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REVIEW

# Breastfeeding and the prevention of breast cancer: a retrospective review of clinical histories

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**Aims and objectives.** To evaluate at what age parous and nonparous women were diagnosed with breast cancer. Factors taken into account for parous women were whether they had breastfed their children, and if so, the length of the lactation period. Other factors considered for both groups were obesity, family histories of cancer, smoking habits and alcohol consumption.

**Background.** Breast cancer is the most common form of cancer in younger women in Western countries. Its growing incidence as well as the increasingly early age of diagnosis led us to carefully analyse its possible causes and the preventive measures to be taken. This is a particularly important goal in epidemiological research.

**Design.** A retrospective study of the clinical histories of patients diagnosed with breast cancer at the San Cecilio University Hospital in Granada (Spain).

**Methods.** In this study, we analysed 504 medical records of female patients, 19–91 years of age, who had been diagnosed and treated for breast cancer from 2004–2009 at the San Cecilio University Hospital in Granada (Spain). Relevant data (age of diagnosis, period of lactation, family history of cancer, obesity, alcohol consumption and smoking habits) were collected from the clinical histories of each patient and analysed. A conditional inference tree was used to relate the age of diagnosis to smoking habits and the length of the lactation period.

**Results.** The conditional inference tree identified significant differences between the age of the patients at breast cancer diagnosis, smoking habits ($p < 0{\cdot}001$) and lactation period if the subjects had breastfed their children for more than six months ($p = 0{\cdot}006$), regardless of whether they had a family history of cancer.

**Conclusions.** Our study concluded that breastfeeding for over six months not only provides children with numerous health benefits, but also protects mothers from breast cancer when the mothers are nonsmokers.

**Relevance to clinical practice.** Nurses play a crucial role in encouraging new mothers to breastfeed their children, and this helps to prevent breast cancer.

**Key words:** breastfeeding duration, breast cancer, prevention

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## Introduction

Breast cancer is the most common form of cancer in women (Ferlay *et al.* 2007, Hery *et al.* 2008, Amaral *et al.* 2010). Currently, worldwide incidence is estimated at 720,000 cases per year, which amounts to approximately 20% of all cancers (Ballantyne 2004). In fact, in developed countries, breast cancer is the leading cause of cancer death in women of 35–

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64 years of age. However, 17–36% of all breast cancers occur in women under the age of 40 (Secginli & Nahcivan 2006).

In recent years, many breast cancer prevention studies have been carried out all over the world. Their main objective was to evaluate how a woman's chance of developing breast cancer was affected by breastfeeding as well as by pregnancy and childbirth. The results of these studies point to the vital role played by both hormonal and reproductive factors in the development of breast cancer (Enger *et al.* 1997, 1998, Gilliland *et al.* 1998, Tryggvadottir *et al.* 2001, Soon *et al.* 2003, Vieira *et al.* 2011).

Regarding the relation between pregnancy and breast cancer, there are two possible hypotheses. The first hypothesis is oestrogen-induced mitosis may be suppressed by estriol, the main oestrogen produced during pregnancy. The second hypotheses is oestrogen-induced mitosis may be suppressed by the hormone prolactin, which is also present at high levels during pregnancy.

High levels of estriol may protect a woman from subsequently developing breast cancer (Bernstein 1993, Clemon & Goss 2001, Clamp *et al.* 2002, Chlebowski *et al.* 2003). However, there is somewhat less agreement concerning the role of prolactin in the disease. There are many authors who claim that a higher prolactin concentration does not increase the risk of breast cancer. However, results of other studies have shown that a significant increase in the concentration of this hormone favours breast cancer cell growth in rats (Donegan 1977).

According to Levine and Dolin (1992), pregnancy reduces the risk of breast cancer because of the excretion of lipophilic carcinogens by the mother through the foetal fat and vernix caseosa. Hakansson *et al.* (1995) and, more recently, Rough *et al.* (2009) reported that human milk causes the vitro apoptosis or the programmed cell death of several varieties of cancer cells.

Despite the results of such studies, there is still much controversy regarding hormones and their possible effects on breast cancer development. One of the reasons for this is the complex etiopathogenic nature of breast tumours. Without a doubt, further studies are needed before a definitive conclusion can be reached (González-Jiménez *et al.* 2012).

Breastfeeding is still another research focus because there seems to be growing evidence that women who breastfeed reduce their risk of developing breast cancer (Aguilar Cordero *et al.* 2010). In the long term, the protection offered by breastfeeding is greater for premenopausal women. This seems reasonable if one considers the risk taken by mothers when they either stop or temporarily interrupt nursing their babies because of the need to take medication.

From a biological perspective, there are various explanations why breastfeeding seems to prevent breast cancer and why it appears to significantly benefit female health. The most probable of these are the hormonal changes that take place during pregnancy and lactation. These include oestrogen reduction and elimination through mammary fluid, the excretion of carcinogenic agents through the breast tissue during the breastfeeding process and the physical changes in mammary epithelial cells, which tend to differentiate, and thus delay ovulation (Freudenheim *et al.* 1997, Stuver *et al.* 1997, Loren *et al.* 2000).

According to a study carried out by Cancer Research UK, the dramatic increase in breast tumours in recent years is closely related to a corresponding decrease in the birth rate as well as to shorter periods of lactation. The results obtained showed that the relative risk of breast cancer decreased by 7·0% for each birth in addition to a decrease of 4·3% for every 12 months of breastfeeding (Kelsey *et al.* 1993, McCredie *et al.* 1998a,b, Woodman 2002).

Despite such studies, many researchers are still sceptical as to the protection against breast cancer potentially afforded by breastfeeding. They claim that the data obtained until now are both insufficient and in many cases, inconsistent. Nevertheless, a slightly lower rate of breast cancer was observed in women who breastfed their children for periods of over 12 months (Nagata *et al.* 2012). Of the women who had given birth, those who were cancer-free were more likely to have breastfed than those who subsequently developed breast cancer (79% as compared to 71%; Islam *et al.* 2012).

These results seem to point to an inverse relation between the length of the breastfeeding period and breast cancer risk. The rate of the decline in the relative risk of breast cancer associated with breastfeeding did not differ significantly for women in developed and developing countries and did not vary significantly because of age or ethnic origin (Beral *et al.* 2002).

In 1997–1999, researchers in Shandong, China, studied breast cancer risk in a group of 404 women as well as in a control group of the same size. They found that for those women who breastfed their children for more than 24 months, the odds ratio was 0·46 (95% confidence interval of 0·27–0·78) when compared with those who breastfed their child for 1–6 months. These data suggest that prolonged lactation reduces breast cancer risk (Zheng *et al.* 2000).

The main objective of the study described in this article was to provide new epidemiological data regarding the relationship between breast cancer and certain aspects of pregnancy and the lactation period. For this purpose, we

initially analysed available scientific data with a view to evaluating breast cancer incidence in relation to pregnancy and breastfeeding.

Our study targeted a group of 504 women in the province of Granada, Spain, who were monitored over a five-year period.

## Aims

Our research study had the following objectives:

- To ascertain whether there is a correlation between age at breast cancer diagnosis, risk factors such as obesity, alcohol consumption and smoking habits, and duration of lactation in women both with and without a family history of cancer.
- To verify whether there were significant differences in the mean age at breast cancer diagnosis of subjects who were smokers and breastfed their children and subjects with a family history of cancer.

## Methods

### Participants

This study is based on the medical records of 504 female patients, 19–91 years of age, who had been diagnosed with breast cancer and treated at San Cecilio University Hospital in Granada from 2004–2009. All of the subjects agreed to participate in the study and signed a written authorisation that allowed access to their records.

### Design

A retrospective study was carried out of the clinical histories of each patient. Relevant data (i.e. age at breast cancer diagnosis, lactation period, family history of cancer, obesity, alcohol consumption and smoking habits) were extracted from the histories of each patient and were analysed. A questionnaire, especially devised to study and record these variables, was elaborated and validated by the members of the research team. It was composed of a total of 20 items to elicit relevant information from the subjects.

To evaluate the nutritional status of each patient, it was necessary to determine their height and weight and thus their body mass index with a view to ascertaining whether they were normal weight, overweight or obese. The standards of the World Health Organization were used for this purpose (World Health Organization 1998). Authorisation for the study was also obtained from the Clinical Research Ethics Committee of the Saint Cecilio University Hospital. This made it possible to access the clinical records of the subjects and begin the study.

As part of our data analysis, we used descriptive statistics, *t*-tests and ANOVA texts to verify the statistical significance of the factors considered in our study. A conditional inference tree was built to obtain the strongest associations between the response variable and the factors. All the calculations were made using the R STATISTICAL SOFTWARE (R Foundation for Statistical Computing, Vienna, Austria) application, PARTY PACKAGE (Hothorn *et al.* 2006).

## Results

A descriptive analysis was carried out on the sample of 504 women. In this research, we considered data related to various risk factors not directly linked to age, namely obesity, alcohol consumption (two or more drinks a day), family history of cancer and smoking habits. A univariate statistical analysis of the dichotomous levels of each factor related to age at diagnosis as a response variable showed that no significance was found for any of the factors with the exception of smoking habits ($t = 5{\cdot}417$; $p < 0{\cdot}001$). However, our results showed that alcohol consumption (Harvey *et al.* 1987) and family history of cancer could contribute to explain differences in a multiple factor model. Unfortunately, the unbalanced group samples (480 to 14) in alcohol consumption did not allow the inclusion of this factor in a more complete model (with another crossing factor).

Additionally, the study sample was subdivided into three groups, depending on the average duration of the lactation period. The first group was composed of nonparous women or parous women who had not breastfed their children. The second group was composed of women who had breastfed their babies for three to six months, and the third group was composed of women who had breastfed for more than six months. Table 1 shows the results.

Using a more general model, we built a conditional inference tree with a view to highlighting the importance of each factor in the differences observed for each level and their corresponding interactions. Conditional inference trees estimate a regression relationship by binary recursive partitioning in a conditional inference framework. Generally speaking, the algorithm works in three stages. The first stage involves testing the global null hypothesis of independence between any of the input variables and the response (which may be multivariate as well). If this hypothesis cannot be rejected, then the process ends. If the hypothesis can be rejected, then the input variable with the strongest association with the response is selected. This association is

measured by a *p*-value corresponding to a test for the partial null hypothesis of a single input variable and the response. In the second stage, a binary split is implemented in the selected input variable. In the third and final stage, steps one and two are recursively repeated.

In this model, age at breast cancer diagnosis was regarded as a dependent variable. Explanatory factors included the subjects' smoking habits, alcohol consumption and duration of lactation period. The first clearly relevant factor given by this model is smoking habits ($p < 0{\cdot}001$). Only one other factor was found to be significant, but this was only for subjects who were nonsmokers. The differences were observed in those women who breastfed their children for more than six months ($p = 0{\cdot}006$), as shown in Fig. 1.

**Table 1** Means, standard deviations and significance values for *t*-tests and ANOVA of age of diagnosis in relation to the factors considered

| Risk factor | *n* | Mean | SD | *t* | *p* |
|---|---|---|---|---|---|
| Obesity | | | | | |
| Yes | 370 | 56·5 | 14·5 | −1·120 | 0·263 |
| No | 134 | 58·1 | 12·0 | | |
| Alcohol consumption* | | | | | |
| Yes | 14 | 47·9 | 11·6 | 2·529 | 0·012 |
| No | 480 | 57·4 | 13·9 | | |
| Family history of cancer | | | | | |
| Yes | 203 | 55·7 | 12·6 | 1·706 | 0·089 |
| No | 301 | 57·8 | 14·6 | | |
| Smoking habits | | | | | |
| Yes | 419 | 58·4 | 13·7 | 5·417 | <0·001 |
| No | 85 | 49·7 | 12·4 | | |

| Lactation period | *n* | Mean | SD | *F* | *p* |
|---|---|---|---|---|---|
| NP or <3 months | 364 | 56·7 | 13·9 | 6·58 | 0·0015 |
| 3–6 months | 109 | 55·5 | 13·9 | | |
| >6 months | 31 | 65·4† | 10·3 | | |

*Ten records without response.
†Nonhomogeneous group (Tukey's HSD *post hoc* test).

Table 2 shows the gains in the mean age of diagnosis for the factors in the conditional inference tree. As can be observed, there is a significant increase in the mean age at diagnosis for nonsmokers with a lactation period of over six months (21·3 years) in comparison with the other groups who breastfed their children for a shorter period of time.

To verify whether there is an interaction between the duration of the lactation period and smoking habits, a multiple regression model was fit. In consonance with the regression tree output, the only significant factors obtained by the regression model were the principal ones, namely smoking habits ($F = 29{\cdot}4$; $p < 0{\cdot}0001$) and lactation period ($F = 4{\cdot}95$; $p = 0{\cdot}002$).

## Discussion

There seems to be an increasing consensus among researchers that pregnancy and breastfeeding protect women from developing breast cancer. Both processes positively affect mammary epithelial differentiation and reduce the levels of

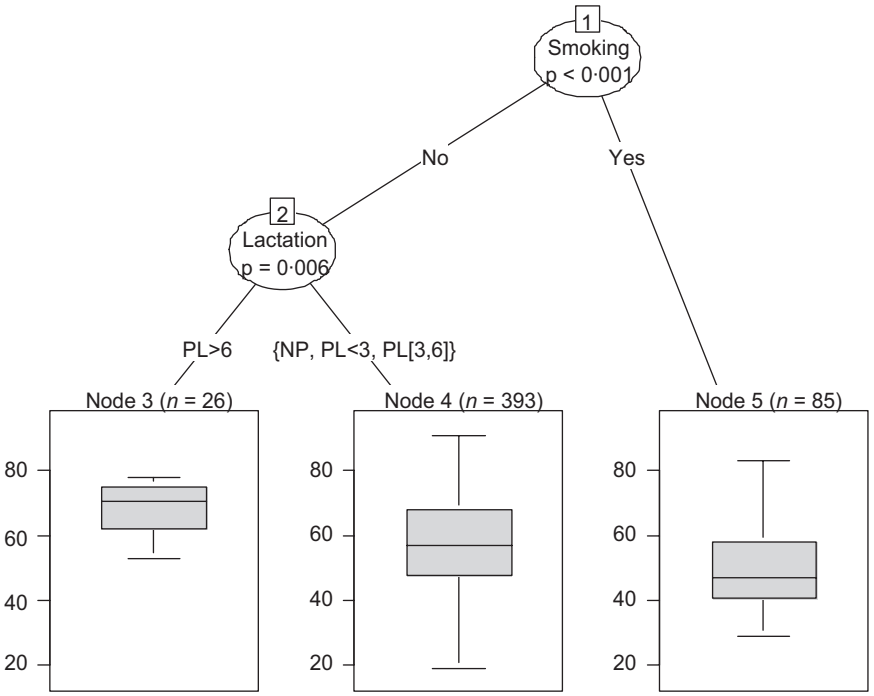


**Figure 1** Conditional tree of Age of Diagnosis for the factors considered.

**Table 2** Differences in the mean age of diagnosis for lactation groups in relation to family history of cancer and smoking habits

| Lactation group | Factor Smoking habits | Entire sample | | |
|---|---|---|---|---|
| | | Mean (SD) | Diff. | *n* |
| No lactation or less <3 months | Nonsmoker | 58·0 (13·8) | 7·3 | 299 |
| | Smoker | 50·7 (12·5) | | 65 |
| 3–6 months | Nonsmoker | 57·0 (13·6) | 10·9 | 94 |
| | Smoker | 46·1 (13·0) | | 15 |
| >6 months | Nonsmoker | 68·4 (7·9) | 21·3 | 26 |
| | Smoker | 47·6 (7·2) | | 5 |
| Total | | | | 504 |

certain hormones, such as oestrogen, which have been linked to breast cancer (Beral *et al.* 2002).

The results of our study show that childbirth and breastfeeding have an inverse relation to the age of breast cancer diagnosis, regardless of the patients' family history of cancer. Generally speaking, it was found that a longer lactation period reduced the risk of breast cancer. Nevertheless, the female smokers in our study were diagnosed with breast cancer at a younger age and obtained no significant benefit in this respect from a longer lactation period. In contrast, female nonsmokers who breastfed for periods of longer than six months tended to be diagnosed for breast cancer much later in life. In fact, our study showed an average gain of 10 years in the mean age at diagnosis with respect to other crossing categories (Table 2). In the case of female smokers, breastfeeding did not produce any benefits in the mean age at diagnosis, and the value was approximately nine years less than for the nonsmokers in the study (Table 1).

These results, based on age at diagnosis, are consistent with those obtained in other breast cancer studies in developed countries. Based on these findings, the incidence of this disease could be reduced from 6·3% to 2·7% (Harvey *et al.* 1987, Kalachc *et al.* 1993, Zheng *et al.* 2001) if women breastfed their children for more than six months. Consequently, the modern tendency not to breastfeed appears to be a crucial factor in the recent increase in breast tumours. This phenomenon has been confirmed by epidemiologic studies indicating that when a woman does not breastfeed her children, this increases her risk of developing breast cancer. In fact, breast cancer risk was found to decrease at a rate of 4·3% for each year that a woman breastfed her child (McCredie *et al.* 1998a,b). Unfortunately, the number of women who increasingly opt for bottle-feeding their babies has largely contributed to the virtual disappearance of breastfeeding.

In conclusion, breastfeeding for periods of over six months not only provides children with numerous health benefits, but also protects the mother from serious diseases such as breast cancer. Accordingly, breastfeeding is a potential ally in the fight against breast tumours. Current scientific data make researchers optimistic about the future reduction of breast cancer risk. It is thus necessary to continue to analyse and study the benefits of breastfeeding in the prevention of breast cancer.

## Relevance to clinical practice

According to other studies (Jiwa *et al.* 2010), the involvement of nurses in the prevention of complex diseases such as breast cancer necessarily involves the promotion of breastfeeding, especially for periods of longer than six months. In addition, nurses have an equally important role as health educators because they are in an excellent position to warn women about specific risk factors for breast cancer such as smoking, alcohol intake and the development of cadres of obesity (Campbell *et al.* 2006).

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## Disclosure

The authors have confirmed that all authors meet the ICMJE criteria for authorship credit (www.icmje.org/ethical_1author.html), as follows: (1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be published.

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