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Maternal Age at the Last Birth and the Risk for Breast Cancer: A Case Control-Retrospective Study and Mini -Review of the Literature

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Abstract

Objective: Maternal age at the last birth and the risk of developing breast cancer were subjects of epidemiologic research, with controversial results. In order to objectively assess the relationship between maternal age at the last birth and the risk of developing breast cancer, we carried out this case control-retrospective study.

Material and Methods: In our case-control retrospective analysis, 342 women who visited two breast clinics in Greece and had given birth to live newborns were analyzed. Women with breast cancer were included in the case group, whereas women without the disease were included in the control group. All women underwent a clinical examination that included a breast ultrasound and, in those who were older than 40 years old, also a digital bilateral mammogram was performed.

Results: Mann-Whitney test observed that p-value = 0.474 and concluded that there is no statistically significant difference in the distributions of maternal age at birth of the last child of the two groups of women and the risk of breast cancer development.

Conclusion: Our study showed no statistically significant relationship between maternal age at the last birth and breast cancer. Further studies with a larger number of patients are mandatory in order to confirm this result.

Keywords: Breast cancer; Maternal age and birth; Breast Malignancy; Breast cancer risk factors

Introduction

Breast cancer is the most frequent cause of death among women [1]. The differentiation of breast tissue, as well as hormonal and immunological profiles, can be impacted by reproductive events and their timing, which may increase the risk of breast cancer [2]. According to studies, breast cancer risk was increased by later menopause, later first birth age, family history of the disease, and adverse delivery [3], while it was decreased by later menarche age, high parity and breastfeeding [4].

The number of pregnancies and the age at first birth are well-known risk factors for breast cancer. Maternal age at the last birth, which is a marker of a later spike of hormones connected to pregnancy, is crucial in the development of gynecological cancer [5]. The association between later maternal age at the last birth and a lower risk of endometrial cancer and epithelial ovarian cancer has been established [6,7]. However, it is still controversial whether or not maternal age at the last birth has an impact on the development of breast cancer.

The present case control-retrospective study was especially aimed to clarify the role of maternal age at the last birth in breast cancer development.

Material and Methods

This study was a case-control retrospective one. We included the data of 342 women who visited two breast clinics in Greece and had given birth to live newborns. Women with

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breast cancer were included in the case group, whereas women without the disease were included in the control group. All women underwent a clinical examination that included a breast ultrasound and, in those who are older than 40 years old, also a digital bilateral mammography was performed. The case-group included 202 women with a histologically confirmed breast cancer history, while the control group included 140 women without a history of breast cancer. The two groups were examined in the same period of time. In all patients, written informed consent was requested. The data were analyzed with SPSS 20 statistical package software. Mann-Whitney test was used for statistical analysis and p-value<0.05 was considered statistically significant.

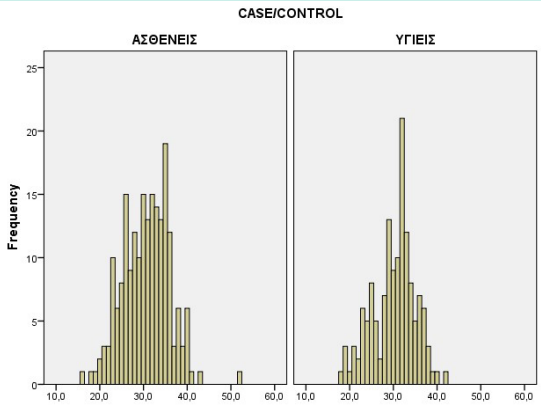

Figure 1: Age of participants at the birth of their last child.

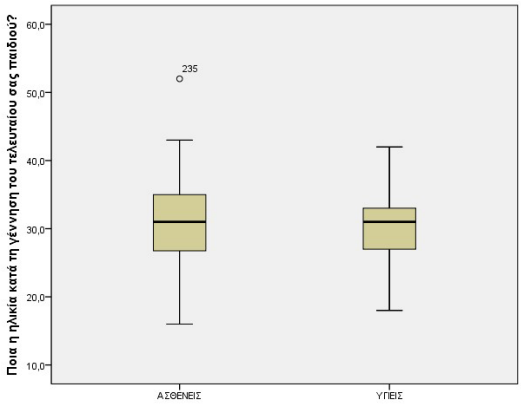

Figure 2: Age of participants at the birth of their last child.

Results

The average age of the patients in the study at the birth of their last child was 31 years old. The minimum value of the patients' age at the birth of their last child was 18 years old and the maximum value of the patients' age at the birth of their last child was 59 years old. In addition, the mean value of the age of the healthy study participants at the birth of their last child was 31 years old. The minimum value of the age of healthy women at the birth of their last child was 16 years old and the maximum value of the age of healthy women at the birth of their last child was 52 years old (Table 1).

Table 1: Average age of participants at the birth of the last child.

Age at the birth of the last child		
	Healthy	**Patients**
N Valid	140	202
Mean	30.143	30.663
Median	31	31
Minimum	18	16
Maximum	59	52

Checking the Association between the Age at Birth of the Last Child and the Risk of Breast Cancer

Mann-Whitney test observed that p-value = 0.474 and concluded that there is no statistically significant difference in the distributions of age at birth of the last child of the two groups of women (Table 2). This can be seen in Histograms 1-2 (Histograms 1-2).

Table 2: Mann-Whitney test for association of age at birth of last child with risk of breast cancer.

Test Statistics[a]	
	Age at the birth of the last child
Mann-Whitney U	13564.500
Wilcoxon W	23434.500
Z	-.717
Asymp. Sig. (2-tailed)	.474
a. Grouping Variable: CASE/CONTROL	

Discussion

While there is strong evidence linking a later maternal age at first live birth to a higher risk of breast cancer, the links between other reproductive ages and cancer risk are less certain [8].

The first full-term pregnancy has two effects on breast cancer risk, increasing the short-term risk and then decreasing the long-term risk. The interaction of these effects with breast cancer risk depends on the age of the woman [9,10].

Pregnancy seems to have a protective effect on women who have their first child at age 35 years old or earlier. Women who become pregnant for the first time later in life are more likely to develop breast cancer [11,12]. After the first pregnancy, the risk of breast cancer rises for around 10 years [11]. There after, the risk is reduced even more than in women who do not have children.

The underlying mechanism that results in this protection remains unclear, but several pathways have been explored, including breast lobe differentiation, cellular differentiation, and the stromal composition that occurs in the mammary gland during and after pregnancy. However, to date, no single cause has been identified and it is likely that the afore mentioned mechanisms interact to provide this protection [13].

One possible reason for the different effects of age on first birth is related to breast cells. More specifically, during pregnancy, breast cells grow rapidly. If there is any genetic damage to the breast cells, it is replicated as the cells grow. This increased genetic damage to the cells can lead to breast cancer. The likelihood of having such genetic damage increases with age. This theory may help explain why women who gave birth to their first child at an older age have a higher risk of breast cancer compared to women who gave birth to their first child at a younger age.

In the Western world, current trends regarding the decreasing number of children per family and the increased age of women at the first full-term pregnancy probably explain the increased incidence of breast cancer, a phenomenon that is also starting to occur in other countries, for example, in Latin America [14].

On the other hand, numerous epidemiological studies have been conducted to investigate the link between maternal age at last birth and the likelihood of acquiring breast cancer. One

study revealed a negative correlation [15] and five studies revealed a substantial positive association between the last birth and the risk of breast cancer [16-20]. The correlation between the short-term increases in breast cancer risk after a live birth may be the cause of the link between breast cancer risk and the last live birth that some studies have indicated [21]. The risk of maternal breast cancer peaks five years after childbirth, and it takes 15 years to minimize the risk [8].

Some studies found that having a child later in life raised the risk of developing breast cancer [22], but other studies revealed that the age at the child's last birth had no greater significance than the age at any intermediate birth [21,23]. According to several researchers, the relationship between the risk of breast cancer and the age at the time of the delivery is partially explained by the association of time since the last birth [24].

Similar to our results, most studies indicated no statistically significant association between maternal age at the last birth and breast cancer [8,23,25-31].

Conclusion

In the current case control-retrospective study no correlation between maternal age at last live birth and breast cancer risk was identified. Further studies with a larger number of patients are mandatory in order to confirm this result.

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