ORIGINAL ARTICLE

WILEY

Clinicopathological features and prognosis of patients with pregnancy-associated breast cancer: A matched case control study

Ruyan Zhang | Xiaoran Liu | Wenfa Huang | Bin Shao | Ying Yan | Xu Liang | Ran Ran | Guohong Song | Lijun Di | Hanfang Jiang | Huiping Li

Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Department of Breast Oncology, Peking University Cancer Hospital and Institute, Beijing, China

Correspondence
Huiping Li, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Department of Breast Oncology, Peking University Cancer Hospital and Institute, No. 52 Fucheng Road, Haidian District, Beijing 100142, China.
Email: huipingli2012@hotmail.com

Ruyan Zhang and Xiaoran Liu contributed equally to this work.

Abstract

Aim: We aimed to clarify tumor features and prognosis of pregnancy-associated breast cancer (PABC) among Chinese women.

Methods: PABC was defined as breast cancer diagnosed during pregnancy or within a year after delivery. Patients with PABC were selected from breast cancer cases of women ≤45 years treated at our institution between December 2012 and December 2017, and one non-PABC control was matched for stage, age, and year of diagnosis for each case.

Results: Forty-one women with PABC were identified (22 diagnosed during pregnancy and 19 within 1 year of delivery). There were significantly more progesterone receptor (PR)- and triple-negative tumors in the PABC (56.1% and 24.4%, respectively) than in the non-PABC group (31.7% and 4.9%, respectively) ($P = .045$ and $.026$, respectively). Human epidermal growth factor receptor 2 positivity was the same in both groups (31.7%). Median disease-free survival (DFS) was 29.0 months (95% confidence interval [CI], 6.5-51.5 months) in the PABC and 40.9 months (95% CI, 22.8-58.8 months) in the non-PABC group ($P = .167$). Median overall survival (OS) was 82.8 months in the PABC (95% CI, 39.3-126.5 months) versus 80.1 months (95% CI, 56.7-103.6 months) in the non-PABC group ($P = .131$).

Conclusion: Histological features were similar in both groups, except that PR- and triple-negative tumors were more frequent in the PABC group. Survival analyses show similar OS for patients with PABC and non-PABC. DFS tended to be shorter in the PABC group; however, this difference was not statistically significant.

KEYWORDS
breast cancer, clinicopathological features, postpartum, pregnancy, prognosis

1 | INTRODUCTION

Pregnancy-associated breast cancer (PABC) is defined as breast cancer diagnosed during pregnancy or the postpartum period (from 1 to 5 years after delivery according to various published studies); the most commonly used definition specifies only 1 year postpartum.

Breast cancer is one of the most common cancers in pregnancy, being diagnosed in about one of 3000 to one of 10 000 pregnancies.[1–3] This incidence is reportedly increasing as more women are delaying childbearing.[1] In previous studies, PABC constituted around 7%, 10%, and 15.6% of all BCs in women below the ages of 45, 40, and 35 years, respectively.[4–6]

Do the clinicopathological features and prognosis of PABC differ from those of non-PABC? This still remains a controversial issue. Previous studies have found that PABC is often diagnosed at an advanced stage due to delay in diagnosis. In some,[7–12] but not all,[13,14] studies, PABC has been found to have more aggressive tumor features, namely, more ER/PR-negative and/or HER2-positive tumors. Additionally, poorer prognosis has been observed in women with PABC than in those with non-PABC in some,[4,12,15–17] but not all,[8,9,18] studies. However, the role of pregnancy in the poor prognosis of breast cancer remains debatable because patients with PABC tend to be young and to present at an advanced stage, these features act as confounding factors. Furthermore, treatment of PABC may be limited or delayed due to concerns for fetal safety. A meta-analysis of PABC by Azim et al that included 30 studies reported worse survival outcomes for patients with PABC even after adjustment for confounding factors.[15–17]

According to data of the Global Cancer Observatory, 15.2% of patients diagnosed with breast cancer in China are aged less than 40 years, which is a much higher percentage than the 5.6% cited for the United States. Accordingly, the rate of PABC maybe higher in China than in the United States. However, there has been little domestic research on this topic in China; in particular, matched case control studies are rare. To better determine the characteristics of PABC in Chinese women, we designed the present matched case-control study.

2 | METHODS

A database of patients aged less than 45 years diagnosed with breast cancer between December 2012 and December 2017 in the Department of Breast Oncology, Peking University Cancer Hospital and Beijing Institute of Cancer Prevention was reviewed. PABC was defined as breast cancer diagnosed during pregnancy or within the year following delivery. After reviewing the medical notes of patients suspected of having PABC to ensure that the diagnosis of breast cancer (BC) was indeed made during pregnancy or in the year following delivery, 41 patients with PABC were enrolled. We matched these 41 PABC cases with 41 non-PABC cases for stage (American Joint Committee on Cancer (AJCC) I, II, III, and IV) and age (±1 year), as well as year of diagnosis secondarily (±1 year), with the aims of comparing tumor characteristics, disease-free survival (DFS), and overall survival (OS) between patients with PABC and non-PABC. Non-PABC cases included patients who were diagnosed as breast cancer when more than 1 year after delivery or who were nulliparous at the time of diagnosis.

The following data were recorded: age at diagnosis, date of diagnosis, family history, pathological characteristics (pathological type, tumor stage [AJCC], tumor size, nodal involvement, tumor grade, status of estrogen [ER], progesterone [PR], and human epidermal growth factor receptor 2 [HER2] expression and Ki67 index), and treatment modalities (type of surgery, chemotherapy, and radiotherapy), date of relapse, and site of relapse. A tumor was considered ER and/or PR positive if >1% of tumor cells demonstrated intranuclear positivity, and Ki-67 cutoff value was set as 25% according to the mean level tested in our pathology laboratory.

DFS was calculated as the interval from initial breast cancer diagnosis to disease recurrence (loco-regional or systemic) or to time of death from BC, or to the date of last follow-up if the patient was disease free. Overall survival (OS) was defined as the interval between initial diagnosis and time of death or date of last follow up.

This is a retrospective, noninterventive study, exempt from ethical review; every patient had signed a consensus that had been approved by Ethic Committee of Peking University Cancer Hospital before receiving any antitumor treatment.

2.1 | Statistical analysis

Differences in clinicopathological features were compared between cases and controls using the χ^2 and Fisher's exact tests. DFS and OS analyses were performed to assess the effect of PABC on survival. Univariate analysis was performed using the Kaplan–Meier method and multivariate analysis performed using Cox's regression model. Differences were considered significant when $P \leq .05$. All statistical analyses were performed using SPSS 19.0 software.

3 | RESULTS

We identified 41 women with PABC, 22 of whom were diagnosed during pregnancy and 19 within 1 year of delivery. Eight of the 41 matched non-PABC control women were nulliparous and 33 were diagnosed more than 1 year after delivery. Selected patient characteristics and tumor histological variables are shown (Table 1).

The median ages at diagnosis of women with PABC and non-PABC were 31.6 (range: 24-42) years and 32.2 (range: 26-42) years, respectively, most of the patients being younger than 35 years (85.3% and 82.9% with and without PABC, respectively). Only two and one patients with PABC and non-PABC had a family history of breast cancer. The most frequent histological type in both groups was invasive ductal carcinoma, which occurred in 92.7% of those with PABC and 95.7% of those with non-PABC. Stage III was the most common stage at presentation, accounting for 22 patients (53.7%) in each group, followed by stage IV, with nine patients (21.9%) in each group. There were no statistically significant differences between the groups in tumor size, node involvement, grade, or Ki-67 index positivity. ER-negative tumors tended to occur more frequently in patients with PABC (43.9%)

TABLE 1 Patient characteristics according to PABC status

	PABC (%) N = 41	Non-PABC (%) N = 41	P-value
Mean age at diagnosis in years (range)	31.6 (24-42)	32.2 (26-42)	Matched
Age ≤ 35 years	35 (85.3)	34 (82.9)	.762
Age > 35 years	6 (14.6)	7 (17.1)	
Timing of diagnosis			NS
During pregnancy	22 (53.7)	NA	
Within 12 months of delivery	19 (46.3)	NA	
Nulliparous	NA	8 (19.5)	
More than 12 months postpartum	NA	33 (80.5)	
Family history			1.0
Yes	2 (4.9)	1 (2.4)	
No	39 (95.1)	40 (97.6)	
Stage			Matched
I	4 (9.8)	4 (9.8)	
II	6 (14.6)	6 (14.6)	
III	22 (53.7)	22 (53.7)	
IV	9 (21.9)	9 (21.9)	
Histology			.286
Ductal	38 (92.7)	39 (95.1)	
Lobular	1 (2.4)	0	
Ductolobular	0	1 (2.4)	
DCIS	2 (4.9)	1 (2.4)	
T stage			.176
T1	7 (17.1)	15 (36.5)	
T2	18 (43.9)	17 (41.5)	
T3	10 (24.4)	6 (14.6)	
T4	6 (14.6)	3 (7.3)	
N stage			.271
N0	8 (19.5)	4 (9.8)	
N1	5 (12.2)	11 (26.8)	
N2	11 (26.8)	12 (29.3)	
N3	17 (41.5)	14 (34.1)	
Grade			.355
I	1 (2.4)	1 (2.4)	
II	26 (63.4)	29 (70.7)	
III	14 (34.1)	9 (22.0)	
No data	0	2 (4.9)	
Ki-67			.319
>25%	28 (68.3)	32 (78.0)	
<25%	13 (31.7)	9 (22.0)	
ER			.106
Positive	23 (56.1)	30 (73.2)	

(Continues)

TABLE 1 (Continued)

	PABC (%) N = 41	Non-PABC (%) N = 41	P-value
Negative	18 (43.9)	11 (26.8)	
PR			.045*
Positive	18 (43.9)	28 (68.3)	
Negative	23 (56.1)	13 (31.7)	
HER2			.839
Positive	13 (31.7)	13 (31.7)	
Negative	26 (63.4)	27 (65.9)	
IHC 2+	2 (4.9)	1 (2.4)	
TNBC	10 (24.4)	2 (4.9)	.026* (Fisher)

*P-values indicate statistically significant.
P-values from chi-square test unless otherwise specified (Fisher exact test).
Abbreviations: DCIS, ductal carcinoma in situ; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; TNBC, triple negative breast cancer.

TABLE 2 Treatment modality according to PABC status

	PABC (%) N = 41	Non-PABC (%) N = 41	P-value
Surgery			.298
No surgery	6 (14.6)	6 (14.6)	
Breast-conserving	8 (19.5)	4 (9.8)	
Mastectomy	27 (65.9)	31 (75.6)	
Neoadjuvant chemo	11 (26.8)	7 (17.0)	.281
Adjuvant chemotherapy	31 (75.6)	32 (78.0)	.840
Adjuvant chemo agent			.703
Anthracyclines only	1 (2.4)	1 (2.4)	
Taxanes only	2 (4.9)	5 (12.2)	
Both	28 (68.3)	26 (63.4)	
Adjuvant radiation therapy	20 (48.8)	26 (63.4)	.181

than in controls (26.8%); however, this difference was not significant (P = .106). Nevertheless, there were more PR-negative and triple-negative tumors in the patients with PABC (56.1% and 24.4%, respectively) than in those without PABC (31.7% and 4.9%, respectively); this difference was statistically significant (P = .045 and .026). The rate of HER2 positivity was the same in both groups (31.7%).

The commonest surgical procedure in both groups was mastectomy with axillary lymph node dissection. More women with PABC (19.5%) than non-PABC (9.8%) underwent breast-conserving surgery. More women with PABC received neoadjuvant chemotherapy (26.8% vs 17%). The number of patients receiving adjuvant chemotherapy was almost the same in the two groups (31 vs 32) and the type of chemotherapy agents was similar in the two groups. Adjuvant radiation therapy was delivered in 20 patients (48.8%) with PABC and 26 (63.4%) non-PABC. No significant difference in treatment modality received was identified between the patients in the two groups (Table 2).
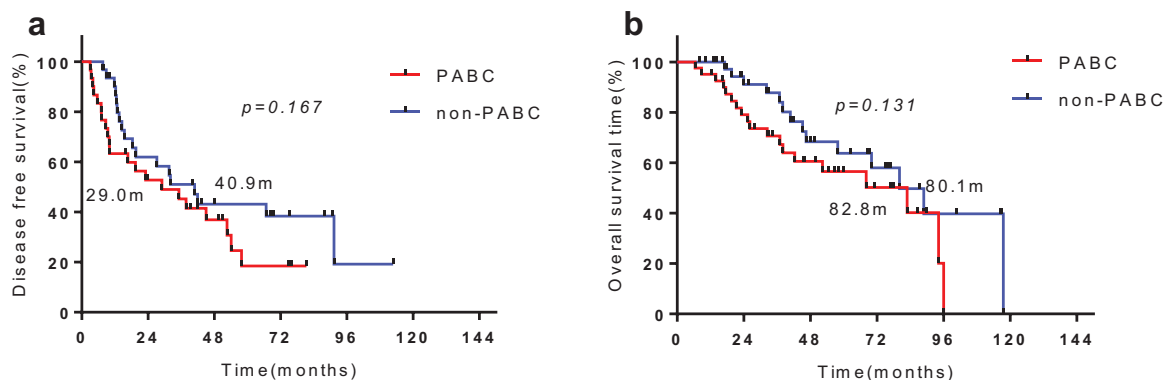
FIGURE 1 A, Disease-free survival (DFS) stratified by pregnancy status (median DFS in those with and without pregnancy-associated breast cancer [PABC] = 29.0 vs 40.9 months, respectively; $P = .167$). B, Overall survival (OS) stratified by pregnancy status (median OS in those with and without PABC = 82.8 vs 80.1 months, respectively; $P = .131$) [Colour figure can be viewed at wileyonlinelibrary.com]

3.1 | Treatment during pregnancy and termination of pregnancy

Two patients received surgery and one patient received chemotherapy during pregnancy, five patients early terminated their pregnancy at their request shortly after they were diagnosed as breast cancer, and the remaining 14 patients did not begin treatment of breast cancer until after delivery mostly due to their concerns for fetal safety.

The two cases received modified radical mastectomy at 25-28 weeks of gestation, and one of the two patients developed epilepsy in more than 1 month after surgery (confirmed to be caused by brain metastasis), then she underwent cesarean section to terminate pregnancy and gave birth to a healthy baby; the other patient also only received surgery with no chemotherapy or targeted therapy (HER2 3+) followed, she maintained pregnancy until 32 weeks, then received a cesarean section, and delivered a live birth.

One case at 32 weeks of gestation received three cycles of cyclophosphamide + Pirarubicin (a semisynthetic anthracycline) + 5-FU (CAF) neoadjuvant chemotherapy during pregnancy and achieved partial remission on ultrasound evaluation (uPR) with no serious complications occurred. Then, the patient delivered a healthy baby at 40 weeks and received one more cycle of CAF chemotherapy before breast-conserving surgery.

During follow-up, 21 patients with PABC (67.7% of 31) and 18 with non-PABC (58.1% of 31) who were diagnosed as having stage I-III disease and had undergone surgery relapsed. Nineteen PABC patients (46.3%) and 14 non-PABC patients (34.1%) died.

The median DFS tended to be worse in PABC patients than non-PABC patients; however, this difference was not statistically significant ($P = .167$; Figure 1A). The median DFS in patients with PABC was 29.0 months (95% confidence interval [CI], 6.5-51.5 months) compared with 40.9 months (95% CI, 22.8-58.8 months) for those with non-PABC (Figure 1A). The median OS was similar in the two groups, tending to be longer in those with PABC (82.8 months; 95% CI, 39.3-126.5 months) compared with 80.1 months (95% CI, 56.7-103.6 months) in those with non-PABC; however, this difference was not statistically significant ($P = .131$) (Figure 1B).

It should be noted that five patients (gestational age was less than 12 weeks in four of them) who terminated pregnancy to treat the cancer were not excluded in the DFS and OS analysis, because these five patients were diagnosed as breast cancer during pregnancy; they met the inclusion criteria for PABC whether they terminated the pregnancy or not. Nevertheless, we did an additional analysis of DFS and OS between the two groups after excluding these five patients, and no significant statistical difference was found—mDFS in PABC and non-PABC: 29.0 versus 39.2 months ($P = .154$); mOS in PABC and non-PABC: 68.1 versus 80.2 months ($P = .249$).

When patients with PABC were divided into two subgroups—breast cancer during pregnancy versus within 1 year after delivery—there were no statistically significant differences in DFS or OS between these subgroups; however, both DFS and OS tended to be longer in the postpartum than the pregnancy group (Figures 2A and 2B). Comparisons between each of these subgroups and their matched control group also showed no statistically significant differences in DFS or OS (Figure 3A-D).

Other prognostic factors (stage, ER, PR, and HER2) were assessed for their effect on DFS and OS in the study patients. On univariate and multivariate analysis, only advanced stage was associated with worse DFS, whereas advanced stage and ER negativity were associated with worse OS.

4 | DISCUSSION

Similar to the results of most studies with or without adjustment for age and stage, ER- and PR-negative tumors were more common in PABC patients than non-PABC patients in our study. We also identified a significantly higher proportion of PR-negative and triple-negative tumors in PABCs, whereas HER2 positivity was the same in the two groups, a finding consistent with some other matched-control studies.[14,18] Besides, other histological features and treatment modality were similar in both groups, the total mastectomy rate was high in both group; actually, breast conservation rate in China is very low, and the rate reported in retrospective studies ranged from 5% to 20%,
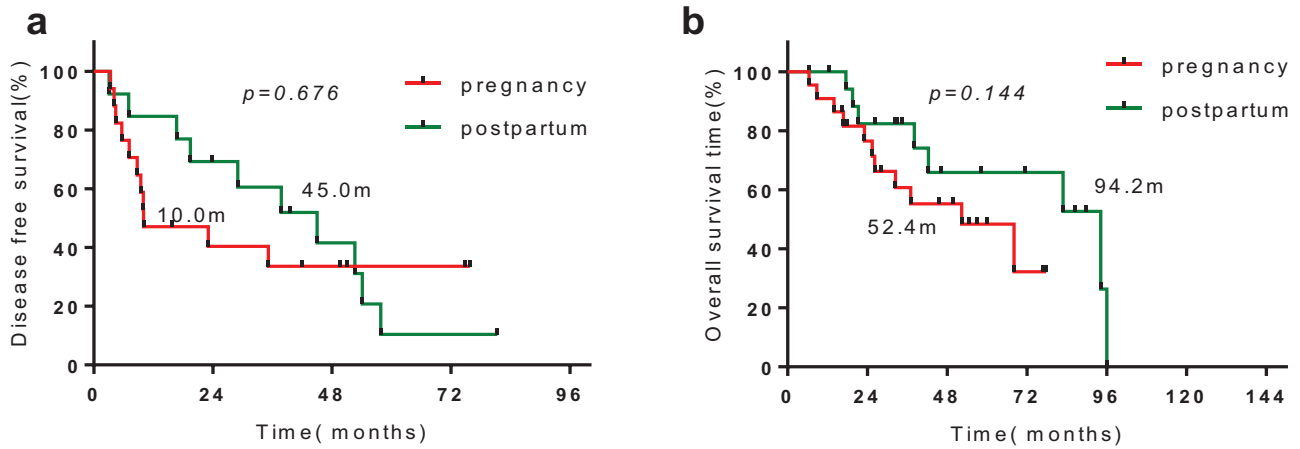
FIGURE 2 A, Disease-free survival (DFS) in the pregnancy and postpartum groups (median DFS = 10.0 months vs 45.0 months; *P* = .676). B, Overall survival (OS) in pregnancy and postpartum groups (median OS = 52.4 vs 94.2 months; *P* = .144) [Colour figure can be viewed at wileyonlinelibrary.com]
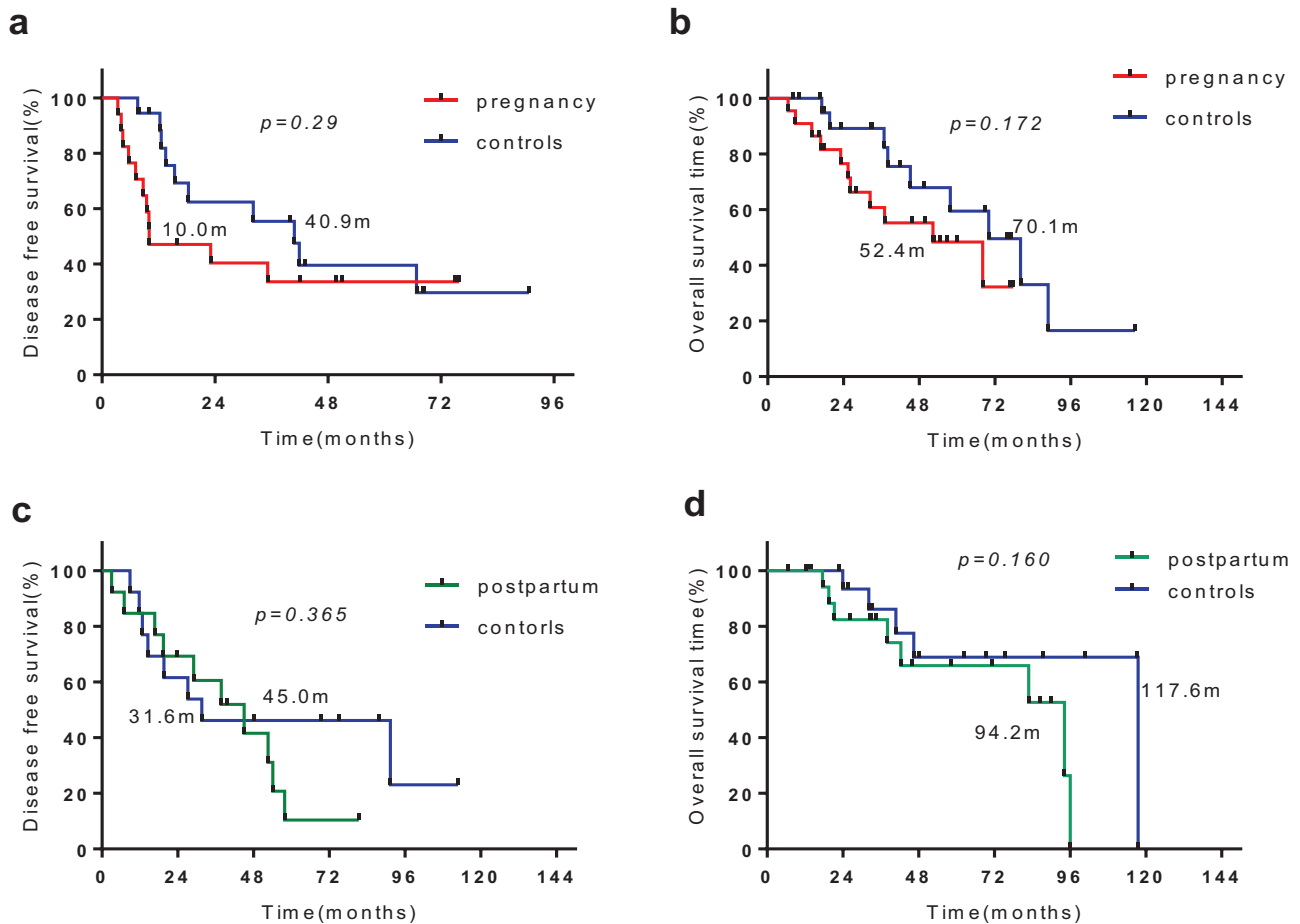
FIGURE 3 A, Disease-free survival (DFS) in pregnancy and control groups (median DFS = 10.0 vs 40.9 months; *P* = .29). B, Overall survival (OS) in pregnancy and control groups (median OS = 52.4 vs. 70.1 months; *P* = .172). C, DFS of postpartum and control groups (median DFS = 45.0 vs 31.6 months; *P* = .365). D, OS of postpartum and control groups (median OS = 94.2 vs 117.6 months; *P* = .160) [Colour figure can be viewed at wileyonlinelibrary.com]

which is caused by a variety of factors including the smaller size of breast in Chinese women than in women of western countries and other.

Awareness is growing that breast cancer can be treated during pregnancy in recent years. A multicenter case-control study shows prenatal exposure to maternal cancer with or without treatment did not impair the cognitive, cardiac, or general development of children in early childhood.[19] However, there were only 129 children enrolled in the study. The main treatment options for pregnant women with breast cancer are surgery and systemic chemotherapy. The largest experience about chemotherapy in pregnancy has been with anthracycline and alkylating agent chemotherapy.[20] There are limited data on the use of taxanes during pregnancy,[21] and a 20-year international cohort study suggested a relationship between platinum-based chemotherapy and small for gestational age, and between taxane chemotherapy and Neonatal Intensive Care Unit (NICU) admission.[22] And the National Comprehensive Cancer Network (NCCN) panels recommend that chemotherapy should not be administered at any point during the first trimester of pregnancy. Modified radical mastectomy has been the most common surgical procedure; breast-conserving surgery is considerable if radiation therapy can be delayed to the postpartum period.[23,24]

However, only three patients received treatment during pregnancy in our study. Two cases received surgery in the second trimester of pregnancy, and one case received CAF agent of neoadjuvant chemotherapy in the third trimester of pregnancy, without serious perinatal complications and congenital defects. Fourteen patients did not begin treatment of breast cancer until after delivery, four of whom were over 30 weeks of gestational age when they were diagnosed as breast cancer; they chose to postpone the treatment to postpartum period after doctors informed them of the feasibility of surgery or chemotherapy during pregnancy and the potential risk to the fetus of the treatment. Many traditional Chinese women believe that health of the fetus was more important to their families than their own; undoubtedly, they had made sacrifices for the health of the fetus.

Despite the higher proportion of triple-negative BC and treatment delay in women with PABC, we did not find a worse prognosis than women with non-PABC who were matched by age and stage. On survival analysis, the median DFS tended to be shorter in women with PABC than in non-PABC; treatment delay in PABC may have contributed to the difference. However, this difference was not significant and the median OS of the two groups were almost the same.

Subgroup analyses compared prognosis of patients with breast cancer diagnosed during pregnancy (BCP) and during postpartum (BCPP) with that of their matched control patients, and compared prognosis between patients with BCP and with BCPP directly. It suggested that BCP groups tended to show worse prognosis than their matched controls and BCPP, but it all failed to reveal significant differences in both DFS and OS. Multivariate analysis also failed to confirm that pregnancy is an independent factor for poor prognosis of PABC. The results of our study tend to support that maybe the poor prognosis of PABC is not related to pregnancy itself but mainly due to the young age of patients and more invasive biological characteristics of tumor.

Actually, the belief that the prognosis of women with PABC is similar to that of women with non-PABC after adjustment for age and stage became more widely accepted after the results of a multicenter study with large sample size were published in 2013. In this study, 311 patients with BCP were compared with 865 patients who did not have associated pregnancies (patients with diagnosis made postpartum were excluded). These two groups were found to have similar survivals after adjusting for known prognostic factors.[9]

At the same year, a prospective study conducted by Litton et al from M.D. Anderson Cancer Center reported a reassuring and intriguing finding: patients with BCP who received chemotherapy during pregnancy had comparable, if not better, survival than did nonpregnant women. The 5-year survival was 77% for pregnant patients and 71% for controls (P = .046).[25]

Both of the above studies focused on the patients with BCP, whereas patients with diagnosis made postpartum were excluded; controls were those patients who did not have associated pregnancies. Some previous studies have found that patients with BCPP have inferior outcomes compared with those with BCP or controls with non-PABC.[4,17,25–27] It must be noted that the number of years after delivery when a breast cancer can be diagnosed as PABC ranged from 1 to 5 years or even longer.[27–29]

A study reported that survival rate for breast cancer diagnosed within 12 months, 13-48 months, and more than 48 months postpartum was 38%, 51%, and 60% respectively, compared with 65% for age-matched nulliparous women.[30] These findings imply that the sooner after delivery the breast cancer is diagnosed, the worse the prognosis, and that the prognosis of nulliparous women is better than that of age-matched postpartum women.

In our study, we defined postpartum PABC as within 1 year after delivery; the non-PABC group included patients diagnosed with breast cancer from 1 to 2 years after delivery and nulliparous women. We found no significant differences in DFS or OS between the 22 patients with BCP and 19 patients with BCPP, and in contrary, the prognosis tending to be superior for BCPP. There are several possible reasons as follows: the two groups were not matched by stage; BCP tended to present at an advanced stage (86.4% [19/22] of BCP and 63.1% [12/19] of BCPP were at stage III-IV when diagnosed); and more treatment delay were found in BCP group as the supplementary table showed. Besides, the sample size of the two groups was too small.

Limitations of our study include the small sample size, treatment delay and termination of pregnancy in women with BCP that may impact the outcome of PABC, and retrospective study design. With a larger sample, it would be possible to divide postpartum breast cancer into more groups according to time between delivery and diagnosis, and to compare the tumor characteristics and prognosis between those groups, as well as with nulliparous women. However, it was difficult for the authors to find more age- and stage-matched controls for PABCs at the same year or closed to the year cancer was diagnosed; and to the best of our knowledge, this is the first age- and stage-matched case control study to explore the tumor features and prognosis of PABC in Chinese women.

5 | CONCLUSIONS

When patients with PABC and non-PABC were matched for age and stage, histological features were similar in both groups, except that PR- and triple-negative tumors were more frequent in the PABC group. Survival analyses show similar OS and DFS for patients with PABC and non-PABC. It failed to confirm that pregnancy is an independent factor for poor prognosis of PABC. Further studies are warranted to further elucidate these points.

ORCID
Ruyan Zhang https://orcid.org/0000-0002-3471-017X

REFERENCES

1. Andersson TM, Johansson AL, Hsieh CC, Cnattingius S, Lambe M. Increasing incidence of pregnancy-associated breast cancer in Sweden. *Obstet Gynecol*. 2009;114:568-572.
2. Stensheim H, Moller B, van Dijk T, Fossa SD. Cause-specific survival for women diagnosed with cancer during pregnancy or lactation: a registry-based cohort study. *J Clin Oncol*. 2009;27:45-51.
3. Lethaby AE, O'Neill MA, Mason BH, Holdaway IM, Harvey VJ. Overall survival from breast cancer in women pregnant or lactating at or after diagnosis. Auckland Breast Cancer Study Group. *Int J Cancer*. 1996;67:751-755.
4. Johansson AL, Andersson TM, Hsieh CC, Cnattingius S, Lambe M. Increased mortality in women with breast cancer detected during pregnancy and different periods postpartum. *Cancer Epidemiol Biomarkers Prev*. 2011;20:1865-1872.
5. Anders CK, Johnson R, Litton J, Phillips M, Bleyer A. Breast cancer before age 40 years. *Seminars in Oncology*. 2009;36:237-249.
6. Beadle BM, Woodward WA, Middleton LP, et al. The impact of pregnancy on breast cancer outcomes in women <or= 35 years. *Cancer*. 2009;115:1174-1184.
7. Genin AS, Lesieur B, Gligorov J, Antoine M, Selleret L, Rouzier R. Pregnancy-associated breast cancers: do they differ from other breast cancers in young women? *Breast*. 2012;21:550-555.
8. Murphy CG, Mallam D, Stein S, et al. Current or recent pregnancy is associated with adverse pathologic features but not impaired survival in early breast cancer. *Cancer*. 2012;118:3254-3259.
9. Amant F, von Minckwitz G, Han SN, et al. Prognosis of women with primary breast cancer diagnosed during pregnancy: results from an international collaborative study. *J Clin Oncol*. 2013;31:2532-2539.
10. Baulies S, Cusido M, Tresserra F, et al. Biological and pathological features in pregnancy-associated breast cancer: a matched case-control study. *Eur J Gynaecol Oncol*. 2015;36:420-423.
11. Rodriguez AO, Chew H, Cress R, et al. Evidence of poorer survival in pregnancy-associated breast cancer. *Obstet Gynecol*. 2008;112:71-78.
12. Johansson ALV, Andersson TM, Hsieh CC, et al. Tumor characteristics and prognosis in women with pregnancy-associated breast cancer. *Int J Cancer*. 2018;142:1343-1354.
13. Middleton LP, Amin M, Gwyn K, Theriault R, Sahin A. Breast carcinoma in pregnant women: assessment of clinicopathologic and immunohistochemical features. *Cancer*. 2003;98:1055-1060.
14. Moreira WB, Brandao EC, Soares AN, Lucena CE, Antunes CM. Prognosis for patients diagnosed with pregnancy-associated breast cancer: a paired case-control study. *Sao Paulo Med J*. 2010;128:119-124.
15. Ali SA, Gupta S, Sehgal R, Vogel V. Survival outcomes in pregnancy associated breast cancer: a retrospective case control study. *Breast J*. 2012;18:139-144.
16. Dimitrakakis C, Zagouri F, Tsigginou A, et al. Does pregnancy-associated breast cancer imply a worse prognosis? A matched case-case study. *Breast Care*. 2013;8:203-207.
17. Azim HA Jr, Santoro L, Russell-Edu W, Pentheroudakis G, Pavlidis N, Peccatori FA. Prognosis of pregnancy-associated breast cancer: a meta-analysis of 30 studies. *Cancer Treat Rev*. 2012;38:834-842.
18. Halaska MJ, Pentheroudakis G, Strnad P, et al. Presentation, management and outcome of 32 patients with pregnancy-associated breast cancer: a matched controlled study. *Breast J*. 2009;15:461-467.
19. Amant F, Vandenbroucke T, Verheecke M, et al. Pediatric outcome after maternal cancer diagnosed during pregnancy. *N Engl J Med*. 2015;373:1824-1834.
20. Germann N, Goffinet F, Goldwasser F. Anthracyclines during pregnancy: embryo-fetal outcome in 160 patients. *Ann Oncol*. 2004;15:146-150.
21. Garcia-Manero M, Royo MP, Espinos J, Pina L, Alcazar JL, Lopez G. Pregnancy associated breast cancer. *Eur J Surg Oncol*. 2009;35:215-218.
22. de Haan J, Verheecke M, Van Calsteren K, et al. Oncological management and obstetric and neonatal outcomes for women diagnosed with cancer during pregnancy: a 20-year international cohort study of 1170 patients. *Lancet Oncol*. 2018;19:337-346.
23. Annane K, Bellocq JP, Brettes JP, Mathelin C. Infiltrative breast cancer during pregnancy and conservative surgery. *Fetal Diagn Ther*. 2005;20:442-444.
24. Kuerer HM, Gwyn K, Ames FC, Theriault RL. Conservative surgery and chemotherapy for breast carcinoma during pregnancy. *Surgery*. 2002;131:108-110.
25. Callihan EB, Gao D, Jindal S, et al. Postpartum diagnosis demonstrates a high risk for metastasis and merits an expanded definition of pregnancy-associated breast cancer. *Breast Cancer Res Treat*. 2013;138:549-559.
26. Madaras L, Kovacs KA, Szasz AM, et al. Clinicopathological features and prognosis of pregnancy associated breast cancer - a matched case control study. *Pathol Oncol Res*. 2014;20:581-590.
27. Hartman EK, Eslick GD. The prognosis of women diagnosed with breast cancer before, during and after pregnancy: a meta-analysis. *Breast Cancer Res Treat*. 2016;160:347-360.
28. Psyrri A, Burtness B. Pregnancy-associated breast cancer. *Cancer J*. 2005;11:83-95.
29. Lyons TR, Schedin PJ, Borges VF. Pregnancy and breast cancer: when they collide. *J Mammary Gland Biol Neoplasia*. 2009;14:87-98.
30. Lee GE, Mayer EL, Partridge A. Prognosis of pregnancy-associated breast cancer. *Breast Cancer Res Treat*. 2017;163:417-421.