The Association of Parity and Breastfeeding with Breast Cancer: A Review

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Abstract

Background: The association between parity and breastfeeding with breast cancer is still conflicting. Therefore, we did an analysis to summarize the recent studies of breast cancer with the subject of parity and breast-feeding.

Materials and methods: The related studies were extracted by a search on PubMed between May 1, 2010 and May 1, 2016. The random-effect model was used. Factors like sensitivity analysis, sub-group analysis, and publication bias were considered.

Results: Twenty-eight papers involving 12,041 breast cancer cases were included in our meta-analysis. The obtained results suggest that breastfeeding was inversely associated with the risk of breast cancer. The association of breastfeeding with in the case of ever breastfeeding compared with never categories were studied. The summary of Odds Ratio for this study was 0.84 (95% Confidence Interval [CI], 0.64-1.32). An inverse association was also found for the longest breastfeeding compared with the shortest categories of breastfeeding with the risk of breast cancer. There is no evidence also for the association of parity and breast cancer in our study.

Conclusion: The results of finding from analysis propose that the number of parities and the longer duration of breastfeeding were inversely associated with the risk of breast cancer.

Keywords: Parity; Breastfeeding; Breast cancer; Parous

Introduction

Breast Cancer (BC) is one most diagnosed type of cancers caused cancer death among women worldwide [1]. According to [2] among 12% of all new cancer cases and 25% of all cancers among women is breast cancer. For instance, according to [2] about 22% of cases of breast cancer in Brazil can be prevented by not drinking alcohol, being physically active and maintaining a healthy weight.

Breastfeeding is hypothesized to reduce the risk of BC primarily through two mechanisms, differentiation of breast tissue and reduction of the lifetime number of ovulatory cycles, but previous reviews of the association between breastfeeding and breast cancer have not consistently found that breastfeeding reduces the risk of breast cancer [3]. Among the research works the parity and breastfeeding are controversial issues, particularly in the number of parities and duration breastfeeding [4,5].

Some researchers have been studied the relation between parity and breastfeeding (BF) in preventing Breast Cancer (BC). Their results demonstrated that parity and BF are preventive for BC patients. For example, the role having BF, the number of breastfed children, the period of breastfeeding, age at first lactation, and period of amenorrhea during lactation. Many studies have been proved that breastfeeding is a preventive factor of breast cancer [6-9].

The main goal of this study is to investigate an analysis of the relationship between parity and breastfeeding with breast cancer based on epidemiological researches were published in the reviewed journals between 2010 and 2016.

The rest of this paper is classified as follows; Section 2 reports the used materials and methods. The obtained results from our review comes in Section 3. The finding from our meta-analysis reported in Section 4.

Materials and Methods

In this section, we provide our search method and strategy to select the state-of-art works first. Second, we explain the study selection process in order to extract the relevant works. Third, we report the data abstraction mechanism from the chosen papers. Finally, we explain statistical methods which have been used in our review.

Search and strategy

We investigated a comprehensive search on studies on PubMed database during the six-year period between May 1, 2010 and May 1, 2016. Our search is limited to the published researches in English with the following keywords and Medical subjects: (breastfeeding OR breast feed OR lactation) AND (breast) AND (parity) AND (cancer OR tumor OR neoplasm). We also reviewed some additional works for the reference information about the relation between the parity and

breastfeeding with breast cancer. In our search results we have selected the following article types; Clinical Trial, Journal Article, and Review. **Figure 1** illustrates the number of extracted papers from our research.
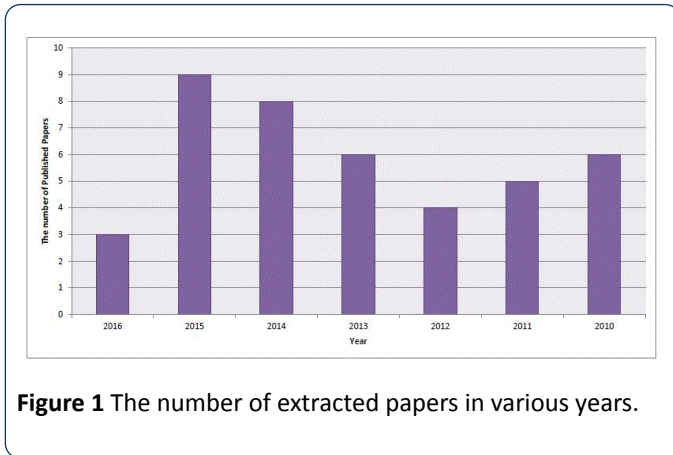

Figure 1 The number of extracted papers in various years.

Study selection

We included the studies which had a case-control, cohort, or cross-sectional studies. Then, we investigate the association between the number of parity, duration of breastfeeding in months and incidence of breast cancer. The selected research works had to present the following concepts; i) the hazard ratio ii) odds ratio (OR) or relative risk (RR) with 95% confidence intervals (CIs). We discarded the studies that did not provide these information. For some studies which are published in different accommodations we have selected the largest number of cases.

Data abstrction

For each chosen paper we performed an investigation on the eligibility and data abstraction. We extracted the following data from each study; list of authors, the year of publication, the region of study and its design, the size of sample study (i.e., the number of cases and controls and cohorts), duration of study for cohorts, the assessment of study for breastfeeding duration including ever, average, and total months, the number of parities, the study estimates adjusted for the works that have CI greater than 95%. If no adjusted estimates were presented, we included the crude estimate. If no estimate was presented in a given study, we calculated it and its CI 95% according to the raw data presented in the article.

Statistical analysis

The gathered data is calculated as the inverse variance-weighted mean of the natural logarithm of multivariate adjusted RR with 95% CI for breastfeeding and breast cancer risk. We used the random-effects model to consider the within-study and between-study variation [10]. Also, we used The Q test and Thompson [11] to assess heterogeneity among selected literature. Meta-regression has used to assess the

potentially important covariate applying substantial impact on between-study heterogeneity [12]. Egger`s regression asymmetry test is used for publication bias [13]. To study the effect of a single study on meta-analysis we use the method in [14-20]. All the statistical analysis were performed with SPSS software on a machine with 4GB of RAM.

Results

The pooled results from our review were reported in this section. We provide a detailed results from each chosen literature here.

Study characteristics

Our search method has identified 324 papers from PubMed. Twenty-eight papers were used in this meta-analysis. **Figure 2** shows the steps that we used to extract the papers. In this study, the number of included papers, which demonstrated 12,041 cases, were published between 2010 and 2016. All of the studies only included parous women in analyses. The detailed characteristics of the papers for parity and breastfeeding were shown in **Tables 1** and **2**, respectively.

Breastfeeding and breast cancer

Twenty-eight papers were used in our meta-analysis. In our meta-analysis, we found that there is an inverse association with the risk of breast cancer of breastfeeding in 11 studies. There was no evidence for this association in seventeen studies. The gathered results suggested that the breastfeeding could reduce the breast cancer risk: summary RR=0.84; 95% CI, 0.64132.

Parity, breastfeeding and breast cancer

Eight studies [4,15-21] comprising 12,041 breast cancer cases investigated the association between ever-breastfeeding and breast cancer risk. The obtained results from the researches do not lead us to a unique fact. For example, some works proved that breastfeeding has a positive result on BC [4,15,17,18,20,21]. They also suggested that the duration of breastfeeding should be greater than 13 months. On contrary, some researchers found that there is not an association between the reduction of BC and breastfeeding [16,19-23]. An inverse result was reported in the studies for the association of parity and BC. Among our studies, six papers suggested that at least one parity could reduce the risk of BC while on the rest papers there is no evidence for this risk.

Results

The pooled results from our review were reported in this section. We provide a detailed results from each chosen literature here.

Table 1 Characteristics of our study in parity and breastfeeding effect on breast cancer.

Reference (year)	Country	Study design	Cases (n)	Category	RR (95% CI)	Adjustment of matched for
Akbari et al. [4]	Iran	PCC	376	ever versus never	1.8 (0.5-5.5)	Adjusted for parity, the count of months of breastfeeding, the number of children, tobacco consumption and fatty diet, family history, and use of hormones.
De Silva et al. [15]	Sri Lanka	PCC	100	> 1 year versus never	1.74 (1.01-3.01)	Adjusted for breastfeeding, parity, age at menarche, menopause, reproductive factors, passive smoking, abortion, alcohol consumption, age, BMI, family history of breast cancer, hormonal contraceptives, use of contraceptives, and level of education.
Alsaker et al. [20]	Norway	PCC	2640	Not mentioned	1.32 (1.02-1.72)	Adjusted for long term survival from breast cancer, parity, number of full term pregnancies, age at menarche, martial status, place of residence, BMI, and the effect of Estrogen Receptor (ER).
Palmer et al. [19]	African American	PCC	4265	Ever versus Never	1.37 (1.06-1.70)	Adjusted for parity, breastfeeding, estrogen receptor, the number of birth, age at first birth, and family history.
Kotsopoulos et al. [21]	seven countries	PCC	3330	Ever versus Never	1.37 (1.06-1.70)	Adjusted for a personal and/or family history of breast and/or ovarian cancer, mutation detection, ages at menarche and menopause, cause of menopause, pregnancy, and breastfeeding history.
S. Shinde et al. [22]	US	PCC	2473	Ever versus Never	0.90 (0.87-0.94)	Adjusted for ethnicity, age at menarche, family history, and age at diagnosis.
Porto et al. [23]	Brazil	PCC	81	Ever versus Never	2.49 (1.175-0.30)	Adjusted for age at diagnosis, age at menarche, reproductive status, live births, breastfeeding, family history of breast cancer, physical activity, cigarette smoking, body mass index, and metabolic syndrome parameters.
Giudici et al. [17]	Italy	PCC	286	Ever versus Never	0.22 (0.090-0.59)	Adjusted for breastfeeding, age at menarche, parity, age at first pregnancy, number of children) with the risk of breast cancers.
Redondo et al. [24]	Spain	PCC	501	Ever versus Never	0.25 (0.080-0.68)	Adjusted for lifetime breastfeeding, mean lifetime breastfeeding duration, age at menarche , age at first full-term pregnancy, parity, age at diagnosis, age at menopause, menopausal status at diagnosis, the number of pregnancies combined with a long breastfeeding period, number of pregnancies, and family history.

Table 2 Characteristics of our study in parity and breastfeeding.

| Reference	Cases	Controls	Parity	Suggested duration of breastfeeding (months)
Iqbal et al. [18]	129 pairs	NA	2	52.7-55.3
De Silva et al. [15]	100	203	1	36-47
Kotsopoulos et al. [21]	3330	1665 pairs	2	≥ 24
Akbari et al. [4]	376	425	1-3	18-24
Alsaker et al. [20]	2640	NA	0-3	13-19
Giudici et al. [17]	286	578	0-2	≤ 12
Palmer et al. [19]	4265	14180	≥ 4	not associated
Ambrosone et al. [16]	786	1015	1-2	no additional benefit to ER+ cancer
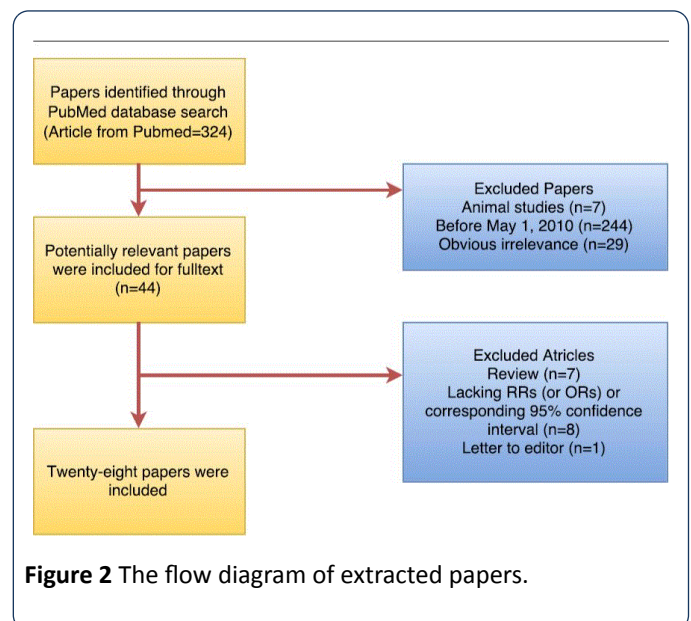
Figure 2 The flow diagram of extracted papers.

Discussion

The obtained results from the meta-analysis of epidemiologic studies illustrated that ever breastfeeding had a reduction on breast cancer compared with never breastfeeding. There is an inverse association also between longest and shortest duration of breastfeeding in these studies.

The pooled results for the association of parity and reduction of breast cancer showed that the parity could reduce the risk of breast cancer. Some studies suggested that at least one parity could reduce the risk of breast cancer.

Several studies have been done to explain the association of breastfeeding and parity with breast cancer [4,24-36]. For instance, Dall et al. [33] found that parity in younger pregnancies decreases breast cancer risk. A protective effect of parity on breast cancer has been reported in [4,19,34].

This meta-analysis included a large amount of sample cases with a large number of controls. The number of cases in this meta-analysis is 12,031 with 19766 controls. The sample size of this study should have provided enough statistical power to determine the association of ever breastfeeding and never breastfeeding in reducing breast cancer risk. It also could provide sufficient statistical power for the association of parity and the risk of breast cancer. Additionally, this study considered several subgroups to evaluate heterogeneity.

This analysis has several limitations. First of all, as a meta-analysis of observational studies, some studies were prone to biases such as selection bias and inherent in the original studies. Furthermore, some studies are adjusted for fewer factors of breast cancer while some others took many factors into account in studying the risk of breast cancer. In addition, some cohort studies provided detailed information of adjustment their results. Thus, more large studies, especially prospective studies, are needed in the future.

Second, some individual studies may introduce bias in an unpredictable direction. For example, in the case of ever breastfeeding and a longer duration of breastfeeding which are associated with other hormone-dependent or reproductive factors, including lower levels of body mass index [37], the study is adjusted for potential confounding factors.

Finally, the huge heterogeneity and a possible publication bias must be considered in the study, especially, this effect can be seen on the gathered results from ever breastfeeding and the total duration of breastfeeding. In spite of multiple subgroups and their sensitivity analyses that were carried out, heterogeneity still existed in our study. As we found in our analysis, the heterogeneity in our results can be found in the category of duration for the duration of breastfeeding and the number of parities. Therefore, we included the studies that are considered both factors in risk reduction of breast cancer. There is also publication bias in our analysis which can produce a problem for our meta-analysis.

In summary, the result of our analysis suggests that breastfeeding, particularly a longer duration of breastfeeding, was inversely associated with risk of breast cancer. Additionally, having at least one parity could reduce the risk of breast cancer among women.

Compliance with Ethical Standards

Conflict of interest

Arezou Babalou has no conflict of interest.

Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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