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Breastfeeding and breast cancer risk reduction in sub-Saharan Africa: a look at the evidence

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Abstract

Although a few studies have been conducted in sub-Saharan Africa (SSA) on the relationship between breastfeeding and breast cancer, the findings have been inconsistent. Given limited research resources in the region, there is a need to critically review the available studies to ascertain the extent to which they support the hypothesis that breastfeeding reduces breast cancer risk given their strengths and weaknesses. A literature search in Medline, Scopus, PubMed, Google Scholar, and a reference list of published studies was conducted. Key studies published outside SSA between 2000-2022 were selected for detailed review based on sample size, geographical distributions and relevance of the findings. All available studies in sub-Saharan Africa were included. Data were extracted from the results sections of the published studies. The findings were summarized using tables and forest plots, The plots were based on R statistical software version 3.4.0 (2017). Data analysis and conclusion were primarily done by comparing the total number of significant findings (based on confidence interval) with the total number of non-significant findings taking into consideration the strengths and weaknesses of the studies. A total of 15 case-control studies, 6 cohort studies across five regions of the world (North America, Europe, Asia, South America, and North Africa) and all available studies (9 case-control studies) from sub-Saharan Africa were reviewed. A reduced risk of breast cancer (especially oestrogen receptor negative breast cancer) associated with having a breastfeeding experience or a longer life duration of breastfeeding was observed in most case-control studies including those from SSA. While most of the available evidence in SSA tended to support the hypothesis that breastfeeding reduces breast cancer risk, there is a need for more robust studies with sufficient sample sizes for subgroup analysis.

Keywords: breast cancer, breastfeeding, risk factor, sub-Saharan Africa

Introduction

Breastfeeding has been described as one of the most effective and cost-effective investments nations can make in the health of their youngest members and the future health of their economies and societies (The United Nations 2017)]. According to WHO, breastmilk provides all the energy and nutrients that the infant needs for the first months of life, and it continues to provide a substantial proportion of the same up to the second year of life (World Health Organisation 2023). It boosts immunity against common childhood diseases as well as impacts children's brain, cognitive, and socio-emotional development(World Health Organisation 2023; Krol & Grossmann 2018).

Moreover, there is evidence that breastfeeding reduces anxiety, negative mood, and stress in mothers(Krol & Grossmann 2018)]. According to the Centre for Disease Control, breastfeeding is beneficial to maternal health because it reduces the mother's risk of noncommunicable diseases such as breast and ovarian cancer, type 2 diabetes, and high blood pressure (Center for Disease Control and Prevention: Division of Nutrition 2021). Similarly, the Continuous Update Panel Project has concluded that there is convincing evidence that breastfeeding reduces breast cancer risk while shorter duration or no breastfeeding experience increases the risk(Research 2010).

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Incidentally, evidence of rising incidence of breast cancer has been reported globally including in sub-Saharan Africa (SSA)(Bray et al. 2018; Azubuike et al. 2018).

This has been attributed among other things to changes in environmental pollution, lifestyles and reproductive behaviors including poor breastfeeding practices among women (Research 2010). Although this conclusion was based primarily on studies from high income countries, similar reports are beginning to emerge in other regions of the world such as sub-Saharan Africa (SSA). Unfortunately, findings of the few available studies in SSA have not been consistent. Nevertheless, given the slow pace of research in the region, there is need to maximise the available evidence by ascertaining to what extent they can guide intervention while waiting for more studies. The aim of this reviews was to present key studies across the globe with emphasis on studies conducted in SSA, while highlighting their strength, limitations. Their findings are synthesized in order to draw conclusion on the current state of evidence. The observations were expected to inform the conduct of more studies in SSA. The review was part of the review of evidence of the association between breast cancer risk of putative risk factors including, parity, breastfeeding, socioeconomic status and physical activity. See supplementary file for the study selection flow chart.

Methodology

The study was a critical review of selected literature from outside of SSA and all available studies in SSA.

Literature search strategy

The literature review was based on published studies in Medline, Scopus, PubMed, Google Scholar, and Google. Additional studies and relevant documents were identified from the reference lists of published papers. These were then retrieved from the web using Google scholar and Google search engines. Key words related to the hypotheses were retrieved individually using the advanced search tools in Medline. These were later combined as appropriate using Boolean operators (AND, OR). For example '(Breast neoplasm or breast cancer) AND reproductive factors AND breastfeeding', '(Breast neoplasm OR breast cancer) AND breastfeeding', '(Breast neoplasm OR breast cancer) AND breastfeeding AND Africa OR sub-Saharan Africa', '(Breast neoplasms OR breast cancer risk) AND parity AND (Africa OR sub-Saharan Africa)', '(Breast neoplasm OR breast cancer) AND parity AND Nigeria, breast cancer risk AND Africa, reproductive factor AND breast cancer risk AND Nigeria', 'Parity AND breast cancer risk AND Nigeria'. Since a search for one exposure of interest retrieved relevant papers for other exposures of interest as well, the search results were combined. For example, a search for parity and breast cancer identified other papers related to breastfeeding, SES, and physical activity (see supplementary file for the flow chart).

Study selection criteria (inclusion and exclusion criteria)

Studies included in the review were those published between the years 2000 and 2022. The specified time frame was to ensure that only current evidence available across the world was included. Furthermore, this was the time frame within which most eligible studies in sub-Saharan African countries were published. The studies were restricted to case-control and cohort study across different regions of the world including North America, Europe, South America, Asia and Africa. cross sectional studies and publications from non-peer reviewed journals were excluded. The search was restricted to papers published in the English language. All peer-reviewed papers included must have relevant titles, abstracts, and full-text contents. This was to ensure that only good quality studies were reviewed. Owing to the number of studies obtained, all the studies that met the eligibility criteria were not reviewed in detail. Owing to large number of studies across the globe, key studies with sufficient sample size and high citation across regions were selected except. However, one study with a unique/unpopular finding was discretionally selected to enhance a balance overview of literature. Given the paucity of studies in sub-Saharan Africa which is the main focus of the review, all available studies in the region irrespective of their limitations were included. High-quality case-control or cohort studies with large sample sizes whose results captured typically the observations and conclusions of other similar studies were selected for detailed review. The rest of the included studies were cited as supportive references.

Data extraction and quality assessment

Data were extracted from the results sections of the published work and the quality was assessed based on the

methodology taking into consideration sample size, study design, confounding, generalisability and other sources of bias. The quality and relevance of the selected studies were further reviewed by two independent experts.

Data presentation and analysis

The findings were summarised with tables and forest plots. The forest plot was based on R statistical software version 3.4.0 (2017). The study-specific estimates were pooled using a random-effect model. Although the interpretation of the overall pooled estimates was problematic due to heterogeneity in the exposure definitions (and the fact that some of the studies were repeated where necessary to show the findings based on subgroup analysis), it was necessary to generate them in order to produce the forest plots in R. The forest plots provide a visual representation of the individual studies and the study specific estimates. This was to reduce the potential for a biased overview of the published evidence since not all literature cited was reviewed in detail. Data analysis and conclusion were primarily done by comparing the total number of significant findings (based on confidence interval) with total number of non-significant finding taking into considerations the strengths and weaknesses of the studies.

Results (Summary)

This review involved 15 case-control studies and 4 cohort studies across five regions of the world- North America, Europe, Asia, South America, and North Africa as summarized in Table 1. Of the 30 studies obtained from the literature search, 7 were conducted in North America, 6 in Europe, 4 in Asia, 1 in South America, 1 in North Africa. The table shows that most studies conducted in Africa have a low sample size (5,969 participants from 9 studies) compared to North America (529,048 participants from 8 studies). Thirteen results reported in these studies suggest that breastfeeding (lactation) was significantly associated with a reduced risk of breast cancer. However, 16 results suggest the presence of a non-significant association between breastfeeding and reduced risk of breast cancer. One study, however, indicated an increased risk of breast cancer with breastfeeding. The forest plots of the study results were shown in Figures 1 and 2. The plots show that most results were in the direction of reduced risk of breast cancer among women who breastfed, although some of these results were not significant.

With respect to SSA, 9 studies were retrieved. Five (5) studies indicated that breastfeeding was associated with breast cancer while the remaining 4 did not indicate such results. The finding with respect to subgroup analysis base on menopausal status and oestrogen receptor status showed inconsistent result.

Variables	Number of studies	Pooled sample size

North America	7	529,048
Mixed (Europe/North America)	2	5,398
Europe	6	85,374
South America	1	1,270
Asia	4	7,589
North Africa	1	800
Sub-Saharan Africa	9	5969
Case control study	24	105,151
Cohort study	6	530,297

Table 1 Relationship between lactation and breast cancer risk: summary of study characteristics by sample size

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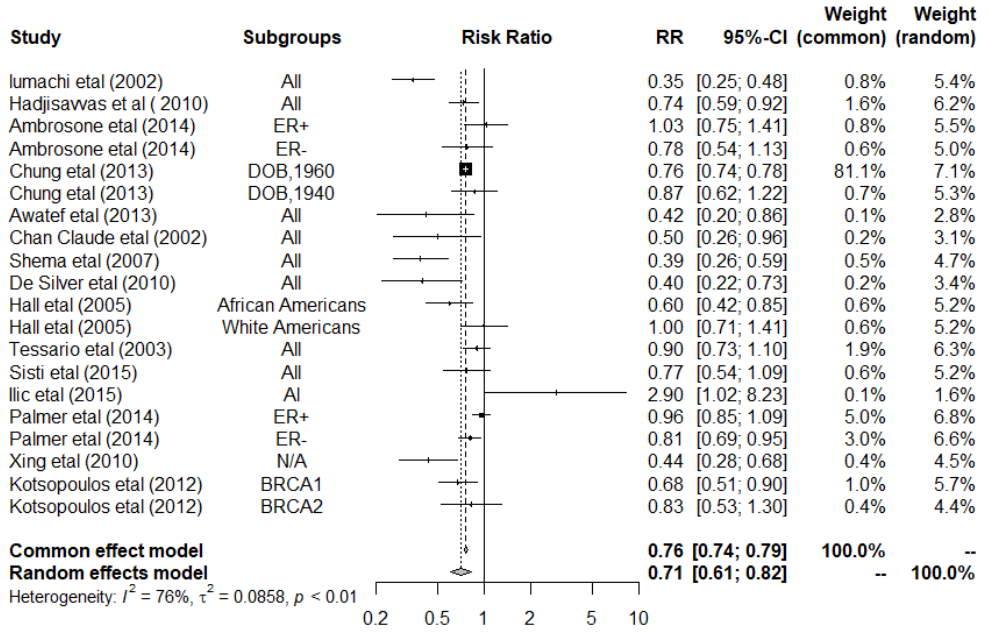
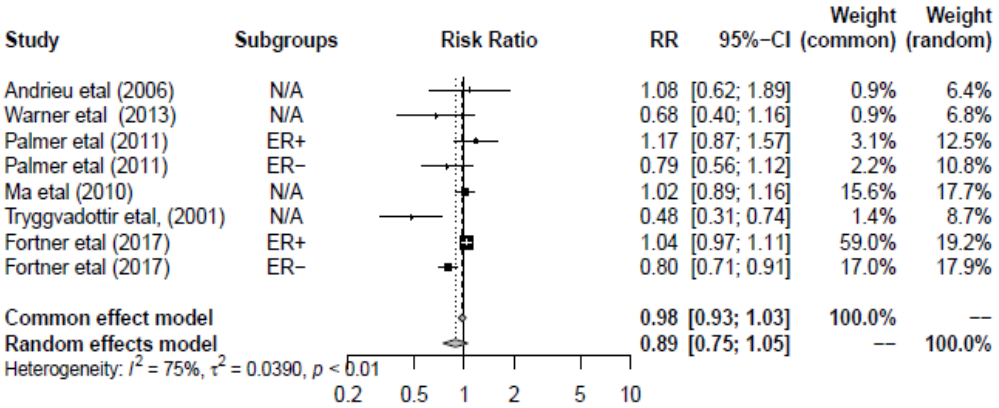


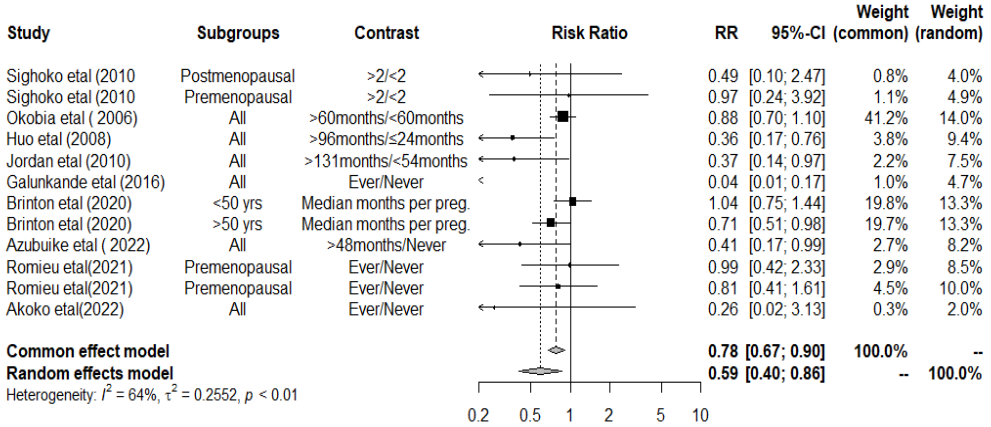
OR (Having ever breastfed, Longer lifetime duration of breastfeeding versus Having never breastfed & shorter lifetime duration of breastfeeding respectively)



RR (Having ever breastfed, Longer lifetime duration of breastfeeding versus Having never breastfed & shorter lifetime duration of breastfeeding respectively)

Forest plots show case-control and cohort studies. Where studies reported analyses by subgroups (oestrogen receptive subtypes,) these are presented separately for each subgroup analysis. The pooled estimate was based on the random effect model. Note that 'RR' which appears on the headings of the plots is automatically generated in R, and represents the rate or risk ratio, in a cohort study, and the odds ratio in a case-control study as specifically stated on the plot x-axis.

Figure 1: Relationship between lactation and breast cancer risk: summary of evidence from outside sub-Saharan Africa using forest plot



OR (Having ever breastfed, Longer lifetime duration of breastfeeding versus Having never breastfed & shorter lifetime duration of breastfeeding respectively)

Forest plot shows all available studies. Where results were separately reported by subgroups (menopausal status and age) these were presented separately. The pooled estimate was based on the random effect model. Note that 'RR' which appears on the headings of the plots is automatically generated in R, and represents the rate or risk ratio, in a cohort study, and the odds ratio in a case-control study as specifically stated on the plot x-axis.

Figure 1: Relationship between lactation and breast cancer risk: summary of evidence from sub-Saharan Africa using forest plot

Detailed review/ Discussion

Observations outside sub-Saharan Africa

Of the 30 studies reviewed, six studies (Figure 1) with contrasting results based on subgroups (oestrogen receptor status, date of birth, ethnicity, breast cancer genes and age) analysis were presented. Hence, the number of results presented was higher than the number of studies reported (Table 1). Several studies in Europe, North America, Israel, Asia, North Africa reported a reduced risk of breast cancer among women who have ever breastfed or breastfed for a longer time compared to women who had never breastfed or had shorter duration of breastfeeding (Shema et al. 2007; Lumachi et al. 2002; Tryggvadóttir et al. 2001),(Hall et al. 2005; Msolly, Gharbi, & Ahmed 2013; Xing, Li, and Jin 2010)(Shema, et al. 2007; Chang-Claude et al. 2000; De Silva et al. 2010)]. For example, a hospital-based case-control study in Sri Lanka observed that women who breastfed for ≥ 24 months during their lifetime had a significantly lower risk of breast cancer than those who breastfed for < 24 months (OR 0.40, 95% CI: 0.22, 0.73)(De Silva, et al. 2010)].A dose-response effect was reported as the duration of lactation increased. The authors, however, noted that while cases were selected from the hospital, controls were selected from clinical settings(De Silva, et al. 2010)]. There could also be limitations associated with small the sample size (n = 303) and limited age range (30-64 years). Nevertheless, similar observations were made in another case-control study in Northern Israel involving 792 participants aged 30-75 years. [OR (> 12yrs. versus < 12yrs. of breastfeeding) 0.3, 95% CI: 0.1, 0.4, p for trend < 0.001](Shema, et al. 2007)]. Although controls in the latter study were hospital-based, the authors showed that their characteristics did not differ from those of women in the general population. Furthermore, a case-control study by Hall and Colleagues observed a reduced risk of breast cancer associated with breastfeeding among African American women aged 20–49yrs, but not among women older than 49 years and Caucasians(white) women[(Hall, et al. 2005)]. This could suggest that the relationship between breastfeeding and breast cancer is modified by age and ethnicity.

There were, however, large case-control and cohort studies in Europe, North America, South America and Asia (n=≥1270) where a significant association between any form of breastfeeding and the risk of breast cancer was not observed (Tessaro et al. 2003; Andrieu et al. 2006; Ambrosone et al. 2014; Warner et al. 2013; Hadjisavvas et al. 2010; Chung et al. 2013; Sisti et al. 2015; Ma et al. 2010).

On the contrary, a study in Serbia observed an increased risk of breast cancer among parous women who have ever breastfed compared to those who have never breastfed (OR 2.90, 95% CI: 1.02, 8.22) as well as among those who have breastfed for ≥ 13months (OR 3.44, 95% CI: 1.15, 10.24)(Ilic, Vlajinac, & Marinkovic 2015). The authors, however, noted that limitations could have arisen from the small sample size of the study (n = 381), the use of non-standardised questionnaires and the inability to determine the eligibility rate of controls. In addition to these reservations expressed by the authors, there could be a problem of multicollinearity or over-adjustment of confounders. For example, adjustment for the number of pregnancies, as well as the number of live birth and abortion history.

Relationship between breastfeeding and risk of breast cancer subtypes

It has been suggested that the relationship between breastfeeding and breast cancer risk could be modified by oestrogen receptor status. The results of the African-American Breast Cancer Epidemiology and Risk (AMBER) consortium study (a case-control study involving 3,698 cases 14,180 controls of African-American origin) for example, showed that breastfeeding was associated with a reduced risk of oestrogen receptor-negative (ER-) breast cancer (OR 0.81, 95% CI: 0.69, 0.95) but not with oestrogen receptor-positive (ER+) breast cancer (OR 1.04, 95% CI: 0.91, 1.18)(Palmer et al. 2014). A similar observation was made by Fortner and colleagues based on data from Nurses' Health Study(Fortner et al. 2019). However, other large case-control studies in the USA and China (n ≥ 1,801) did not suggest that oestrogen or hormone receptor status could significantly modify the association between breastfeeding and risk of breast cancer(Xing, Li, and Jin 2010; Ambrosone, et al. 2014; Palmer, et al. 2014; Palmer et al. 2011). Nevertheless, results of these latter studies showed the effect sizes tended to be lower (protective) for ER- compared to ER+ breast cancer even when the findings were not significant, (Palmer, et al. 2011; Ambrosone, et al. 2014).

On the contrary, a longer duration of breastfeeding associated with an increased risk of both ER+ and ER- breast cancer among women born in 1950 and 1960 was reported in South Korea (Chung, et al. 2013). The report

suggested that a longer duration of breastfeeding was associated with increased risk of both ER+ and ER- breast cancer among women born in 1950 and 1960. The authors attributed their findings to possible differences in risk profiles associated with the cohorts as well as a potential misclassification error. Notably evidence of an effect modification by breast cancer gene (BRCA) types was suggested in a matched case-control study of 1,665 pairs of women with a deleterious mutation in either BRCA1 (n = 1,243 pairs) or BRCA2 (n = 422 pairs) (Kotsopoulos et al. 2012). The findings of this study showed that Increased duration of breastfeeding was associated with a higher risk reduction in BRCA 1 than BRCA2 cases (Kotsopoulos et al. 2012). It was not clear what role the differences in sample sizes might have played in the observed differences in risk reduction.The notable gap in sample sizes of BRCA 1 and BRCA2 cases should, however, be considered when interpreting the findings.

The studies reviewed suggest that breastfeeding could protect against breast cancer, especially oestrogen receptor-negative and BRCA1 breast cancer subtypes. However, the observation of a non-significant association between breastfeeding and breast cancer subtypes in several large case-control studies strongly suggests the need for more studies.

Observations from sub-Saharan Africa

A reduced risk of breast cancer associated with breastfeeding has been reported in Africa (Huo et al. 2008; Jordan et al. 2013; Galukande et al. 2016; Azubuike et al. 2022). For example, a Nigerian study reported a decrease of 7% for every 12 months of breastfeeding (p for trend = 0.005) (Huo, et al. 2008). The authors, however, acknowledged the possibility that the use of multiple imputations to replace missing data might introduce bias. Furthermore, generalisability could be an issue since > 80% of the participants were from the Yoruba ethnic population of Nigeria. Nigeria has more than 300 ethnic groups (National Population Commission (NPC) [Nigeria] & ICF International 2014). Nevertheless, the observation was consistent with the findings of a recent Nigerian study which included both participants from southern and northern Nigeria without applying multiple imputation in the analysis (Azubuike, et al. 2022). Although the authors of this latter study acknowledged the potential for selection bias, the distribution of key reproductive factors was shown to be consistent with the population parameters. Notably, while a population-based study in Ghana did not observe a significant risk of breast cancer with increased duration of breastfeeding among all women, it observed a significant risk reduction among older women and women with oestrogen receptor positive breast cancer(Figueroa et al. 2020). This contradicted the findings of Azubuike and colleagues who observed a significant risk reduction among all women, younger women and women with oestrogen receptor negative breast cancer(Azubuike, et al. 2022) .

It is not clear if this could be attributed to subtle population differences (for instance in age distribution) or differences in study methodologies. Hence, there is need for more studies in the region to confirm these findings. On the contrary, other studies from the region did not observe a significant association between breastfeeding and the risk of breast cancer (Okobia et al. 2006; Sighoko et al. 2013). These studies, however may have been limited by their sample sizes (n< 500). All the same, although the forest plot of SSA studies (Figure 2) seem to support the hypothesis that breastfeeding reduces the risk of breast cancer in the region, the plot may be limited by the obvious heterogeneity among the available studies. Nevertheless, given that 5(2 of which were population-based study) out of the 9 available studies indicated a risk reduction in breast cancer associated with breastfeeding practice, promotion of breastfeeding and improved breast-feeding practice may hold a potential for a reduced risk of breast cancer in the region. Nevertheless, the contradiction in findings especially with respect to the role of oestrogen receptor status requires further investigation based on studies with large sample sizes.

Limitations and strength

The potential for selection bias especially among the international studies included in this review may not be ruled out since this study cannot be described as a systematic review despite the systematic approach adopted. The description and the analysis of the results did not take into full consideration the heterogeneities among studies. The key strength of the study, however, is its comprehensiveness. To the best of my knowledge, all the available key

studies from subsaharan Africa were included. Hence, it provides a basis for relevant stakeholders to make informed decision based on the current state of evidence, as well as a direction for future investigation.

Conclusion

There was substantial evidence (especially from case control studies) that breastfeeding reduces breast cancer risk among women globally. This, however, was not observed in all studies, especially cohort studies. Most available studies in sub-Saharan Africa showed tendencies towards a reduced risk of breast cancer associated with breastfeeding. Of the 9 SSA studies cited, 5 indicated that that breastfeeding can protect against breast cancer, while the remaining four provided no such indication. The available findings on the modifying role of age and oestrogen receptor status on the relationship breastfeeding and breast cancer were not consistent. Hence, well-designed studies are needed to draw valid conclusions that will be generalizable to the region. Since most of the studies that observed a non-significant association between breastfeeding and breast cancer risk have sample sizes ≤ 500, studies with higher sample sizes would be desirable. While more investigation is highly recommended, the promotion of breastfeeding as part of a strategy for breast cancer prevention in the subregion is substantially supported by this review.

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