

Poor survival rate of pregnancy-associated breast cancer in Asian countries

Dear Editor,

Asia has a lower incidence of breast cancer than North America, Oceania, and Western Europe. However, breast cancer rates have been rising fast in recent decades.¹ Breast cancer cases in Asian countries now constitute 40% of all cases diagnosed globally, and mortality due to breast cancer has similarly risen among Asian women.¹ With an estimated age-standardised rate of 29.1 per 100,000, the rate of breast cancer incidence in Asia is projected to range from one-fourth to one-third of those in high-risk regions.² Due to the increase in the prevalence of breast cancer along with delayed childbirth and low parity, pregnancy-associated breast cancer (PABC) cases are subject to rise in Asian countries. This article aims to raise awareness on PABC, which is rare but increasingly common.

Breast cancer that develops during or within a year after pregnancy is known as PABC, and it poses a diagnostic and treatment challenge. PABC can be described as breast cancer occurring during pregnancy or within 1 year of childbirth.³ It can also involve cases of breast cancer identified within 2 years of delivery⁴ or 5 years after childbirth.⁵ The definition of PABC varies, which could lead to different conclusions about the relationship between pregnancy, postpartum stage and breast cancer.

PABC patients in Asian populations studied had a lower survival rate than their non-pregnant counterparts.^{6,7,8,9,10} A study on Japanese women observed poorer prognoses in breast cancer patients with recent childbirth, than in individuals who had given birth less recently or were nulliparous. The 5-year survival rate of Japanese women with less than 2 years of pregnancy and PABC was 64.3% compared to 90.6% in non-PABC women.⁶ In a Korean population, survival was significantly shorter in PABC patients with a 5-year survival rate of 80.11%, compared to non-PABC patients at 95.99%; similarly, 5-year survival rate was lower in patients with postpartum breast cancer at 77.15% compared to non-PABC group at 95.97%.⁷ In a Taiwanese population, the 5-year survival rate in the antepartum PABC group was 65.7% while that in the postpartum group was 81.8%; and in the non-PABC group was 90.5%. No significant differences were observed in overall survival among the 3 groups ($P=0.15$).⁸ In a retrospective study of 110 women with breast cancer in Saudi Arabia, 33 patients in the pregnant group died. The 5-year survival rate of PABC

was 65% and 82% in non-PABC patients ($P=0.002$). Disease-free survival of PABC was 47.5% compared with 65.4% in the non-PABC group.⁹ In a nationwide population-based study, 30,230 breast cancer patients from 2002 to 2014 were identified from the cancer registry in Taiwan. Among them, 90 cases were antepartum, 347 were identified within 1 year after delivery, and 1,993 were identified from 1 to 5 years after delivery. In the study, a total of 2,920 patients died from breast cancer by the end of 2014, and breast cancer was the leading cause of mortality in 89% of the patients.¹⁰ Among breast cancer patients in India, the 3-year overall survival rate in the antepartum group was 74.2% (95% confidence interval [CI] 58.3–94.4) and in the postpartum group was 62.8% (95% CI 47.9–82.3).¹¹

Women who had breast cancer and recent previous pregnancies less than 2 years were 2.9 times more likely to die than non-PABC women (hazard ratio [HR] 2.9, 95% CI 1.05–4.56; $P=0.036$).⁶ Postpartum breast cancer in Korean women was related to a worse survival rate (HR=1.57, 95% CI 0.82–2.99; $P=0.1708$).⁷ On the other hand, breast cancer during pregnancy was not related to a lower risk of survival, with a multivariable HR of 1.09 (95% CI 0.15–7.91; $P=0.9355$).⁷ In a Taiwanese study, all postpartum breast cancer patients had a greater mortality rate compared to those without a pregnancy history. Antepartum PABC cases had an HR of 1.9 (95% CI 1.17–3.12), and postpartum PABC cases had an HR of 1.92 (95% CI 1.48–2.48).¹⁰

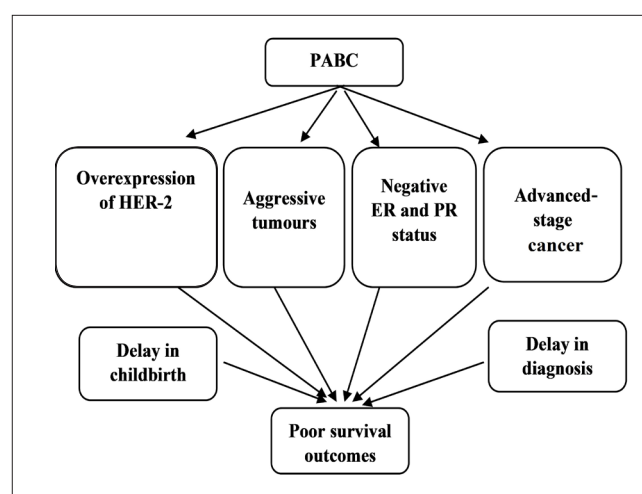


Fig 1. Factors contributing to poor survival in PABC.
ER: estrogen; receptor; HER-2: human epidermal growth factor receptor 2; PABC: pregnancy-associated breast cancer; PR: progesterone receptor

Fig. 1 shows possible factors for poor survival observed in PABC women. The factors include aggressive tumours, advanced-stage cancer, and overexpression of human epidermal growth factor receptor 2 (HER-2) along with the negative status of estrogen receptor (ER) and progesterone receptor (PR).¹² These factors, combined with a delay in diagnosis and childbirth, can lead to poor survival outcomes, as observed in several studies. Aggressive tumour features in young breast cancer patients who had just given birth were noted in a study conducted on Japanese women.⁶ Tumours of >5cm size were more common in the pregnant (21.1%) and postpartum groups (18.4%) than in non-pregnant women (7.9%).¹⁰ Similarly, a higher proportion of negative ER and PR status has been found in the PABC group.^{7,9,10} Advanced-stage cancer was more common in PABC women than in the non-PABC group in a study on Saudi women. This was significant ($P=0.01$) in 55.7% of patients with advanced-stage cancer in the PABC group compared with 36.7% in the non-PABC group.⁹ In Taiwanese women studied, advanced-stage cancer was more prevalent in those with a breast cancer diagnosis during gestation (16.7%) and within 1 year of childbirth (18.4%) than those without any record of pregnancy (9.7%).¹⁰ PABC patients who delivered within 2 years had a significantly more advanced stage, larger size, more axillary lymph node involvement, higher histological grade, and more progesterone receptor negative, HER2 positive, and triple negative tumours than those who had given birth less recently or women who never gave birth.⁶ Overexpression of HER-2 has also been common in PABC cases. A retrospective study from a tertiary medical centre in Taiwan reported overexpression of HER-2 in the PABC group (47.6%) than in their non-pregnant counterparts (19.7%).⁸ Similarly, overexpression of HER-2 was noted in the PABC group in the Saudi population⁹ and the Chinese population.¹³ Another study on Taiwanese women also reported higher expression of HER-2 in 36.36% of pregnant women and 26.5% of postpartum cases compared to 24.57% of those without a recent pregnancy record. Overexpression was also common in 32% of patients with >1 to ≤2 years postpartum PABC and 29.56% of those with >2 to ≤5 years postpartum PABC.¹⁰

In conclusion, a low survival rate for PABC was prevalent in different populations across Asia. However, most PABCs had favourable maternal and fetal outcomes and delivered healthy infants.^{11,13} For any comparison for survival between PABC and non-PABC patients, staging is the main prognostic factor that should be adjusted or matched. We would like to highlight the importance of understanding the behaviour of PABC in Asian women and developing required treatment plans.

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REFERENCES

1. Kim Y, Yoo KY, Goodman MT. Differences in incidence, mortality and survival of breast cancer by regions and countries in Asia and contributing factors. *Asian Pac J Cancer Prev* 2015;16:2857-70.
2. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer* 2015;136:E359-86.
3. Keyser EA, Staat BC, Fausett MB, et al. Pregnancy-associated breast cancer. *Rev Obstet Gynecol* 2012;5:94-9.
4. Gooch JC, Chun J, Kaplowitz E, et al. Pregnancy-associated breast cancer in a contemporary cohort of newly diagnosed women. *Breast J* 2020;26:668-71.
5. 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;138:549-59.
6. Nagatsuma AK, Shimizu C, Takahashi F, et al. Impact of recent parity on histopathological tumor features and breast cancer outcome in premenopausal Japanese women. *Breast Cancer Res Treat* 2013;138:941-50.
7. Choi M, Han J, Yang BR, et al. Prognostic Impact of Pregnancy in Korean Patients with Breast Cancer. *Oncologist* 2019;24:e1268-76.
8. Yang YL, Chan KA, Hsieh FJ, et al. Pregnancy-associated breast cancer in Taiwanese women: potential treatment delay and impact on survival. *PLOS ONE* 2014;9:e111934.
9. Suleman K, Osmani AH, Hashem H, et al. Behavior and outcomes of pregnancy associated breast cancer. *Asian Pac J Cancer P* 2019;20:135-8.
10. Chuang SC, Lin CH, Lu YS, et al. Association of pregnancy and mortality in women diagnosed with breast cancer: A Nationwide Population Based Study in Taiwan. *Int J Cancer* 2018;143:2416-24.
11. Bajpai J, Simha V, Shylasree TS, et al. Pregnancy associated breast cancer (PABC): Report from a gestational cancer registry from a tertiary cancer care centre, India. *Breast* 2021;56:88-95.
12. Genin AS, Lesieur B, Gligorov J, et al. Pregnancy-associated breast cancers: do they differ from other breast cancers in young women? *Breast* 2012;21:550-5.
13. Jin YC, Du JX, Fu SM, et al. A retrospective clinical study of patients with pregnancy-associated breast cancer among multiple centers in China (CSBrS-008). *Chin Med J (Engl)* 2021;134:2186-95.

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