extracted from hospital medical records and included:

- Epidemiological data: age, parity, family history of cancer, gestational age at diagnosis.
- Clinical data: presenting symptoms, consultation delay, tumor size, presence of inflammatory signs or lymphadenopathy.
- Paraclinical data: breast imaging, staging investigations, histopathological profile, hormone receptor status, HER2 status, and molecular subtype.
- Therapeutic data: surgery, chemotherapy, radiotherapy.
- Outcome and follow-up: recurrence and survival.

2.6. Statistical Analysis

Data were entered and analyzed using SPSS software version 26. Quantitative variables were expressed as mean \pm standard deviation or median, depending on data distribution. Qualitative variables were presented as frequencies and percentages. Due to the limited sample size, no comparative or multivariate analyses were performed.

2.7. Ethical Considerations

The study was approved by the Ethics Committee of Hassan II University Hospital, Fez. All patients were managed in accordance with the principles of the Declaration of Helsinki, with strict respect for data confidentiality.

3. Results

3.1. Epidemiological and Clinical Characteristics

The twelve included patients accounted for 3.1% of the 387 breast cancer patients managed in the department during the study period. The mean age was 35 years, and 57% of the patients were multiparous. Breast cancer was diagnosed during pregnancy in all cases (100%), with a mean gestational age of 20 weeks of amenorrhea.

The main mode of presentation was self-detection of a breast lump, reported in 70% of patients, with a mean consultation delay of 4 months (Table 1).

Table 1. Epidemiological and clinical characteristics of the patients (n = 12).

Variables	Values
Number of patients	12
Mean age (years)	35 \pm 3.8
Multiparous	57%
Diagnosis during pregnancy	100%
Mean gestational age at diagnosis (weeks)	20
Mode of presentation: self-detected breast lump	70%
Mean delay before consultation (months)	4 \pm 1.2

3.2. Tumor Characteristics and Histopathological Profile

Bilateral breast involvement was observed in two cases. The mean tumor size was 30 mm. Local inflammatory signs were present in 50% of patients, and suspicious axillary lymphadenopathy was identified in 33% of cases. Metastatic disease at diagnosis was found in 16.7% of patients, predominantly involving bone metastases. Regarding the histopathological profile, invasive carcinoma of no special type (NST) accounted for 95% of cases, with SBR grade II - III tumors observed in 85%. Hormone receptors (ER/PR) were negative in 50% of patients, HER2 overexpression was detected in 25%, and the triple-negative subtype was identified in 16.7%

of cases (**Table 2**).

Table 2. Tumor characteristics and histopathological features.

Variables	Values
Mean tumor size (mm)	30 ± 10
Inflammatory signs	6 (50%)
Suspicious axillary lymph nodes	4 (33%)
Metastatic disease at diagnosis	2 (16.7%)
Invasive carcinoma, no special type (NST)	11 (95%)
Histological grade (SBR II - III)	10 (85%)
Hormone receptor-negative tumors	6 (50%)
HER2-positive tumors	3 (25%)
Triple-negative breast cancer	2 (16.7%)

Regarding the diagnostic work-up, breast ultrasound was performed in all patients and represented the first-line imaging modality. Mammography with abdominal shielding was performed in selected cases when clinically indicated. Histological confirmation was obtained by core needle biopsy in all cases. Biopsy was performed at the time of clinical suspicion, regardless of gestational age, allowing diagnosis during pregnancy, with most cases identified during the second trimester. The physiological breast changes associated with pregnancy, combined with delayed consultation, contributed to the diagnostic delay observed in our series.

Based on the TNM classification, most tumors corresponded to locally advanced disease, with a predominance of T2 lesions and frequent clinical axillary lymph node involvement. Bilateral breast involvement was uncommon. Metastatic disease at diagnosis was limited but present, mainly involving bone metastases.

The initial staging work-up was adapted to pregnancy to minimize fetal exposure to ionizing radiation and relied on clinical examination, breast and axillary ultrasound, chest radiography with abdominal shielding, and liver ultrasound. Abdominopelvic ultrasound was performed as part of routine obstetric follow-up. High-radiation imaging modalities, such as computed tomography and bone scintigraphy, were avoided during pregnancy and deferred to the postpartum period when required. Overall, most non-metastatic patients were diagnosed at advanced clinical stages, predominantly stage II or III.

3.3. Therapeutic Management

All patients received multidisciplinary management, involving medical oncologists, surgeons, and obstetricians, in order to reconcile oncological treatment with pregnancy monitoring.

- Operability assessment: Tumors were deemed operable in 10 out of 12 cases.
- Breast surgery: Performed in 83% of patients (10/12), including 6 mastectomies and 4 lumpectomies, chosen according to tumor size, location, and gestational age, in close coordination with the obstetrician. Axillary dissection was performed depending on nodal involvement.
- Chemotherapy: All patients received chemotherapy:
 - Neoadjuvant: 6 cases (50%)
 - Adjuvant: 4 cases (33.3%)
 - Palliative: 2 cases (16.7%)

Chemotherapy regimens were primarily anthracycline-based, consisting of doxorubicin or epirubicin combined with cyclophosphamide (AC or EC protocols), administered every three weeks. In patients requiring sequential therapy, taxanes (mainly paclitaxel) were introduced after completion of anthracyclines when gestational age allowed. Systemic treatment was initiated after the first trimester in all cases, predominantly during the second trimester, in accordance with international recommendations to minimize teratogenic risk. No major treatment delays or significant dose reductions were reported during pregnancy. No severe maternal toxicity was observed, and no treatment discontinuation was required. Fetal monitoring was conducted regularly through coordinated obstetric follow-up, with no immediate complications attributable to in utero exposure to chemotherapy. In the postpartum period, treatment was completed or intensified according to tumor subtype. Patients with HER2-positive tumors received anti-HER2 therapy (trastuzumab) after delivery. Endocrine therapy was initiated postpartum in hormone receptor-positive patients, mainly with tamoxifen, following completion of chemotherapy and radiotherapy when indicated.

- Radiotherapy: No patient received radiotherapy during pregnancy.
- Obstetric follow-up and coordination: Regular ultrasound monitoring, assessment of fetal well-being, and adjustment of treatments according to maternal tolerance. Therapeutic decisions were discussed in multidisciplinary tumor board meetings.
- Additional measures: Psychological support, counseling on delayed breastfeeding, and postpartum planning of complementary treatments (radiotherapy or hormonal therapy when indicated).

3.4. Obstetrical and Neonatal Outcomes

Obstetrical outcomes were favorable in the majority of cases. The mean gestational age at delivery was 37 weeks, with most deliveries occurring at or beyond 37 weeks of gestation. Vaginal delivery was achieved in the majority of patients, while cesarean section was performed for obstetrical indications. Birth weights were appropriate for gestational age. Apgar scores at 5 minutes were satisfactory in all newborns. Two neonates (16.7%) required short-term admission to the neonatal intensive care unit due to prematurity. No congenital malformations or major growth restrictions were reported.

All patients who received chemotherapy during pregnancy were treated after the first trimester, predominantly during the second and third trimesters. No immediate neonatal complications were directly attributable to in utero exposure to chemotherapy.

3.5. Oncological Outcomes and Survival

The mean follow-up duration was 18 months. During follow-up, disease recurrence was observed in six patients (50%). Recurrences were categorized as locoregional when involving the ipsilateral breast or regional lymph nodes (10%), contralateral breast recurrence (20%), and distant metastasis (20%). Distant relapse represented a significant proportion of recurrence events (Figure 1).

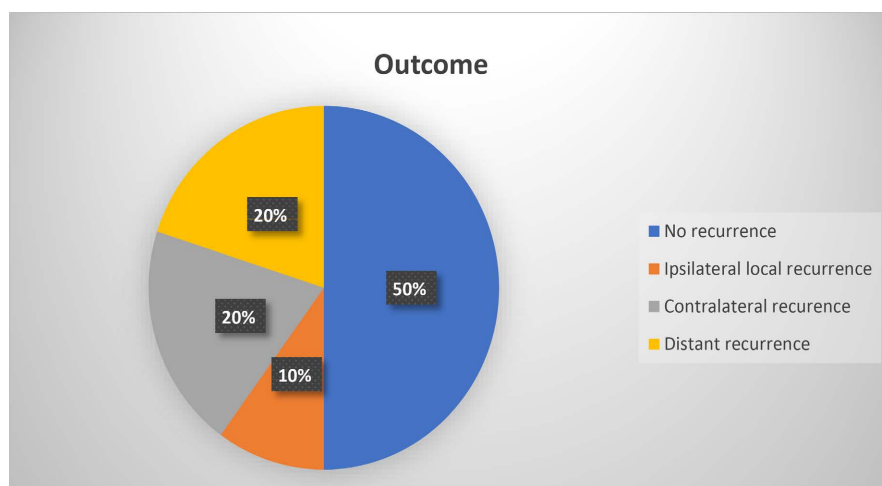


Figure 1. Disease course of patients with pregnancy-associated breast cancer.

Disease-free survival (DFS) was defined as the time from initial diagnosis to the first documented recurrence (locoregional, contralateral, or distant) or last follow-up. Overall survival (OS) was defined as the time from diagnosis to death from any cause or last follow-up. At the time of analysis, the estimated disease-free survival rate was 50%, while the overall survival rate was 83.3%, with two deaths occurring in patients presenting with advanced-stage disease at diagnosis.

4. Discussion

Pregnancy-associated breast cancer (PABC) remains a rare and complex clinical entity, representing 3.1% of breast cancer cases diagnosed in our series, which is consistent with published epidemiological data, estimating its frequency between 0.2% and 3.8% of breast cancers in young women [1] [2]. This rarity can be explained partly by the low proportion of pregnant women affected by cancer and partly by the physiological changes of pregnancy, which complicate clinical examination and radiology, often causing diagnostic delays [3] [4].

The mean age at diagnosis of 35 years in our series is comparable to that reported in other studies, where the mean age typically falls within the third and

fourth decades of life [1] [5]. This concordance confirms that PABC predominantly affects women of childbearing age.

The diagnostic delay, illustrated in our series by a mean gestational age of 20 weeks at diagnosis and initial presentation via self-detected breast lump, reflects a well-known issue: glandular and physiological breast changes complicate clinical examination and radiologic interpretation, often leading to prolonged diagnostic delays [3] [5] [6]. This partly explains the more advanced stage at presentation, as reported in North African and international series [2] [4].

From a histopathological perspective, the predominance of invasive carcinoma of no special type (NST), frequent expression of unfavorable profiles (ER/PR negative, HER2 positive, or triple-negative), and high proportion of SBR grade II - III tumors suggest increased biological aggressiveness of PABC, as highlighted by several authors [3] [6] [7]. These features are often associated with poorer prognosis, necessitating a carefully adapted therapeutic approach.

Management of PABC must be multidisciplinary and individualized. In our series, all patients received chemotherapy, generally administered after the first trimester to reduce teratogenic risk, in accordance with international recommendations for breast cancer treatment during pregnancy [3] [6] [8]-[10]. Breast surgery was performed in the majority of non-metastatic patients, respecting both oncological and obstetric principles. Radiotherapy was deferred until the postpartum period due to fetal risks. Postpartum treatments were adapted according to tumor subtype, including initiation of anti-HER2 therapy and hormonal therapy when indicated. No severe maternal toxicity was reported, and fetal monitoring was conducted regularly.

The evolution of our non-metastatic patients was marked by 5 recurrences (50%), including 10% local recurrences, 20% contralateral recurrences, and 20% distant recurrences, with 2 deaths recorded. These results highlight the high risk of recurrence even after apparently adequate treatment [2] [7] [9]. Some studies suggest, however, that after adjustment for stage and tumor characteristics, the prognosis of PABC may not differ significantly from that of non-pregnant patients with similar cancers [9]-[11], emphasizing the importance of early diagnosis and optimal management.

From an obstetric perspective, most pregnancies were carried to term or near-term (mean gestational age 37 weeks), with favorable neonatal outcomes. Two newborns required neonatal intensive care due to prematurity. No major congenital malformations were observed. These outcomes were monitored in relation to timing of chemotherapy exposure [5] [6] [10] [12] [13].

In conclusion, our series confirms that PABC is often associated with delayed diagnosis and marked histopathological aggressiveness. Early, guideline-based multidisciplinary management remains crucial to optimize both maternal prognosis and obstetric outcomes [10] [12] [13]. However, several limitations must be acknowledged: the small sample size limits statistical power, and availability of some data, such as long-term overall survival and extended neonatal outcomes,

remains limited. Multicenter studies with prolonged follow-up are needed to better define long-term prognosis and evaluate the impact of different therapeutic strategies [2] [10] [11].

5. Conclusion

Our series highlights the specific characteristics of pregnancy-associated breast cancer (PABC) in a Moroccan context, detailing its clinical, biological, and therapeutic features. Our observations confirm that PABC is frequently diagnosed at a late stage and exhibits aggressive histopathological profiles, underscoring the need for heightened vigilance in pregnant patients. The study also demonstrates the effectiveness of a multidisciplinary management approach, integrating surgery, appropriately timed chemotherapy, and obstetric follow-up, which allows for optimal oncological treatment while preserving pregnancy. Finally, our results emphasize the importance of awareness programs, early screening, and coordinated care to reduce diagnostic delays and improve both maternal and fetal prognosis in this specific population. This study thus provides a valuable contribution to local knowledge of PABC and serves as a basis for future multicenter research aimed at refining therapeutic strategies and management recommendations.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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