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# Breast cancer during pregnancy: a retrospective study on obstetrical problems and survival

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ABSTRACT

*Objectives:* Breast cancer is one of the most common cancers occurring in pregnancy. Data on survival of these patients and their obstetrical complications are still limited.
*Study design:* We conducted a case–control, retrospective study to evaluate the overall survival (OS) of 22 patients with breast cancer in pregnancy (BCP) and 45 non-pregnant women with breast cancer (BC) matched for age, stage and hormonal status.
*Results:* Survival of BCP and BC patients using Kaplan–Meier analysis was similar (86.4% in cases and 80% in controls $p = 0.392$) and BCP patients had survival consistent with the stage of the disease, providing that the treatment had been in agreement with the recommended protocols. The overall incidence of premature delivery was 54.6% and complications were observed in three newborns out of 23 (13%).
*Conclusions:* Preterm labor induction without any obstetrical indication following woman's request to continue chemotherapy outside pregnancy can be reduced by explaining the risks of early delivery and the lack of effects of many chemotherapeutic regimens on the fetus.


## 1. Introduction

Breast cancer is one of the most common carcinomas occurring in pregnancy [1,2]. In a study by Stensheim et al. [3] the most frequent malignancy diagnosed during pregnancy was melanoma, but regional differences and specific cancers treated in specific hospitals mean reliable data are lacking. Pregnancy-associated breast cancer (PABC) includes breast cancer diagnosed during pregnancy (BCP) and up to one year after delivery. The incidence of BCP is likely to increase in the near future due to a decrease in the age of breast cancer onset: in Italy the incidence of breast cancer in non-pregnant women below 45 years of age rose from 16.39% per 100,000 in 1980 to 26.57 per 100,000 in 2010 [4]. Moreover, an increase in age of childbearing in women from western countries has also been reported [5].

As pointed out by Oduncu et al. [6], there is a conflict between maternal chemotherapy and fetal well-being once BCP has been diagnosed. The mother would require immediate treatment but the optimal therapy may be at high risk for the fetus. In fact diagnosis of BCP in the first trimester limits treatment options because the administration of chemotherapy might be harmful to the fetus [7]. This is why cytotoxic treatments are postponed to the 2nd trimester.

Unlike BCP, when the breast tumor appears within one year after delivery the maternal treatment is not influenced by the trimester of pregnancy. The inclusion in many case–control studies of tumors diagnosed up to one year after delivery might explain conflicting results on the prognosis of PABC. It is important to point out that some treatments during pregnancy are not in line with data in the literature, due to different strategies from different physicians [8]. The lack of adherence to protocols can further explain different results.

BCP is usually considered to have an unfavorable prognosis, although the poor prognosis may simply reflect a more advanced disease stage at diagnosis, because of physiological changes induced in the mammary gland by pregnancy-related hormones. These changes make breast cancer more difficult to diagnose, or diagnosis can be delayed due to reluctance in performing mammography during pregnancy. Moreover some studies indicate that tumors occurring during pregnancy might be more aggressive

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during the puerperium, showing a different prognosis, possibly due to specific cell modifications associated with these two different physiological periods [9].

We conducted a case–control, retrospective study to evaluate the overall survival (OS) of a group of pregnant versus non-pregnant women, matched for age and stage of breast cancer. Moreover, we investigated the effect of chemotherapy during pregnancy, the obstetrical complications and timing of delivery.

## 2. Material and methods

We included as cases 22 pregnant women with breast cancer diagnosed between 1st January 2004 and 15th March 2013 with available data on age at primary diagnosis, tumor histology, size, histological grading, nodal status and hormonal expression. We excluded patients with breast cancer diagnosed up to one year after delivery or with incomplete information.

All patients were enrolled in the Department of Gynecological, Obstetrical and Urological Sciences and Department of Surgery Pietro Valdoni University Sapienza in Rome. As controls for OS we considered 45 age-matched patients with breast cancer referred to our center in the same time interval. Informed consent was obtained from all patients or their relatives to use their pathological and clinical data for this retrospective study.

Surgery consisted of radical mastectomy or quadrantectomy followed by lymph node dissection. Conservative surgery was followed by radiotherapy in the puerperium. Chemotherapy before delivery consisted of standard cycles of FEC (cyclophosphamide 500 mg/m$^2$ day 1, epirubicin 70 mg/m$^2$ day 1, 5-fluorouracil 500 mg/m$^2$ day 1, every 21 days) or EC (epirubicin 100 mg/m$^2$ + cyclophosphamide 500 mg/m$^2$ every 21 days) or epirubicin alone 100 mg/m$^2$ every 21 days.

Patients who were alive were censored at the time of the last follow-up (15th March 2013). Survival (in years) was defined as the period between the first diagnostic biopsy and the last follow-up or death date. The distribution of covariates according to breast cancer at baseline was analyzed using the $\chi^2$ test and the Fisher's exact test for categorical variables, while the *t*-test was used to verify if a relationship held for quantitative variables. The association was considered statistically significant when $p < 0.005$. BCP and BC overall survival analyses were conducted using the Kaplan–Meier method, and the log-rank test was used to determine whether the differences in survival curves (BCP and BC patients) are due to chance ($p < 0.005$). Statistical analysis was performed using the SPSS 17.0 software for Windows (SPSS Inc., Chicago, IL, USA).

## 3. Results

### 3.1. Patient characteristics and treatments

Mean maternal age at diagnosis in our BCP group was 37.2 ± 3.2 years ($n = 22$) (mean and standard deviation), and mean age in controls was 39.3 ± 6.9 years ($n = 45$) ($p = 0.094$). The mean gestational age at diagnosis of BCP patients was 29.2 ± 6.6 weeks (min 5–max 37 weeks). The characteristics of cases and controls are reported in Table 1. There were no statistically significant differences between cases and controls regarding lymph node status ($p = 0.763$), site of lesion ($p = 0.585$), tumor classification ($p = 0.815$), tumor grading ($p = 0.434$), estrogen receptor (ER) status ($p = 0.117$) and histological type (lobular or ductal) ($p = 0.120$).

In the BCP group, 10 radical mastectomies and in 12 quadrantectomies followed by lymph node dissection were performed. In the control group, 18 radical mastectomies and 27 quadrantectomies followed by lymph node dissection were performed. Conservative surgery was followed by radiotherapy in both cases and controls, but in the BCP group radiotherapy was performed during the puerperium. During pregnancy FEC was administered to 1 case, EC was administered to 4 BCPs and epirubicin alone was administered to another 4 cases (Table 2). In the BCP group, 9 out of 22 patients received neoadjuvant chemotherapy (40.9%). Chemotherapy given after childbirth is reported in Table 2, which also reports local treatments in BCP patients. Chemotherapy after childbirth consisted of standard cycles of FEC, standard cycles of CMF (cyclophosphamide + methotrexate + 5-fluorouracil), EP (epirubicin + paclitaxel), FEC + docetaxel, E + CMF, EC + pegylated liposomial doxorubicin + CDDP (cisdichlorodiamminoplatinum) or P (paclitaxel) + CDDP. In one

**Table 1**
Population characteristics by group of patients.

| | | | Groups of patients | | | *p*-Value |
|---|---|---|---|---|---|---|
| | | | Case (BCP) | Control (BC) | Total | |
| Status at (15_3_2013) | Alive | *N* | 19 | 36 | 55 | 0.392[a] |
| | | % | 86.4% | 80.0% | 82.1% | |
| | Death | *N* | 3 | 9 | 12 | |
| | | % | 13.6% | 20.0% | 17.9% | |
| Age | | *n* | 22 | 45 | 67 | 0.095[b] |
| | | Mean | 37.2 | 39.3 | 38.6 | |
| | | SD | 3.18 | 6.895 | 5.99 | |
| Site of lesion | Left | *n* | 9 | 19 | 28 | 0.585[c] |
| | Right | | 13 | 24 | 37 | |
| | Right/Left | | 0 | 2 | 2 | |
| pTNM classification (tumore) | T1 | *n* | 10 | 24 | 34 | 0.815[c] |
| | T2 | | 7 | 13 | 20 | |
| | T3 | | 5 | 8 | 13 | |
| pTNM classification (linfonodi) | N0 | *n* | 11 | 19 | 30 | 0.763[c] |
| | N1 | | 8 | 17 | 25 | |
| | N2 | | 3 | 9 | 12 | |
| Grading | 2 | *n* | 10 | 18 | 28 | 0.375[a] |
| | 3 | | 11 | 27 | 38 | |
| Histological type | Lobular | *n* | 2 | 11 | 13 | 0.120[a] |
| | Ductal | | 20 | 34 | 53 | |
| ER expression | – | *n* | 12 | 16 | 28 | 0.112[a] |
| | + | | 10 | 29 | 39 | |

[a] Fisher's exact test.
[b] *t* test for equality of means.
[c] Pearson chi-square.