



Pregnancy and Lactation: Risk or Protective Factors for Breast Cancer?

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Abstract

Pregnancy and lactation represent the most effective protective elements against breast cancer; counter-intuitively breast cancer incidence shows a small but noticeable increase up to 5 years after delivery. The cumulative effect is however favourable and women show a reduction in breast cancer risk which is proportional to the total duration of lactation and to the number of full-term pregnancies.

Keywords

Breast cancer · Breastfeeding · Cancer risk · Pregnancy · Protective factors

27.1 Overview

The increasing incidence of breast cancer has been partially attributed to changing patterns of lifestyle including reproductive factors. Later marriage, fewer pregnancies, and shorter duration of breastfeeding are known to influence the risk of breast cancer.

27.2 Pregnancy and Breastfeeding as Protective Factors for Breast Cancer

27.2.1 Pregnancy

The protective role of pregnancy on breast cancer development was established 50 years ago, with the publication of a paper discussing the protective role of parity on breast cancer and the varying effect of age at first pregnancy [1]. This observation; however, was not novel: the effect of pregnancy (and breastfeeding) on breast cancer was suggested by Ramazzini in the 18th century. He was the first to report that breast cancer was particularly frequent in convents. This information is still relevant because even today nuns have a higher mortality risk from breast cancer [2]. Later studies established that protection is increased by an increase in the number of pregnancies and time of breastfeeding. The

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mechanism behind this protective effect is not clear, and a role for mammary stem cells has been suggested [3].

Parous women have a reduced mortality for all cancers and for breast cancer specifically [4], and this effect is particularly evident for full-term pregnancy at an early age. Recently, reproductive behaviors have been studied in relation to different subtypes of breast cancer, and it has been shown that parity reduces the risk of luminal breast cancer but not that of HER2-positive or triple-negative breast cancer (TNBC). On the contrary, age at first pregnancy has a different effect in that old age at first pregnancy increases the risk of luminal breast cancer but not that of HER2-positive breast cancer or TNBC [5]. The effect of parity in *BRCA*-mutated women appears to be less consistent, with differences according to the gene involved [6].

27.2.2 Breastfeeding

Several studies have shown the protective effect of breastfeeding on breast cancer, and it has been suggested that incidence of breast cancer in developed countries could be impressively reduced if childbearing behavior (parity, duration of breastfeeding) of women in developed countries was similar to that of women in developing countries [7]. A detailed analysis of molecular subtypes of breast cancer showed that not all types are reduced to the same extent and that breastfeeding reduces the risk of luminal breast cancer and TNBC [5, 8, 9] but not that of HER2-positive cancer [5]. Breastfeeding also plays a protective role for women carrying a *BRCA* mutation, but this has been shown in *BRCA-1*-mutated cases, and not yet in *BRCA-2*-positive patients [10].

27.3 Pregnancy as a Risk Factor for Breast Cancer

Most breast cancers are sporadic, and the etiology of the disease is not well understood; although it is now clear that some external factors such as the pattern of reproductive behavior can

modulate the risk. Many epidemiological studies have indicated that the long-term protective effect of pregnancy on the risk of breast cancer is preceded by a short-term adverse effect, with an increase in breast cancer risk for the first 5 years after delivery as compared with other periods afterward [11] (see also Chap. 23). As reported by Bruzzi et al. [12], the relative risk for breast cancer in women who had given birth to a child during the previous 3 years was 2.66 compared with women whose last childbirth had occurred 10 years ago, or more. The risk slowly decreased thereafter.

Along with these data, a study on Swedish women published by Lambe et al. [13] comprising approximately 75,000 patients reported that primiparous women were at a higher risk of breast cancer than nulliparous women for up to 15 years after childbirth and at a lower risk thereafter. The excess of risk was most pronounced among those who were older at the time of first delivery (odds ratio, 1.26; 95% CI, 1.10–1.44; 5 years after delivery among women who were 35 years old at the first delivery). Some years later, the same group reported a case-control study [14] comparing primiparous with nulliparous women and showed that a transient increase in maternal breast cancer risk peaked 5 years following delivery (odds ratio, 1.49; 95% CI, 1.01–2.20) and leveled off 15 years postpartum. Women who had given birth to two children had a transient increase in risk that was lower at its peak than that of primiparous women, occurring about 3 years following the second delivery. This time window of 5 years postpartum may define the latent period required for pregnancy hormones to promote the progression of normal breast cells toward early stages of malignant transformation.

Despite this slight increase in breast cancer risk after delivery, an extensive body of epidemiological studies has proved a strong and lifelong protective effect of early full-term pregnancy [1, 11, 15, 16]. This protective effect is at least 50% for a pregnancy occurring before the age of 20 years, meaning that women that had an early pregnancy develop 50% fewer cancers compared with nulliparous women. On the other hand, there is an overall increase in the risk of breast

tumors for first pregnancies after the age of 35 years [17].

Regarding breast cancer subtype, a meta-analysis [5] of 15 studies including 21,941 cancer patients and 864,177 controls showed that parity was associated with a 25% risk reduction of developing a luminal subtype (OR, 0.75; 95% CI, 0.70–0.81; $P < .001$), but advanced age at first birth was associated with an increased risk of developing a luminal subtype (OR, 1.15; 95% CI, 1.00–1.32; $P = .05$). The data above show that there is a nonlinear relationship between breast cancer incidence and time interval since delivery.

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