Original Article

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Protective Factors Against Breast Cancer Development: A Retrospective Study on Breastfeeding and Fertility

Meme Kanseri Gelişimine Karşı Koruyucu Faktörler: Emzirme ve Doğurganlık Üzerine Retrospektif Bir Çalışma

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ABSTRACT

Objective: Breast cancer (BC) is the most common type of cancer among women. Various risk and protective factors play a role in its development. This study evaluates the association between parity, breastfeeding, and age at BC diagnosis among women with BC.

Methods: Between January 2016 and December 2023, data from follow-up records of 1,014 patients diagnosed with BC and admitted to our hospital's radiation oncology clinic for radiotherapy treatment were analyzed. The collected data were statistically analyzed using Microsoft Access and SPSS 25.0.

Results: When patients with BC were grouped into those under and over the age of 55, a significant association was found between parity and later age at BC diagnosis (odds ratio: 2.02, 95% confidence interval: 1.29-3.16; p<0.002). When the number of live births was evaluated, having more than one live birth was associated with a later age at BC diagnosis (p<0.001). Regarding breastfeeding status, the proportion of patients diagnosed with BC under the age of 55 was 70.4% in the non-lactation group, whereas this rate was approximately 55.1% in the lactation group. This finding suggests that lactation may contribute to delaying the age of BC diagnosis (p<0.001).

ÖZ

Amaç: Meme kanseri (MK), kadınlar arasında en sık görülen kanser türüdür. Hastalığın gelişiminde birçok risk faktörü ve koruyucu faktör rol oynamaktadır. Bu çalışma, MK olan kadınlarda parite, emzirme ve MK tanı yaşı arasındaki ilişkiyi değerlendirmektedir.

Yöntemler: Ocak 2016 ve Aralık 2023 tarihleri arasında, hastanemiz radyasyon onkolojisi kliniğine MK tanısı ile radyoterapi tedavisi için başvuran 1.014 hastanın takip dosyalarındaki veriler incelenmiştir. Elde edilen veriler, Microsoft Access ve SPSS 25.0 programları kullanılarak istatistiksel analizlere tabi tutulmuştur.

Bulgular: MK tanısı alan hastalar, 55 yaş altı ve üstü olarak gruplandırıldığında, gebelik oranları karşılaştırılmış ve gebelik lehine anlamlı bir fark bulunmuştur (olasılık oranı: 2,02, %95 güven aralığı: 1,29-3,16; p<0,002). Gebelik sayıları değerlendirildiğinde, birden fazla çocuk sahibi olmanın MK tanısının daha ileri bir yaşta konulmasıyla ilişkili olduğu saptandı (p<0,001). Emzirme durumuna göre yapılan incelemede, laktasyon olmayan hasta grubunda 55 yaş altı MK görülme oranı %70,4 iken, laktasyon öyküsü olan grupta bu oran yaklaşık %55,1 olarak saptanmıştır. Bu bulgu, emzirmenin MK tanı yaşını geciktirici bir etkiye sahip olabileceğini göstermektedir (p<0,001).

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ABSTRACT

Conclusion: BC is a multifactorial disease with an increasing incidence. Our study demonstrates that parity and breastfeeding are significantly associated with the age at BC diagnosis. These findings should be interpreted as associations within a BC cohort rather than direct estimates of BC risk Future research will help to further explore these interactions in greater detail.

Keywords: Breast cancer, age at diagnosis, parity, breastfeeding

ÖZ

Sonuç: MK, birçok faktörün etkilediği kompleks bir hastalıktır ve görülme sıklığı giderek artmaktadır. Çalışmamız, gebelik sayısı ve emzirmenin, MK tanı yaşı ile anlamlı şekilde ilişkili olduğunu göstermektedir. Bu bulgular, MK riskini doğrudan yansıtmak yerine, MK tanısı almış hasta grubundaki ilişkileri göstermektedir. Gelecekteki araştırmalar, bu etkileşimlerin daha ayrıntılı bir şekilde incelenmesine katkı sağlayacaktır.

Anahtar Kelimeler: Meme kanseri, tanı yaşı, parite, laktasyon

Introduction

Breast cancer (BC) is the most common malignant tumor among women and the second most frequently diagnosed cancer worldwide (1,2). It is estimated that 2.3 million new cases occur annually, making it the fourth leading cause of cancer-related death globally (3).

Despite the increased availability of screening programs and advances in treatment, the incidence of BC continues to rise. This trend has been attributed to factors such as improved living standards, the use of hormone replacement therapy, and lower parity rates, particularly in developing countries (4,5).

Various reproductive (e.g., early menarche, nulliparity, hormone use, parity, and breastfeeding) and anthropometric (e.g., height, weight, waist circumference) factors have been identified as influencing the risk of BC development (6-9). Parity, defined as the number of live births, and breastfeeding, which is considered a significant protective factor, are of particular interest due to their hormonal impact on breast tissue. This study aims to highlight the significance of lactation and parity among known risk factors and to investigate their association with age at diagnosis among women diagnosed with BC.

Methods

This retrospective study included 1014 patients who were presented to our clinic between January 2016 and December 2023, were diagnosed with BC and received radiotherapy. Data were collected on patients' age at diagnosis, age at menarche and menopause, lactation history, smoking and alcohol use, hormone replacement therapy, comorbidities, and genetic background. These data were obtained from outpatient follow-up records.

Approved by Clinical Research Ethics Committee of University of Health Sciences Türkiye, Kartal Dr. Lütfi Kırdar City Hospital (approval no: 2024/010.99/2/38 date: 27.03.2024).

Statistical Analysis

Statistical analyses were conducted using Microsoft Access (Microsoft Corp., Redmond, WA, USA) for data management and SPSS version 25.0 (SPSS Inc., Chicago, IL, USA) for statistical testing. Odds ratios (OR) and 95% confidence intervals (CIs) were calculated to assess associations between reproductive factors and age at BC diagnosis. The chi-square test was used for categorical data analysis.

Parity was recorded based on the number of live births. Breastfeeding status was evaluated as a binary variable (yes/no), based on the presence of a history of lactation.

Results

The mean age of all patients diagnosed with BC (n=1.014) was 52 years, while the mean age at diagnosis among the postmenopausal group was 59 years. Table 1 summarizes the distribution of risk factors assessed in patients diagnosed with BC.

Parity and lactation status were compared between patients under and over the age of 55, as well as between premenopausal and postmenopausal groups, using chi-square analysis. Regarding breastfeeding, the proportion of patients under 55 who had no history of lactation was 70.4%, whereas this proportion was approximately 55.1 % in the group with a history of lactation (OR: 1.94, 95% CI: 1.35-2.80; p<0.001) (Table 2); additionally,

Table 1. Distribution of risk factors in patients diagnosed with breast cancer (n=1,014)

Risk factor	Category	n (%)
Age	≥55	429 (42.4)
	<55	585 (57.6)
Marital status	Single	121 (11.9)
	Married	860 (84.8)
	Widowed	33 (3.3)
Menopausal status	Premenopausal	436 (43.0)
	Postmenopausal	578 (57.0)
Lactation status	Yes	845 (83.3)
	No	169 (16.7)
Smoking	Yes	289 (28.5)
	No	725 (71.5)
Alcohol consumption	Yes	36 (3.6)
	No	978 (96.4)
Hormone replacement therapy	Yes	97 (9.6)
	No	917 (90.4)
Family history (breast cancer in family)	Yes	429 (42.3)
	No	585 (57.7)

Table 2. Analysis of reproductive risk factors in breast cancer patients aged <55 years (n=585) and ≥55 years (n=429)

Lactation			OR (95% CI)	p-value
No	119 (70.4)	50 (29.6)	1.00 Ref.	
Yes	466 (55.1)	379 (44.9)	1.94 (1.35-2.80)	<0.001
Nulliparous	77 (72.0)	30 (28.0)	1.00 Ref.	
Parous (≥1 live birth)	508 (56.0)	399 (44.0)	2.02 (1.29-3.16)	<0.002
Parity				
1-2	345 (70.0)	148 (30.0)	1.00 Ref.	
≥3	240 (46.1)	281 (53.9)	2.73 (2.13-3.50)	<0.001

Outcome: diagnosis age ≥55 (vs <55)
OR: Odds ratio, CI: Confidence interval

lactation status was associated with age at diagnosis when analyzed across menopausal status (p<0.001).

Among postmenopausal patients under 55 years of age, the proportion without lactation was 38.7%, compared to 24.9% among those who had breastfed, indicating a statistically significant difference (p<0.001).

When parity rates were compared between patients diagnosed with BC below and above the age of 55, parity was associated with a significantly later age at BC diagnosis (OR: 2.02, 95% CI: 1.29-3.16; p<0.002). Further analysis showed that having more than one live birth was associated with a later age at diagnosis (p<0.001).

Among patients with a history of three or more live births, 46.1% were diagnosed before the age of 55, whereas this proportion was 70% among those with two or fewer live births (OR: 2.73, 95% CI: 2.13-3.50; p<0.001).

Discussion

One limitation of this hospital-based study is that some responses were based on patient recall, which may have introduced variability in the data. However, as one of the major referral centers for BC cases on the Anatolian side of İstanbul, we believe the findings may be reflective of the broader population in Türkiye.

Previous studies have demonstrated that various factors, including hormones, age, genetic predisposition, and lifestyle, contribute to the incidence of BC (10,11). Age is considered one of the most important risk factors (12,13), with increasing incidence observed as age advances (14,15). McPherson et al. (16) reported that 2 out of every 1,000 women aged 50 were diagnosed with BC, while Vogel (17) found that women over 50 had a significantly higher risk of developing the disease.

Another study analyzed the association between age at diagnosis and relative survival, showing that women aged 45-49 had the best prognosis, with higher survival rates than younger patients (18). In urban areas of India, the highest incidence was observed among women aged 40-49, whereas in rural areas, it was found in the 65-69 age group (19). A study conducted in Northern India reported that 26% of diagnosed patients were under the age of 35 (20). Epidemiological data from the United States (US) have shown an increase in BC incidence among young women in recent years, accompanied by poorer long-term outcomes. These patients are also more likely to face treatment-related complications such as infertility, psychosocial distress, and chronic conditions, emphasizing the need for multidisciplinary and individualized treatment strategies in this population (21).

In our study, the proportion of patients under the age of 55 was relatively high and statistically significant. This may indicate a decreasing age at diagnosis due to improved screening programs or a shift in risk factors associated with developing countries.

In epidemiological studies, lactation is considered a protective factor against BC (22). Consistent with this literature, breastfeeding has been associated with a reduced risk of BC; however, in our cohort, breastfeeding history was associated with a later age at diagnosis rather than direct risk reduction. This finding supports the hypothesis that prolonged and gradual involution following lactation may influence breast tissue remodeling and carcinogenesis. During pregnancy, breast tissue proliferates in preparation for lactation. The filling of alveoli with milk and the subsequent weaning phase trigger breast tissue involution and remodeling. This process is characterized by denser stroma, altered collagen composition, increased inflammation and proliferation, and elevated expression of estrogen and progesterone receptors. When breastfeeding is prolonged and gradually discontinued, the breast undergoes what is referred to as "gradual involution", which may provide additional protection against carcinogenesis (23). These associations may be partly explained by hormonal mechanisms, including prolonged suppression of estrogen exposure during pregnancy and lactation, as well as long-term hormonal differentiation of breast tissue.

In a 2002 study by Collaborative Group on Hormonal Factors in BC, which included 50,302 women diagnosed with invasive BC and 96,973 controls from 30 countries, an inverse relationship was observed between breastfeeding duration and BC risk. The study demonstrated that each year of breastfeeding was associated with a 4.3% reduction in relative BC risk, for both localized and metastatic tumors (24).

A 2023 study by Chen et al. (25) showed that breastfeeding might reduce BC incidence by suppressing oncogene expression in progenitor cells, modulating the cellular microenvironment via calcium, secretory immunoglobulin A, and alpha-lactalbumin, and supporting normal involution processes. Similarly, Ye et al. (26) reported a protective association between breastfeeding and BC risk mediated through decreased breast tissue density. Furberg et al. (23) also found that even limited breastfeeding slightly reduced BC risk among both younger and older parous women. Consistent with these findings, our study demonstrated a significant association between breastfeeding history and earlier vs later age at diagnosis.

Parity is another reproductive factor associated with BC outcomes through hormonal mechanisms. Not only the number of live births but also the exclusivity and duration of breastfeeding contribute to breast tissue remodeling, potentially reducing carcinogenic transformations. Prolonged and exclusive breastfeeding appears to support involution and hormone regulation.

A large national cohort study from Norway investigated the relationship between parity and BC before age 55, finding that early age at first and last birth and high parity were associated with a reduced risk. The protective effect of high parity was most pronounced in women whose first birth occurred before the age of 20, while it was minimal in those who gave birth at or after age 30 (27). A population-based case-control study in Sweden also demonstrated a significant association between higher parity and reduced BC risk (28). Similarly, a Chinese case-control study showed a statistically significant trend of increasing BC risk with decreasing number of full-term pregnancies (29). In a US based population cohort of older women, having five or more live births was found to be protective compared to having only one or two (30).

Study Limitations

One of the potential study limitations is that, due to its retrospective design, there may be missing or inaccurate data in patient records, and bias may arise regarding the accuracy of self-reported information. Additionally, measurement errors may occur in variables such as menopause age and breastfeeding duration. Changes in healthcare policies and screening programs between 2016 and 2023 may have influenced the study results.

Conclusion

BC is a multifactorial disease with a rising incidence worldwide. This study demonstrates that higher parity and a history of breastfeeding are significantly associated with a later age at BC diagnosis. Although causal or risk-reducing effects cannot be inferred due to the retrospective design and the absence of a control group, these findings are consistent with existing epidemiological literature suggesting a potential protective role of reproductive factors. Further prospective, population-based studies are needed to clarify the complex biological mechanisms underlying these relationships.

Ethics

Ethics Committee Approval: Approved by Clinical Research Ethics Committee of University of Health Sciences Türkiye, Kartal Dr. Lütfi Kırdar City Hospital (approval no: 2024/010.99/2/38 date: 27.03.2024).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.T., Concept: D.G., Design: Ş.K.G., Data Collection or Processing: A.A., Analysis or Interpretation: N.A., Literature Search: R.Y., Writing: N.Ç.

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