Breastfeeding and Breast Cancer Risk: Our Experience and Mini-review of the Literature

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ABSTRACT

Background: According to data from World Health Organization, breast cancer constitutes the second most common diagnosed malignancy after lung cancer and the second leading cause of death among women in 2020, worldwide. The protective role of breastfeeding in the emergence of breast malignancy has been mentioned in several studies, indicating the important part it can have in the effort of reducing breast cancer’s incidence.

Objective: To investigate a possible association between breastfeeding and breast cancer risk in Greek women.

Methods: Totally, 391 women participated in our case-control retrospective study. In the case group included 238 women with breast cancer, while in control group 153 women without breast cancer who were enrolled in two breast clinics in Greece. All women were examined clinically and with breast ultrasound, while those older than 40 years old also with bilateral digital mammography.

Results: The x² (chi-square) test found a statistically significant reverse correlation between breast cancer and breastfeeding ≥12 months (cumulative) (p = 0.001). It was observed that the percentages of patients who breastfed ≥12 months were lower than those of healthy women.

Conclusion: Breastfeeding and particularly the cumulative period of ≥12 months is related to the maximum of the protection from breast cancer.

Keywords: Breast cancer, Breastfeeding, Lactation, Breast Malignancy, Breast cancer risk factors.

1. BACKGROUND

According to data from World Health Organization, breast cancer constitutes the second most common diagnosed malignancy after lung cancer and the second leading cause of death among women in 2020, worldwide (1). Similarly, in Europe, including Greece, breast cancer was also in this period of time the second most frequent detected cancer after lung cancer and the second cause of mortality for women. Analytically, in Greece the incidence rate was 27.5% (1). Breast cancer mortality varied among countries and related to woman’s age, however, little variation exists across Human Development Index (HDI) levels (67.0-88.4 per100,000) in women (2).

It has been discovered that genetic, environmental, reproductive and lifestyle-related factors are implicated to the development of this disease. Family history or breast cancer mutation of BRCA1 and/or BRCA2 genes, early age at menarche and late age at menopause, low number of full-term pregnancies, late age at first completed pregnancy, short cumulative breastfeeding duration, high endogenous amount of estrogen, increased BMI, complex benign breast diseases, high breast mammographic density and alcohol consumption are strongly related factors for breast cancer (3-7). Low physical activity and smoking are also related with increase breast cancer risk but in lower intensity. The protective role of breastfeeding in the emergence of breast malignancy has been mentioned in several studies, indicating the important part it can have in the effort...
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of reducing breast cancer’s incidence. The possible mechanisms of the protective effect of breastfeeding are unclear until now and more investigation is needed. Nevertheless, some theories have been proposed. During breastfeeding, the circulation hormones such Estradiol, Prolactin and Growth hormone is reduced and by this way the risk of breast malignancy decreased. Another biological explanation regarding the protection of breastfeeding concerns

Table 1. Cumulative breastfeeding months

| Cumulative breastfeeding months | CASE/CONTROL | Total |
|---------------------------------|-------------|-------|
|                                 | Patients    | Healthy |       |
| Count                           | 35          | 13     | 48    |
| % within Breastfeeding          | 72.9%       | 27.1%  | 100.0%|
| % within CASE/CONTROL           | 14.7%       | 8.5%   | 12.3% |
| % of Total                      | 9.0%        | 3.3%   | 12.3% |
| <1 month                        | Count       | 44     | 12    | 56    |
| % within Breastfeeding          | 78.6%       | 21.4%  | 100.0%|
| % within CASE/CONTROL           | 18.5%       | 7.8%   | 14.3% |
| % of Total                      | 11.3%       | 3.1%   | 14.3% |
| 1-3 months                      | Count       | 32     | 17    | 49    |
| % within Breastfeeding          | 65.3%       | 34.7%  | 100.0%|
| % within CASE/CONTROL           | 13.4%       | 11.1%  | 12.5% |
| % of Total                      | 8.2%        | 4.3%   | 12.5% |
| >3-6 months                     | Count       | 20     | 22    | 42    |
| % within Breastfeeding          | 47.6%       | 52.4%  | 100.0%|
| % within CASE/CONTROL           | 8.4%        | 14.4%  | 10.7% |
| % of Total                      | 5.1%        | 5.6%   | 10.7% |
| >6-9 months                     | Count       | 26     | 13    | 39    |
| % within Breastfeeding          | 66.7%       | 33.3%  | 100.0%|
| % within CASE/CONTROL           | 10.9%       | 8.5%   | 10.0% |
| % of Total                      | 6.6%        | 3.3%   | 10.0% |
| >9-11 months                    | Count       | 9      | 11    | 20    |
| % within Breastfeeding          | 45.0%       | 55.0%  | 100.0%|
| % within CASE/CONTROL           | 3.8%        | 7.2%   | 5.1%  |
| % of Total                      | 2.3%        | 2.8%   | 5.1%  |
| >12-24 months                   | Count       | 22     | 40    | 62    |
| % within Breastfeeding          | 35.5%       | 64.5%  | 100.0%|
| % within CASE/CONTROL           | 9.2%        | 26.1%  | 15.9% |
| % of Total                      | 5.6%        | 10.2%  | 15.9% |
| >24-36 months                   | Count       | 8      | 17    | 25    |
| % within Breastfeeding          | 32.0%       | 0.8%   | 100.0%|
| % within CASE/CONTROL           | 3.4%        | 11.1%  | 6.4%  |
| % of Total                      | 2.1%        | 4.4%   | 6.4%  |
| >36 months                      | Count       | 2      | 3     | 5     |
| % within Breastfeeding          | 40.0%       | 60.0%  | 100.0%|
| % within CASE/CONTROL           | 0.8%        | 2.0%   | 1.3%  |
| % of Total                      | 0.5%        | 0.8%   | 1.3%  |
| Not at all                      | Count       | 40     | 5     | 45    |
| % within Breastfeeding          | 88.9%       | 11.1%  | 100.0%|
| % within CASE/CONTROL           | 16.8%       | 3.3%   | 11.5% |
| % of Total                      | 7.7%        | 1.3%   | 11.5% |
| Total                           | Count       | 238    | 153   | 391   |
| % within Breastfeeding          | 60.9%       | 39.1%  | 100.0%|
| % within CASE/CONTROL           | 100.0%      | 100.0% | 100.0%|
| % of Total                      | 60.9%       | 39.1%  | 100.0%|
the status of the epithelial cells of parous mammary gland which are more differentiated and less proliferative and by this way less prone to malignant mutation (8). Remarkably, type III lobules are developed only during pregnancy and type IV lobules which are fully mature appear under the influence of hormonal changes only during lactation (9). The protection of mammary cells against cancerous mutation is enhanced through breastfeeding which contributes to their final differentiation making them less susceptible to malignant transformation. Finally, the process of apoptosis that occur during breastfeeding removes from breast ductal tissue mammary cells with initial DNA mutation and therefore decreases the risk of breast cancer development (10). On the other hand, breastfeeding has also some challenges e.g. mastitis, abscess, chronic inflammation and possible due to the traumatic procedure of breast pumping etc. not very frequently (11), but the balance between breastfeeding or not, is clearly pro breastfeeding. Nevertheless, as it was mentioned above, more investigation should be conducted in order to clarify the protective role of breastfeeding.

2. OBJECTIVE
To investigate a possible association between breastfeeding and breast cancer risk in Greek women.

3. MATERIAL AND METHODS
This research is a case-control bicentric study. We collected the data of breast cancer patients who consulted in two breast clinics in Greece, between 2016 and 2019. The 391 participants included in the study were divided in two groups. More specifically, the case-group included 238 women (60.9%) with breast cancer confirmed after breast surgical procedure by the histopathological analysis. On the other hand, the control group included 153 healthy women (39.1%), who were examined with clinical examination, breast ultrasound and/or bilateral digital mammography without evidence for breast cancer. All the women of the two different groups were assessed in the same period of time, after a written informed consent.

The information regarding breastfeeding and the possible relationship with the presence or absence of breast cancer was analyzed using SPSS 20 software. Moreover, Chi-square test ($\chi^2$) was performed in order to calculate the p-value. A statistical significant result was considered if p-value was inferior to 0.05.

4. RESULTS
By calculating cumulatively the breastfeeding months of all participants, 48 out of 391 participants (12.3%) of the survey either did not have a pregnancy or did not breastfeed at all because they had not given birth to a living newborn. Of these, 5 (72.9%) were breast cancer patients and 13 (27.1%) were healthy. 56 (14.5%) of the 391 participants of this study breastfed for <1 month. Of these, 44 (78.6%) were breast cancer patients and 12 (21.4%) were healthy. 49 of the 391 (12.5%) participants breastfed for 1-3 months. Of these, 32 (65.3%) were breast cancer patients and 17 (34.7%) were healthy. 42 of the 391 (10.7%) participants breastfed for a period of >3-6 months. Of these, 20 (47.6%) were patients and 22 (52.4%) were healthy. 39 of the 391 (10%) participants breastfed for >6-9 months. Of these, 26 (66.7%) were breast cancer patients and 13 (33.3%) were healthy. 20 of the 391 (5.1%) participants breastfed for a period of >9-11 months. Of these, 9 (45%) were breast cancer patients and 11 (55%) were healthy. 62 of the 391 (15.9%) participants breastfed for a period of >12-24 months. Of these, 22 (35.5%) were patients and 40 (64.5%) were healthy. 25 of the 391 participants (6.4%) breastfed for a period of >24-36 months. Of these, 8 (32%) were breast cancer patients and 17 (68%) were healthy. 5 of the 391 (1.3%) participants breastfed for >36 months. Of these, 2 (40%) were breast cancer patients and 3 (60%) were healthy. Finally, 45 of the 391 participants (11.5%) did not breastfeed at all by personal choice. Of these, 40 (88.9%) were breast cancer patients and 5 (11.1%) were healthy.

Simply put, of the 238 breast cancer patients, 35 (14.7%) either had no pregnancy or did not breastfeed at all because they had not given birth, 44 (18.5%) breastfed for <1 month, 32 (13.4%) breastfed for 1-3 months, 20 (8.4%) breastfed for >3-6 months, 26 (10.9%) breastfed for >6-9 months, 9 (3.8%) breastfed for >9-11 months, 22 (9.2%) breastfed for >12-24 months, 8 (3.4%) breastfed for >24-36 months, 2 (0.8%) breastfed for >36 months and 40 (16.8%) did not breastfeed at all by choice. In addition, of the 153 healthy participants in the study, 15 (8.5%) either had no pregnancy or did not breastfeed at all because they had not given birth to a live newborn, 12 (7.8%) breastfed for <1 month, 17 (11.1%) breastfed for 1-3 months, 22 (14.4%) breastfed for >3-6 months, 15 (8.5%) breastfed for >6-9 months, 11 (7.2%) breastfed for >9-11 months, 40 (26.1%) breastfed for >12-24 months, 17 (11.1%) breastfed for >24-36 months, 5 (2%) breastfed for >36 months and 5 (3.3%) did not breastfeed at all by personal choice (Table 1).

The $\chi^2$ (chi-square) test found a statistically significant reverse correlation between breast cancer and a cumulative breastfeeding ≥12 months (p = 0.001) (Table 2). It was observed that the percentages of breast cancer patients who breastfed >12 months were lower than those of healthy women.

5. DISCUSSION
In our study, the association between longer cumulative breastfeeding and breast cancer’s incidence reduction was proved. Particularly, we observed that participants referring breastfeeding’s duration for one year or longer presented the lowest risk of breast cancer. Throughout the years the role of breastfeeding as a protective factor against breast cancer has been extensively investigated in several

| Chi-Square Tests          | Value | df | Asymp. Sig. (2-sided) |
|---------------------------|-------|----|-----------------------|
| Pearson Chi-Square        | 63.797 | 8  | .000                  |
| Likelihood Ratio          | 66.187 | 8  | .000                  |

Table 2. Breastfeeding correlation test ≥12 months (cumulatively) with the risk of breast cancer
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Breastfeeding as a modifiable factor seems to be of protective effect. Thus, it is an urgent need for women all over the world to be informed about the benefits of breastfeeding as protector factor of breast cancer. Moreover, this positive effect has more evidence when breastfeeding is performed for cumulative period of ≥12 months, this duration seems to allow the maximum of the protection.

6. CONCLUSION

Breastfeeding provides benefit to the infant and to the mother. Regarding breast cancer mostly studies as our proved that breastfeeding particularly more than 1 year has a protective effect. Thus, it is an urgent need for women all over the world to be informed about the benefits of breastfeeding as protector factor of breast cancer. Moreover, this positive effect has more evidence when breastfeeding is performed for cumulative period of ≥12 months, this duration seems to allow the maximum of the protection.

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