

Systematic Review

Breastfeeding Impact on Cancer in Women: A Systematic Review

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Keywords:

Breastfeeding Breast cancer Ovarian cancer Breastfeeding benefits

Received: February 1, 2024 Revised: February 19, 2024 Accepted: February 25, 2024 Published: March 8, 2024

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Citation: Abdullah AS, Ali HO, Muhammed HM, Pashtiwan LRA, Ali RM, Ahmed NHA. Breastfeeding Impact on Cancer in Women: A Systematic Review. Barw Medical Journal. 2024 Mar 8;2(1):47-55.

https://doi.org/10.58742/2xcsfx91

Abstract

Introduction

Many studies have emphasized the impact of breastfeeding on the health of both the mother and the infant, especially its impact on the different types of cancers that can develop in the mother. Due to the ongoing conflict regarding whether or not breastfeeding reduces, increases, or has no impact on the risk of cancer, this systematic review was conducted to settle this conflict and shed light on the issue.

Methods

The CINAHL, PubMed/MEDLINE, Cochrane Library, Web of Science, and EMBASE databases were thoroughly searched to identify any studies published in the English Language up to November 25th, 2023.

Results

Out of the initial 170 papers the systematic search brought, 16 of them met all the criteria and were left to be included in the study. A sum of 29,100 patients were included in the study with 19,905 of them having breastfed. A total of 14,817 patients were developing different types of cancer and within them, breast cancer was the most frequent. Furthermore, there seemed to be a majority association between breastfeeding and cancer in the mother as most of the studies concluded that breastfeeding is observed to decrease the risk.

Conclusion

The majority of studies support the hypothesis that breastfeeding and breastfeeding duration both lower the risk of cancer, especially breast cancer, developed in the mother.

1. Introduction

Breast feeding, also referred to as nursing, is the physiological process whereby a mother feeds breast milk to her infant. This can be performed either directly from the breast or through pumping the breast and bottle-feeding the infant [1]. As far as

contents go, it is made up of all of the nutrients required by an infant within the first 6 months of life [1,2]. Although the exact composition of human breast milk varies based on environmental factors such as the maternal diet, it is mainly composed of the necessary carbohydrates, fats, proteins, vitamins, minerals, and water the infant requires [2,3].

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Furthermore, breastfeeding also provides the infant with the bioactive molecules that take part in organ development, microbial gut colonization, and immune maturation, among others [4]. According to the World Health Organization (WHO), breastfeeding is recommended to be initiated within the first hour of life, given exclusively for up to 6 months, and continued for 2 years; however, women usually do not breastfeed for the recommended time frame given by health experts [5,6]. This is very problematic not only for the infant but also for the mother since breastfeeding has been linked with numerous short-term and long-term health improvements in the mother [7]. In the short run, breastfeeding has been associated with postpartum weight loss in the mother, while in the long term, improvement in diabetes, metabolic, and cardiovascular health are among the benefits. One other benefit breastfeeding is associated with is cancers of the reproductive system in women. Breastfeeding has been observed to decrease the risk for reproductive cancers and this could be attributed to the reduced lifetime exposure to certain hormones like estrogen [8]. According to a meta-analysis conducted by the Collaborative Group on Hormonal Factors in Breast Cancer, both breastfeeding and the average lifetime duration of breastfeeding were inversely correlated with breast cancer [9]. On the contrary to the aforementioned studies, there are studies on the opposite end of this spectrum that found out that breastfeeding is associated with a more aggressive type of breast cancer as well as an earlier presentation [10].

As a result of the ongoing conflict on the impact of breastfeeding on cancer in the mother and the lack of a solid association establishment, we aim to conduct a systematic review with the hope of enlightening the literature with a more definitive correlation.

2. Methods

2.1. Study design

The guideline that was chosen in this systematic review was the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.

2.2. Data sources and search strategy

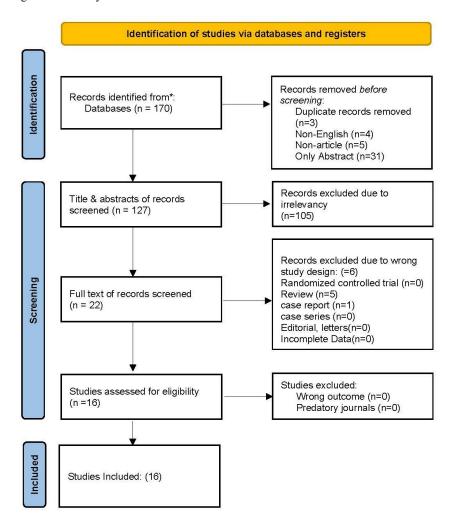


Figure 1. Study selection PRISMA flow chart.

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	11	Over- weight	N/A	N/A	N/A	N/A	N/A	N/A	4372	277	36	125	N/A	1169	N/A	382	N/A	N/A
er	BMI	Normal	N/A	N/A	N/A	N/A	N/A	N/A	1284	312	64	104	N/A	988	N/A	1824	N/A	N/A
Risk factor associated with cancer	parity	>3	*_	132	*	301	105	N/A	2201	N/A	N/A	94	N/A	N/A	*(383	N/A	1130
ociated	Mean parity	1-3	1.87*	1138	2.3*	330	71	N/A	3756	N/A	N/A	94	N/A	N/A	4.0*	1843	N/A	2230
actor ass	A.O.M.I.Y	<u>≥</u> 12	12.8*	N/A	13.2*	N/A	N/A	414	4649	N/A	95	N/A	N/A	N/A	16*	N/A	N/A	988
Risk f	A.O.	<12	12	N/A	13	N/A	N/A	15	1308	N/A	8	N/A	N/A	N/A	1	N/A	N/A	3364
	B.F.D.I.M	× ×	3.5*	478	7.1*	N/A	63.9*	N/A	11.0*	N/A	N/A	N/A	N/A	499	12.0*	705	325	978
	B.F.	1-5	6	365	7	N/A	63	N/A	11	N/A	N/A	N/A	N/A	640	12	878	573	954
2		В.	1930	1249	357	616	901	326	4398	592	50	198	1871	1159	1441	1583	868	2336
2	V 0	D.D.C	965	748	0	341	512	217	3254	0	50	121	2546	1653	2403	1345	1244	3833
2	S 0	D.C	965	853	510	347	389	217	2703	592	50	108	2546	586	2403	881	1231	436
Ţ.		>20				464			1548			98		2122				
Age (year)	•	49	39*	41.5*	54.7*	143	48.7*	44.9*	850	59.9**	N/A	79	54*	116	N/A	N/A	54.5*	N/A
Ì		\ \ \ \ \				81			305			54		0				
E	1ypes of	developed	Breast Cancer	Breast Cancer	Breast Cancer	Breast Cancer	Breast Cancer	Breast Cancer	Breast Cancer	Breast Cancer	Breast Cancer	Breast Cancer	Breast Cancer	Endometrial Cancer	Breast Cancer	Epithelial Ovarian Cancer	Ovarian	Epithelial Ovarian Cancer
	N. of	patients	1930	1601	510	889	901	434	5957	592	100	229	2546	2239	2403	2226	2475	4269
	Publication	date	2004	2006	2012	1975	1971	2015	2020	2013	2017	2000	2014	2000	1977	2012	2009	1990
	Study	design	Cohort	Cohort	Cohort	Case Control	Case Control	Case Control	Case Control	Cohort	Case Control	Case Control	Case Control	Case Control	Cohort	Case Control	Case Control	Case Control
	Country	Country	Canada	Germany	Spain	South Africa	Lebanon	Ethiopia	United States	Sweden	United States	Korea	United States	United States	Japan	United States	United States	United States
	Author	Author	Jernström et al. (12)	Andrieu et al. (13)	Redondo et al. (14)	Anderson et al. (15)	Abdou-Daoud et al. (16)	Mengesha et al. (17)	Sangaramoorthy et al. (18)	Gustbée et al. (10)	Afzal at al. (19)	Do et al. (20)	Lehman et al. (21)	Newcomb et al. (22)	Ing et al. (23)	Jordan et al. (24)	Titus-Ernstoff et al. (25)	Gwinn et al. (26)

* Mean, ** Median, N.O.P. W.B.: Number of Patients Who Breastfed, B.F.D.I.M: Breast Feeding Duration in Months, N.O.P.W.D.C: Number of Patients Who Developed Cancer, T.O.C.D: Type of Cancer Developed, A.O.M.I.Y: Age of Menarche In Years, N.O.P.I.M: Number of Patients in Menopause, A.O.P.: Age of Pregnancy, O.C.P: Oral Contraceptive Pills, B.M.I: Body Mass Index (Normal = 18.5-24.9), (Overweight= >25)

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Through the CINAHL, PubMed/MEDLINE, Cochrane Library, Web of Science, and EMBASE databases, a systematic search was conducted to identify studies published up to November 25th, 2023. The search was done using these keywords: (breastfeeding cancer OR Breastfed OR metastatic OR metastasis OR metastases OR cancers OR carcinoma OR lactation OR malignancy OR malignant OR carcinomas). The search was limited to studies in the English language.

2.3. Eligibility criteria

Only studies that met these inclusion criteria were included in this systematic review: 1) Studies that were either a cohort or a case-control study. 2) The study included patients who breastfed. 3) The association of breastfeeding was studied with the probability of developing cancer in the mother.

2.4. Study selection and data items

Two different researchers first worked on screening the titles and the abstracts of the mentioned studies and selecting them based on the previously mentioned inclusion criteria. Whenever there was a disagreement or a conflict among the researchers, a third researcher joined in to settle the conflict

2.5. Data items

Multiple data were collected from the included articles, including the year of publication, first author, country, study design, breastfeeding, breastfeeding duration, number of patients who developed cancer, type of cancer-associated, age of menarche, parity, BRCA1/BRCA2 mutation, use of oral contraceptive, smoking, and menopausal status.

2.6. Data analysis and synthesis

The extracted data were used in qualitative synthesis. They were re-analyzed using the Statistical Package for Social Sciences (SPSS) 26.0 software for quantitative synthesis. Summary tables with relevant variables were designed which were presented as frequency, mean, and percentage.

3. Results

3.1. Study selection

The systematic search initially came up with a total of 170 articles. Before further screening, 3 duplicates, 4 non-English, 31 only abstract articles, and 5 non-articles were removed from the 170 papers. Among the remaining 127, titles and abstracts were screened, of which a further 105 studies were excluded since they were irrelevant. Out of the remaining 22 articles that were screened, a total of 6 of them were excluded as a result of the wrong study design. This left only 16 articles to be screened to find possible wrong outcomes or predatory journals; However, none were found. Finally, the remaining 16 articles were all deemed eligible and were included in the systematic review. The detailed PRISMA flow chart is shown in Figure 1.

3.2. Characteristics of the included studies

All of the studies included in this review were either a cohort or a case-control study. Out of the 16 studies, 7 of them were conducted in the United States making it the most contributing country. Apart from the United States, other countries such as Canada, Germany, Spain, South Africa, Lebanon, Ethiopia, Sweden, Korea and Japan were all included. Table 1 provides all of the necessary information regarding the studies included.

3.3. Participants

A total of 29,100 patients were included in this systematic review. Among the patients with known age groups, those with an age of 50 or more years were the most common. Furthermore, breast cancer was found to be by far the most common form of cancer associated with breastfeeding, followed by ovarian and then endometrial cancer. Out of the 29,100 patients, a total of 19,905 of them breastfed making up 68.4% of the patients. Number of patients developing all types of cancers was 14,817 with 69.7% of them breastfeeding.

3.4. Main findings

The United States researchers published 7 studies which was the country with the most (43.75%) number of studies. Eleven studies (68.75%) were case-control, and 5 (31.25%) studies were cohort (table 1'). Among the 14,817 patients who developed cancer, 11,688 (78.9%) were breast cancer followed by ovarian cancer (2548, 17.2%) (Table 2). Of those 14,817 patients who developed cancer, 10,327 of them reported a history of breastfeeding making up (69.7%) of the cancer patients. Among the total 16 studies, 12 (75%) of them conclude that breastfeeding decreases the risk of cancer, 3 of them (18.75%) conclude that there is no significant association while b

1 study (6.25%) implies that breastfeeding is observed to be associated with a more aggressive type of breast cancer (table 3).

Table 2: Frequency and percentages of different variables such as age group, country of study, study design, type of cancer developed, breastfeeding and its duration, BMI, smoking, OCP, Menopausal status, BRCA1/BRCA2 mutations as well as the final conclusion provided in the studies regarding the association between breastfeeding and cancer.

Variables	Number of patients (29,100)	References [10-25]
Age	Number of patients (29,100)	
<40	440 (1.5%)	[14,17,19,21]
40 - 49	1,188 (4.1%)	[14,17,19,21]
<u>≥</u> 50	4,220 (14.5%)	[14,17,19,21]
Others	23,252 (79.9%)	[10-13,15,16,18,20,22-25]
Country of study	Number of studies (16)	
Canada	1 (6.25%)	[11]
Germany	1 (6.25%)	[12]
Spain	1 (6.25%)	[13]
South Africa	1 (6.25%)	[14]
Lebanon	1 (6.25%)	[15]
Ethiopia	1 (6.25%)	[16]
United States	7 (43.75%)	[17,18,20,21,23-25]
Sweden	1 (6.25%)	[10]
Korea	1 (6.25%)	[19]
Japan	1 (6.25%)	[22]
Study design	Number of studies (16)	
Cohort Study	5 (31.25%)	[10-13,22]
Case Control	11 (68.75%)	[14-21,23-25]
Type of Cancer Developed	Patients with Cancer (14,817)	
Breast Cancer	11,688 (78.9%%)	[10-20,22]
Endometrial Cancer	586 (3.95%)	[21]
Ovarian Cancer	2548 (17.2%)	[23-25]
Breast Feeding	Number of Patients (29,100)	
Patients who breastfed	19,905 (68.4%)	[10.25]
Patients who did not breastfed	9,195 (32.4%)	[10-25]
Breast Feeding Duration	Number of patients who breastfed (19,905)	
1-5 months	3,410 (17.1%)	[12,21,23-25]
>5 months	2,985 (15%)	[12,21,23-25]
Others	13,510 (67.9%)	[11,13-20,22,24]
BMI	Number of Patients (10,835)	
Normal	4,474 (41.3%)	[10 17 10 21 22]
Overweight	6,361 (58.7%)	[10,17-19,21,23]
Others	Number of Patients (29,100)	
Smoker	3,044 (10.5%)	[11,16,10,21,23]
Oral Contraceptive Pill	6,451 (22.2%)	[11,17,20,24,25]
No of patients in Menopause	5,619 (19.3%)	12,14,16-19,22,24]
BRCA1/BRCA2 Mutation	2,566 (8.8%)	[11,12]

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Table 2: Continued...

Breast feeding association on cancer	Number of studies (16)	
Increases the risk	1 (6.25%)	[10]
Decreases the risk	12 (75%)	[11,13,14,16,17,19-25]
Has no impact	3 (18.75%)	[12,15,18]

4. Discussion

Breastfeeding is considered the most important protective factor for the lives of infants [26]. Murphy et al. conducted a study to investigate the impact of exclusive breastfeeding for a minimum duration of 90 days and the incidence of illness in infants. The findings indicated that breastfeeding for 90 days and more was associated with a significant decrease in the likelihood of being admitted to the hospital, the number of nights spent in the hospital, and also the proneness for developing respiratory diseases such as chest infections, asthma, and common colds [27]. Furthermore, many studies emphasize the role of breastfeeding in the immune development of the infant since the primary milk produced by the mother is rich in immunologically active molecules and various other key nutrients and vitamins [26]. Breastfeeding the infant early in life has been observed to result in developed immunity against numerous diseases while also keeping the infant devoid of malnutrition issues [28,29]. Despite the many known benefits of breastfeeding, it is found that only 37% of children younger than 6 months are breastfed exclusively in low- and middle-income countries and that the prevalence of breastfeeding at 12 months is lower than 20% in the majority of the high-income countries [30]. In our review and among the 29,100 patients included, 19,905 patients which made up 68.4% of the total patients breastfed.

These data indicate that breastfeeding has not yet reached the optimal prevalence in the majority of the countries globally and as previously focused on, this poses a problem not only for the infants but also for the mother due to the many health benefits the mother can obtain from breastfeeding [26,27]. According to Victoria et al., 823,000 deaths in children younger than the age of 5 and up to 20,000 deaths from breast cancer can be prevented each year only by scaling up the level of breastfeeding to a nearuniversal level [30]. Breastfeeding has many impacts on both the physiological and the psychological health of the mother. According to Labbok, breastfeeding can reduce the amount of postpartum blood loss by increasing the rate at which the uterine contracts. Furthermore, it can lower the severity of anemia while also mediating certain physiological changes that can protect the mother against infections, especially bladder. Interestingly, breastfeeding is seen to lower the risk of spinal and hip fractures in postmenopausal women despite the apparent bone loss [31]. Psychologically, breastfeeding mothers do report lowered stress, negative mood, and anxiety when compared to mothers who are stuck to formula feeding [32]. Among the many impacts of breastfeeding on the mother's health, the association of breastfeeding by the mother and its correlation with the different types of cancer developed in the mother is the one of utmost importance.

Cancers of the reproductive system such as ovarian and breast cancer are among the most commonly correlated cancers with breastfeeding. Among the 14,817 patients who developed breast cancer in our review, breast cancer was observed to be the most common form of cancer with 11,688 (78.9%) of the patients developing it, followed by ovarian cancer with 2548 (17.2%) patients and endometrial cancer with 586 (3.95%) patients. Many studies conclude that breastfeeding results in a lower risk of developing cancers of the reproductive system, especially of the breast. This could be attributed to the endogenous hormonal changes lactation inflicts, mainly the lowering of estrogen and the increase of prolactin production. This will lower the overall lifetime exposure to estrogen which then thereby indirectly inhibits the growth of cancer cells in the breast [33]. Other studies focus on other roles of lactation such as the extended terminal differentiation of the mammary gland epithelial cells which can make the breast tissue more resistant to carcinogenic and subsequently reduce the risk of breast cancer [34]. Oral contraceptive pills (OCP) are also frequently assessed to determine their impact on cancer development due to their significant hormonal changing properties. Information regarding OCP and various other factors such as smoking, menopausal status, BMI, and the presence of BRCA1/BRCA2 mutations have all been gathered in this review and listed in

According to Stordal et al., for every 12 months of breastfeeding, the risk of developing breast cancer is reduced by 4.3% [35]. Other studies have further emphasized this inverse relationship of breastfeeding duration with the development of breast cancer. Gajalakshmi et al. conducted a study that revealed a statistically significant linear trend between the duration of breastfeeding and the reduced risk of breastfeeding [36]. Within our patients, only 3,410 (17.1%) out of the total 19,905 patients who breastfed had a breastfeeding history of 1 to 5 months while the other patients mostly had longer durations. Ovarian cancer is another form of cancer in the mother that seems to be associated with breastfeeding so much so that women with a breastfeeding history of more than 13 months are found to be 63% less likely to develop ovarian tumors when compared to women with a breastfeeding history of less than 7 months [37]. Jordan et al. also performed a study to study the association between breastfeeding and its duration with the risk of developing epithelial ovarian cancer. They concluded that among the women who breastfed, the longer the duration of breastfeeding, the lower the risk of developing ovarian cancer [23]. Other researchers such as Afzal et al. and Abdou-Daoud et al. similarly tried to study the relationship between breastfeeding and its role as a protective factor in reducing the risk of cancer in the mother; however, they found no significant role between them [15,18].

Table 3: Breastfeedin	ig charactei	Number	tudy and the final cor Breast feeding duration		Number of	udy yielded with	regards to the hypothesis.	
Study Authors	Number of patients in study	of patients who breastfe d	1-5 months	>5 month s	patients who developed cancer	Type of cancer developed	Conclusion	
Jernström et al. (11)	1930	1930	3.	5*	965	Breast Cancer	In women with BRCA1 mutation, 1 or more years of breastfeeding was associated with decreased risk of breast cancer by 45%.	
Andrieu et al. (12)	1601	1249	365	478	853	Breast Cancer	Breastfeeding was not associated with the risk of breast cancer.	
Redondo et al. (13)	510	357	7.	1*	510	Breast Cancer	Breastfeeding is associated with reduced odds of triple negative breast cancer as compared to luminal A breast cancers.	
Anderson et al. (14)	688	616	N/A	N/A	347	Breast Cancer	Breastfeeding probably protects premenopausal women from developing breast cancer, especially women of white ethnicity.	
Abdou-Daoud et al. (15)	901	901	63	.9*	389	Breast Cancer	Breastfeeding duration was not found to be a protective factor against breast cancer.	
Mengesha et al. (16)	434	326	N/A	N/A	217	Breast Cancer	Breastfeeding was associated with reduced risk of both HR+ and ER-PR-breast cancer among Hispanic women.	
Sangaramoorthy et al. (17)	5957	4398	11	.0*	2703	Breast Cancer	Breastfeeding, among other factors such as family history of breast cancer and being in menopause, is associated with reduced risk of breast cancer.	
Gustbée et al. (10)	592	592	N/A	N/A	592	Breast Cancer	Patients with excessive milk production seemed to have a more aggressive type of breast cancer as well as an earlier presentation.	
Afzal at al. (18)	100	50	N/A	N/A	50	Breast Cancer	Breastfeeding did not have a significant role in breast cancer.	
Do et al. (19)	229	198	N/A	N/A	108	Breast Cancer	Lactation and more importantly breastfeeding duration reduce the risk of breast cancer.	
Lehman et al. (20)	2546	1871	N/A	N/A	2546	Breast Cancer	Breast feeding decreases the incidence of cancer.	
Newcomb et al. (21)	2239	1159	640	499	586	Endometrial Cancer	Lactation is inversely correlated with breast cancer.	
Ing et al. (22)	2403	1441	12	.0*	2403	Breast Cancer	Three to fourfold increase in risk of cancer in the unsuckled breast for patients aged 55 and over.	
Jordan et al. (23)	2226	1583	878	705	881	Epithelial Ovarian Cancer	Among women who have had the opportunity to breast feed, ever breast-feeding and increasing durations of episodes of breast-feeding are associated with a decrease in the risk of ovarian cancer	
Titus-Ernstoff et al. (24)	2475	898	573	325	1231	Ovarian Cancer	Breastfeeding is strongly associated with decreased risk of ovarian cancer; however, this is mainly if the last-born child is breastfed.	
Gwinn et al. (25)	4269	2336	954	978	436	Epithelial Ovarian Cancer	Breastfeeding is among the factors associated with decreased risk of epithelial ovarian cancer.	

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Contrary to the previously aforementioned studies, Gustbée et al. observed earlier presentation and even more aggressive form of breast cancer type amongst the women who breastfed when compared to those who did not [10].

5. Conclusion

We conducted this systematic review to shed light on the different conclusions researchers have gathered over the years regarding this matter. Out of the 16 studies included in this review, 12 (75%) of them show a reduced risk of cancer development in the mother when breastfeeding. Due to the other studies not reaching the same conclusion, we advocate other researchers to further study this topic to come up with a stronger correlation and possibly the settlement of this conflict.

Declarations

Conflicts of interest: The author(s) have no conflicts of interest to disclose.

Ethical approval: Not applicable.

Patient consent (participation and publication): Not applicable.

Funding: The present study received no financial support.

Acknowledgments: None to be declared.

Authors' contributions: FHK was a major contributor to the conception of the study, as well as to the literature search for related studies. BAA, ASA, SO, and HOA were Involved in the literature review, the writing of the manuscript, and data analysis and interpretation. HMM, LRAP, and RMA Literature review, final approval of the manuscript, and processing of the tables. NHAA, KMH, AMM, and AMS were involved in the literature review, the design of the study, and the critical revision of the manuscript. BAA and FHK Confirmation of the authenticity of all the raw data. All authors approved the final version of the manuscript.

Data availability statement: Not applicable.

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