

# Breastfeeding as a Protective Factor against Breast Cancer: A Systematic Review

## Abstract

Breast cancer accounts for 24.5% of all cancer cases and 14% of all cancer deaths in women globally. Breastfeeding is thought to lower the risk of breast cancer mainly through two mechanisms; differentiation of breast tissue and a decrease in the total number of ovulatory cycles throughout a woman's lifetime. The objective of this systematic review is to investigate the published literature that studied breastfeeding and its duration as a possible protective factor for the development of breast cancer. PubMed, Web of Science, Science Direct, EBSCO, and Cochrane library were searched. Study articles were screened by title and abstract using Rayyan QCRI then a full-text assessment was implemented. Fifteen studies published between 2000 and 2022 with a total of 27315 breast cancer patients were included. Most included studies reported that breastfeeding and its longer duration play a protective role against breast cancer. Only three studies reported no association between breastfeeding and breast cancer development. So, our systematic review found that breastfeeding, especially breastfeeding of longer duration, was considered a protective factor against breast cancer. Therefore, it was advised that data on breastfeeding duration should be gathered by researchers in order to possibly lower the incidence of breast cancer. If breastfeeding offers protection against breast cancer, a more thorough analysis of potential confounders may shed light on how this protection is achieved. This systematic review reported that breastfeeding, especially breastfeeding of longer duration, was considered a protective factor against breast cancer.

**Keywords:** Breast cancer, Breastfeeding, Malignancy, Systematic review

## Introduction

Breast cancer accounts for 24.5% of all cancer cases and 14% of all cancer deaths in women globally. About half of all breast cancer cases and 60% of all cancer deaths are thought to occur in economically developing nations.<sup>[1]</sup> Breast cancer is the most often diagnosed type of cancer.<sup>[2]</sup> Breast cancer incidence rates have been rising in many African and Asian nations while declining in some western countries since 2000.<sup>[3]</sup>

Many investigations have been made to locate and measure the effects of related genetic and environmental risk factors. Other risk factors include early menarche, or before age 10, later maternal age at first full-term pregnancy (between 30 and 40 years), and brief breastfeeding intervals.<sup>[4]</sup>

Breastfeeding is thought to decrease women's risk of breast cancer through two main mechanisms. The first is the differentiation of breast cells, where they are changed to produce milk after

pregnancy, reducing the sensitivity of the breast tissues to carcinogenic effects (estrogens), and the second is breastfeeding which reduces lifetime exposure to the mitogenic effect of estrogens, preventing ovulation.<sup>[5]</sup> The destruction of the damaged DNA cells is aided by releasing a carcinogen from human milk and the exfoliation of the breast tissues. As a result, the responsiveness to mutations is reduced.<sup>[6]</sup> As a result, it is believed that lactation amenorrhea may influence the decline in breast cancer by lowering hormone levels.<sup>[7, 8]</sup> The history and length of breastfeeding were considered potential protective factors because of this.<sup>[9]</sup> Although some studies have supported this theory, their results have been ambiguous because of the various breastfeeding practices that can influence the hormonal changes in a woman's body during lactation.<sup>[10]</sup> As a result, some studies' findings<sup>[11, 12]</sup> did not support the link between breastfeeding and breast cancer.

Various studies and reviews have independently identified various risk factors

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for breast cancer.<sup>[13]</sup>

### Study objective

The objective of this systematic review is to investigate the published literature that studied breastfeeding and its duration as a possible protective factor for the development of breast cancer.

### Materials and Methods

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were adhered to in this systemic review.

### Study design

The systematic review approach was followed in the study.

### Study condition

This review examines research that looked into breastfeeding and its duration as a possible protective factor for the development of breast cancer.

### Search strategy

To find the relevant literature, a comprehensive literature search was done in four main databases, EBSCO, PubMed, Web of Science, and Cochrane Library. Only the articles written in English were considered. Each database's specific requirements were taken into account. In order to find the appropriate studies, the following keywords were transformed into Mesh terms in PubMed; "Breastfeeding," "Risk factor," "Hazardous factor," "Protective factor," "Breast cancer," "Breast carcinoma," and "Breast malignancy." The "OR" and "AND" Boolean operators were combined with the relevant keywords. English, full-text publications, freely accessible articles, and human trials were all included in the search results.

### Selection criteria

#### Inclusion criteria

According to the following criteria, subjects were chosen for inclusion based on their relevance to the research; breast cancer patients whose breastfeeding period had been investigated as a potential risk factor.

#### Exclusion criteria

The results of any additional papers, ongoing studies, or reviews of existing studies without the mentioned inclusion criteria as their primary goal were dismissed.

### Data extraction

Rayyan (QCRI) was employed to find replicates of the various studies.<sup>[14]</sup> The relevance of the abstracts and titles was assessed based on a limited inclusion/exclusion criterion set. All the papers that met the inclusion criteria were perused entirely by the reviewers. The authors discussed how to resolve any disagreements. The qualified study was included using a data extraction form that was created. The data obtained from the files included; participant number, authors, Clinical Cancer Investigation Journal | Volume 11 | Issue 5 | September – October 2022

study year, title, design, mean age, family history of breast cancer, mean duration of breastfeeding, and main findings.

### Risk of bias assessment

The qualitative data synthesis used the non-randomized studies ROBINS-I technique<sup>[15]</sup> to assess the quality of the included research. The reviewers investigated and fixed any discrepancies in the quality assessment.

### Strategy for data synthesis

In order to provide a qualitative overview of the included study components and results, summary tables containing the data gathered from the eligible studies were created. After the systematic review's data extraction procedure was finished, choices were made about utilizing the data from the included study articles. Some studies were excluded as they did not align with the study's aims, even though they met the full-text inclusion criteria.

### Results and Discussion

#### Search results

Fifty-two duplicate studies were removed from the total 942 results of the search. Six hundred-one studies were released after the screening of the titles and abstracts. Ten out of the 289 reports sought for retrieval were not found, leaving a total of 279 articles. Finally, a full-text assessment was performed on these, and; 180 were excluded for wrong study outcomes, 50 for unavailable data breastfeeding, and 32 for the wrong population type. Seventeen eligible study articles were included in this systematic review. The included studies was presented according to our study objectives (**Table 1**). The study selection process summary is indicated in **Figure 1**.

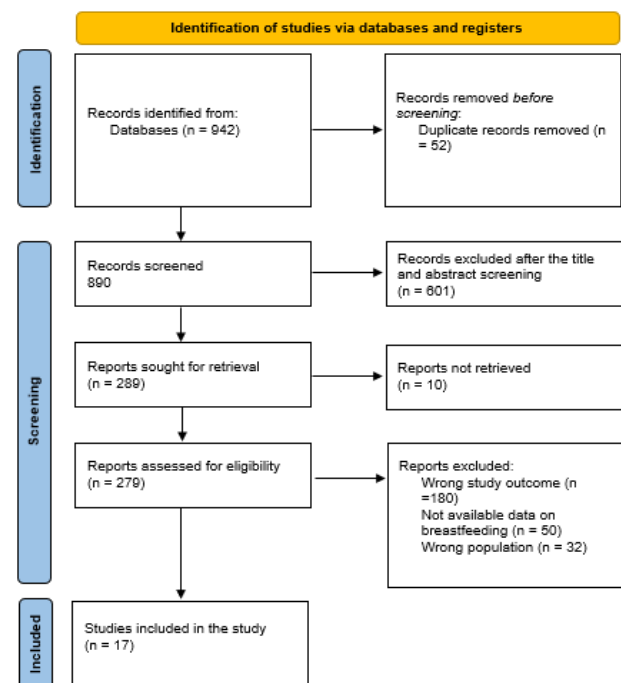


Figure 1. PRISMA flowchart of the study selection process.

**Table 1. A summary of characteristics of the included study articles.**

Study	Study design	Country	Total Participants	Mean age (y)	Family history of breast cancer (%)	Mean duration of breastfeeding (Months)	Key findings	ROBINS-I
Sangaramoorthy <i>et al.</i> , 2019 <sup>[16]</sup>	Retrospective study	USA	2703		12	11	Breastfeeding was associated with a lower risk of breast cancer in Hispanic women, as shown in other populations.	High
Ilic <i>et al.</i> , 2015 <sup>[17]</sup>	Case-control	Serbia	191	35-80	6.8	0 to $\geq 13$	Breastfeeding was linked to an increased risk of breast cancer.	Moderate
González-Jiménez <i>et al.</i> , 2014 <sup>[18]</sup>	Retrospective study	Spain	504	NA	40.3	NA	Breastfeeding for periods of more than six months protects mothers from serious conditions, including breast cancer, especially non-smoker women.	Moderate
Butt <i>et al.</i> , 2014 <sup>[19]</sup>	Prospective cohort	Sweden	13531	57.7	NA	0 to $\geq 13$	Breast cancer subgroups did not show any significant results, and breastfeeding duration was not linked to breast cancer risk.	Moderate
Kumar <i>et al.</i> , 2014 <sup>[20]</sup>	Case-control	India	128	25-78	NA	NA	Breastfeeding significantly lowers breast cancer risk; therefore, promoting breastfeeding and raising awareness of this disease through information, education, and communication campaigns are urgently needed.	Moderate
Stecklein <i>et al.</i> , 2017 <sup>[21]</sup>	Retrospective study	USA	82	23-78	NA	0.5 - 66	A scarcity of breastfeeding history may indicate a worse prognosis in parous women with inflammatory breast cancer.	High
Fernández-Aparicio <i>et al.</i> , 2022 <sup>[22]</sup>	Retrospective study	Spain	524	19-91	55	NA	Subjects who had breastfed their infants for more than three months, on average, had breast cancer at a more advanced age.	Moderate
Alsaker <i>et al.</i> , 2011 <sup>[23]</sup>	Retrospective study	Norway	2640	NA	NA	14.7 $\pm$ 13	Breastfeeding appears to have little impact on the survival of breast cancer patients.	Low
Akbari <i>et al.</i> , 2011 <sup>[24]</sup>	Case-control	Iran	376	45.9 $\pm$ 9.5	22.8	12.4 $\pm$ 9.04	Full-term pregnancies and parities significantly decreased breast cancer risk with effective breastfeeding.	Moderate
Tryggvadóttir <i>et al.</i> , 2001 <sup>[25]</sup>	Case-control	Iceland	993	NA	NA	11.25	Breastfeeding lowers the risk of breast cancer diagnosed in people under 40, and it may also provide some protection for cases diagnosed in older people.	High
Awatef <i>et al.</i> , 2010 <sup>[26]</sup>	Case-control	Tunisia	400	48.9	1.25	73–108	Breastfeeding was linked to a decreased risk of breast cancer in pre and postmenopausal women.	Moderate
Lord <i>et al.</i> , 2008 <sup>[27]</sup>	Case-control	USA	969	55-64	NA	NA	The fact that breastfeeding offers extensive protection against breast cancer may be used to advocate for breastfeeding among these women.	Moderate

Tessaro <i>et al.</i> , 2003 <sup>[28]</sup>	Case-control	Brazil	250	47 ± 6.5	NA	6 - 25	Breastfeeding and breast cancer did not correlate.	High
Chang-Claude <i>et al.</i> , 2000 <sup>[29]</sup>	Case-control	Germany	553	20-52	12.3	NA	In primarily premenopausal women, prolonged breastfeeding has a protective effect against breast cancer.	Moderate
Gajalakshmi <i>et al.</i> , 2009 <sup>[30]</sup>	Case-control	India	898	NA	NA	NA	Premenopausal women who breastfeed for an extended period have a significantly lower risk of developing breast cancer.	Low
Shinde <i>et al.</i> , 2010 <sup>[31]</sup>	Retrospective study	USA	2473	NA	33.5	2.22 ± 4.31 (Per child)	The absence or small duration of breastfeeding was independently linked to triple-negative breast cancer in women with invasive breast cancer.	High
De Silva <i>et al.</i> , 2010 <sup>[32]</sup>	Case-control	Sri Lanka	100	NA	16	NA	Long-term breastfeeding significantly lowers the risk of breast cancer, and a dose-response relationship has been shown to support this protective effect.	Moderate

## Characteristics of the included studies

Seventeen study articles were incorporated in this review, with 27315 patients who developed breast cancer. Four studies were conducted in the USA,<sup>[16, 21, 27, 31]</sup> two in Spain,<sup>[18, 22]</sup> two in India,<sup>[20, 30]</sup> one in Serbia,<sup>[17]</sup> one in Sweden,<sup>[19]</sup> one in Norway,<sup>[23]</sup> one in Iran,<sup>[24]</sup> one in Iceland,<sup>[25]</sup> one in Tunisia,<sup>[26]</sup> one in Brazil,<sup>[28]</sup> one in Germany,<sup>[29]</sup> and one in Sri Lanka.<sup>[32]</sup> Eleven studies were case-control,<sup>[17, 20, 24-30, 32]</sup> six were retrospective in nature,<sup>[16, 18, 21-23, 31]</sup> and one was a prospective study.<sup>[19]</sup> Patients with a family history of breast cancer ranged from 1.25%<sup>[26]</sup> to 55%.<sup>[22]</sup> All included studies reported that breastfeeding and its longer duration play a protective role against breast cancer and significantly decrease its incidence. Only four studies reported no association between breastfeeding and breast cancer development.<sup>[17, 19, 23, 28]</sup> One study demonstrated a worse prognosis of breast cancer in women with short breastfeeding duration.<sup>[21]</sup>

This systematic review is inconclusive as it lacks the quantitative factor to provide a precise finding regarding breastfeeding as a protective factor against breast cancer development. Moreover, this systematic review's papers did not provide consistent results regarding the relationship between ever breastfeeding versus never breastfeeding and the risk of breast cancer.

This study reported that most included studies demonstrated an independent and significant association between breastfeeding and its duration and breast cancer development. Breastfeeding was an important protective factor against breast cancer. Similarly, a previous systematic review and meta-analysis reported that women are more protected against breast cancer the longer they breastfeed. The high incidence of breast cancer in developed nations is primarily attributed to the absence or short lifetime duration of breastfeeding, which is typical of women in these nations.<sup>[33]</sup>

In contrast, other reviews have reported that breastfeeding has

no strong association with breast cancer risk, comprising a review of 15 articles published between 1989 and 2001,<sup>[34]</sup> a review of 22 articles included postmenopausal women,<sup>[35]</sup> and a review of two large prospective analyses from high-income countries.<sup>[36]</sup> But other studies have discovered a weak but statistically significant protective association between ever breastfeeding and breast cancer. There was a 20% reduction in breast cancer risk for women who had ever breastfed, per a review of 21 studies published between 1985 and 1996.<sup>[37]</sup>

The lack of a standardized protocol for categorizing the lifetime number of breastfeeding months for analysis is one of the difficulties in comparing studies of accumulated breastfeeding duration and determining its actual impact on breast cancer risk. The difficulty in determining how breastfeeding affects breast cancer risk is not just this. For instance, it might be crucial to divide any analysis of the risk of breast cancer into groups based on menopausal status. Breastfeeding is only believed to be protective (or at least more protective) against breast cancer in premenopausal women, according to some previous studies.<sup>[38, 39]</sup>

The potential physiological mechanisms that breastfeeding may protect against breast cancer must also be considered in epidemiological studies. According to the differentiation theory, research on breast cancer and lactation is necessary to evaluate the distinct effects of lactation and pregnancy. Three population groups, including nulliparous women, parous women who have never breastfed, and parous women who have breastfed, should, at the very least, be taken into account. The number of pregnancies and total months of breastfeeding could be used to segment further the group of women who have breastfed. The pregnancy's number and woman's age during her first full-term pregnancy are also important considerations because they may affect her risk of developing breast cancer and may be linked to the differentiation of her breast tissue.<sup>[40, 41]</sup>



In this systematic review, only three studies found no connection between breastfeeding and the development of breast cancer.<sup>[19, 23, 28]</sup> Why breastfeeding would lower the risk of breast cancer is unclear. Although several mechanisms have been proposed, a biological explanation for the inverse relationship between breastfeeding and breast cancer risk has not been sufficiently clarified. According to one theory, breastfeeding results in long-term endogenous hormonal changes, including possibly decreased estrogen and increased prolactin production. This could result in a woman's cumulative estrogen exposure being lower, inhibiting the development or growth of breast cancer cells.<sup>[28, 42]</sup>

The mammary gland epithelium or the stromal tissue surrounding it may undergo permanent changes due to reproductive factors, and the occurrence and timing of pregnancy may be associated with the most noticeable effects.<sup>[43, 44]</sup> The effects may also depend on the underlying genetic susceptibility for breast cancer,<sup>[43]</sup> and the tissue changes could make the breast more or less susceptible to carcinogenic factors. As a result, it is conceivable that variables such as age at menarche, when pregnancies occur, whether or not women breastfeed, and age at menopause could cause or prevent particular types of aggressive breast cancer.<sup>[45]</sup>

## Conclusion

Our systematic review of 17 studies of different designs published between 2000 and 2022 found that breastfeeding, especially breastfeeding of longer duration, was considered a protective factor against breast cancer. Therefore, it was advised that data on breastfeeding duration should be gathered by researchers in order to possibly lower the incidence of breast cancer. If breastfeeding offers protection against breast cancer, a more thorough analysis of potential confounders may shed light on how this protection is achieved.

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## Conflict of interest

None.

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## Ethics statement

None.

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