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The Effect of Breastfeeding on Cervical Dysplasias

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Abstract

Objective

The aim of this study was to investigate the relationship between breastfeeding and precancerous cervical lesions.

Materials and Methods

This prospective descriptive study was conducted at a tertiary training and research hospital between September 1, 2023, and November 1, 2023. A total of 229 patients who attended the gynecology outpatient clinic and provided information regarding their breastfeeding experiences were included in the study. Patients with abnormal cervical cytology composed the study group (n = 98), whereas those with normal cytology composed the control group (n = 131). The breastfeeding experiences of both groups were then compared in relation to their cervical cytology results.

Results

The smear results of the control group were normal; however, among the study group, 61.2% had atypical squamous cells of undetermined significance (ASCUS), 15.2% had high-grade squamous intraepithelial lesions (HSILs), and 22.2% had low-grade squamous intraepithelial lesions (LSILs). Human papillomavirus (HPV) positivity was detected in 48% of the study group, whereas it was detected in 9.2% of the control group. The mean duration of breastfeeding in the study group was significantly shorter than that in the control group (14.11 ± 2.96 months versus 23.60 ± 3.35 months; $p < 0.05$). Furthermore, we found that the number of individuals who breastfed for 13–36 months (35.1%) was the greatest in the control group, whereas the number of individuals who breastfed for 6–12 months (34.7%) was the greatest in the study group ($p < 0.05$). Within the study group, the mean breastfeeding duration for the ASCUS subgroup (13.02 ± 1.33 months) was significantly greater than that for both the HSIL (5.91 ± 0.98 months) and LSIL (5.91 ± 0.98 months) subgroups ($p < 0.05$). Moreover, the total duration of breastfeeding and HPV positivity were identified as the most significant parameters affecting the risk of abnormal cytology; patients who breastfed for < 6 months presented a 5.399-fold greater risk of abnormal cytology than did those who breastfed for > 36 months, and HPV-positive patients presented a 26.369-fold greater risk of abnormal cytology.

Conclusion

Similar to its effects on various other cancers, breastfeeding and its duration clearly have beneficial effects on cervical intraepithelial neoplasia. Early recognition of the precancerous stage of cervical cancer—potentially the first cancer type that could be eradicated through comprehensive screening and

control strategies—is crucial. In light of the multitude of benefits that breastfeeding offers for women's health, including its role in the prevention of gynecological cancers, we advocate the implementation of effective policies aimed at increasing breastfeeding rates.

INTRODUCTION

Despite being largely preventable and treatable, cervical cancer remains a significant public health issue, particularly affecting young and socioeconomically disadvantaged women in developing countries. In low-income countries, it is still the second most common type of cancer and the third leading cause of cancer-related death. It has been well established that early screening can substantially reduce mortality associated with cervical cancer. In 2020, the World Health Organization (WHO) launched the "Cervical Cancer Elimination Initiative," reemphasizing that cervical cancer is preventable and setting a goal of eradicating this disease by the next century. The initiative recommended that each country develop its own control policy and emphasized the importance of vaccination, screening, and treatment. Human papillomavirus (HPV) is the most significant etiological factor in the development of cervical neoplasia, accounting for over 95% of cervical cancer cases.

A crucial feature of cervical cancer is underscored by the fact that 90% of deaths attributable to this disease occur in low- to middle-income countries and by the potential for a substantial reduction in mortality through effective screening and preventive measures (1). Regular screening programs implemented in high-income countries have proven highly effective in the early detection of premalignant lesions, thereby preventing prolonged and costly treatments, reducing both mortality and morbidity, and averting the need for complex interventions (2). Cervical dysplasias, which are precursors to cervical cancer, are also referred to as cervical intraepithelial lesions and are classified as low-grade squamous intraepithelial lesions (LSILs) or high-grade squamous intraepithelial lesions (HSILs). Although these lesions are generally associated with high-risk HPV infections and can be managed with timely diagnosis and appropriate follow-up, they carry the risk of progression to cervical cancer if left untreated. Therefore, regular screening for early detection and follow-up is of paramount importance. In addition to HPV, factors such as the immune system, hormonal influences, and lifestyle choices contribute to the development of cervical dysplasia. Breastfeeding, which offers numerous benefits for maternal health, induces significant physiological changes during the postpartum period. Its effects on modulating the immune system and enhancing cellular immunity may play a potential role in the regeneration of the cervical epithelium. However, the direct effects of breastfeeding on the persistence of HPV infection or on cervical dysplasia have not yet been fully elucidated. The relationship between breastfeeding and the incidence of breast, ovarian, and endometrial cancers has been extensively studied, and an inverse relationship between the duration/frequency of breastfeeding and cancer risk has been established (3). However, research on the relationship between breastfeeding and precancerous cervical lesions remains limited.

The aim of this study was to investigate the relationship between breastfeeding and precancerous cervical lesions.

MATERIALS AND METHODS

This prospective study was conducted at a tertiary training and research hospital in Ankara, the capital of Turkey, between September 1, 2023, and December 1, 2023. Ethical approval for the study was obtained from the ethics committee of the hospital (Ankara Atatürk Sanatoryum Training and Research Hospital Clinical Research Ethics Committee) on August 23, 2023 (Approval Number: 2012-KAEK-15/2772). The universal principles of the Helsinki Declaration were applied and informed consent was obtained from all participants. The study was carried out among women who presented at the Gynecology Outpatient Clinic during the specified period. They were enrolled in the cervical cytology screening program, underwent a cotest, and consented to participate. Women aged 25–65 years (the age range for Pap smear screening as recommended by the Turkish Ministry of Health), who had previously given birth, had no history of cervical cancer and/or precancerous cervical lesions, and whose last childbirth occurred at least 2 years prior, were included. Adolescents, women with a known chronic illness, any history of malignancy, those who had undergone a hysterectomy, who had immunosuppressive diseases or treatments, who had conditions that could preclude breastfeeding (e.g., maternal HIV positivity, galactosemia, etc.), who had a history of precancerous cervical lesions, whose last childbirth was < 2 years ago, or who were smokers were excluded from the study.

A total of 229 patients meeting the criteria during the designated period were enrolled in the study; patients with abnormal cervical cytology were included in the study group (n = 98), whereas those with normal cytology formed the control group (n = 131).

After receiving detailed information about the study and providing written consent, the participants completed a sociodemographic information form and breastfeeding history with the assistance of the investigator. Cervical cytology reports were retrieved and recorded from the hospital's information system.

The breastfeeding experiences of the study and control groups were then correlated with their cervical cytology results for comparison.

At our institution, cervical cytology samples are prepared via a liquid-based Pap test (Max-Prep, Dong-gu, Kwangju, South Korea). The cells were collected from the cervical canal via an endocervical plastic brush and then placed in 10 ml Max-Prep cytology solution containers before being delivered to the hospital's pathology laboratories. Cervical cytology and histology samples were interpreted by expert pathologists via the 2001 Bethesda system classification for cervical cytology reports. To minimize bias, all cervical cytology samples collected during the study period were evaluated and reported by the same pathologist.

For the HPV test, after visualizing the cervix, samples were obtained via an appropriate brush in a scraping manner and processed in hospital laboratories via HPV solution containers (Tek-PathPap test preservative solution, 10 ml). The results were reported as either negative or high-risk types (16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68).

Statistical analysis

The data obtained in the present study were analyzed via IBM SPSS Statistics 27 software. Descriptive statistics are reported as the means and standard deviations for normally distributed variables and as median (minimum and maximum) values for nonnormally distributed variables. The normality of the variables was assessed via the Shapiro–Wilk and Kolmogorov–Smirnov tests. For comparisons among multiple variables that did not exhibit a normal distribution, the Kruskal–Wallis test and the Mann–Whitney U test were used, whereas Spearman's correlation test was applied for correlation analyses. The relationships between two categorical variables were examined via Pearson chi-square (χ^2) cross-tabulation. Factors affecting the status of abnormal cytology were evaluated via binary logistic regression: the backward LR model. A p value of < 0.05 was considered to indicate statistical significance in all analyses.

RESULTS

The demographic characteristics of the patients are presented in Table 1. There were no statistically significant differences between the groups with respect to age, education level, employment status, income level, gravida, or parity ($p > 0.05$). In the study group, the smear results presented in Table 1 indicate that 61.2% of the participants had ASCUS, 15.2% had HSIL, and 22.2% had LSIL. In contrast, the smear results in the control group were normal. A statistically significant difference was observed in HPV positivity between the groups; 47 patients (48.0%) in the study group were HPV positive, whereas 12 patients (9.2%) in the control group were HPV positive ($\chi^2 = 44.124$; $p < 0.001$).

Table 1
Demographic characteristics of the study and control groups

	Study		Control		p value
	Number (n)	Percentage (%)	Number (n)	Percentage (%)	
Total	98	% 42.7	131	% 57.3	
Educational level					**0.319**
Primary and Secondary School	16	%16.3	13	% 9.9	
High School	46	% 46.9	70	% 63.4	
University	36	% 36.8	48	% 36.7	
Educational Level of the Spouse					**0.187**
Primary and Secondary School	11	% 12.2	7	% 5.6	
High School	40	% 44.4	65	% 51.6	
University	39	% 43.4	54	% 42.8	
Employment status					**0.987**
Employed	42	% 42.9	56	% 42.7	
Unemployed	56	% 57.1	75	% 57.3	
Income level					**0.084**
Below minimum wage	24	% 24.5	20	% 15.3	
Minimum wage	29	% 29.6	55	% 42	
Above minimum wage	45	% 45.9	56	% 42.7	
Marital status					**0.244**
Married	89	% 90.8	126	% 96.2	
Single	2	% 2	1	% 0.7	
Divorced	7	% 7.2	4	% 3.1	
Smear results					
Normal	0	0	131	%100	
ASCUS	61	% 61.2	0	0	

	Study		Control		p value
	Number (n)	Percentage (%)	Number (n)	Percentage (%)	
LSIL	22	% 22.2	0	0	
HSIL	15	% 15.2	0	0	
HPV					**< 0.001**
Positive	47	% 48	12	% 9.2	
Negative	51	% 52	119	% 90.8	
	Median	**[min–max]**	**Median**	**[min–max]**	**p value**
Age	29	[25–44]	31	[25–42]	**0.129**
Gravida	2	[1–7]	2	[1–6]	**0.509**
Parity	2	[1–4]	2	[1–6]	**0.056**
Time from last birth (years)	3	[2–6]	3	[2–5]	**0.532**
Normal delivery (number)	1	[0–4]	1	[0–5]	**0.577**
Cesarean section (number)	0	[0–4]	0	[0–4]	**0.507**

Table 2
Comparison of total and mean breastfeeding durations between the study and control groups

	Study (n = 98)		Control (n = 131)		p value		
	n	(%)	n	(%)			
Breastfeeding duration < 6 months 6–12 months 13–36 months > 36 months	31 34 24 9	31.6 34.7 24.5 9.2	16 41 46 28	12.2 31.3 35.1 21.4	χ^2 = 17.724 p = 0.001		
	$\bar{X} \pm S.S.$	**Median [Min–Max]**	$\bar{X} \pm S.S.$	**Median [Min–Max]**			
Breastfeeding duration	14.11 ± 2.96	13,0 [2.0–80.0]	23.60 ± 3.35	15	5.60 ± 0.83	5.0 [2.0–14.0]	Z=-3.393 p < 0.001

İn Table 2, a statistically significant difference in total breastfeeding duration was detected between the groups. The number of individuals who breastfed for 13–36 months (35.1%) was the greatest in the control group, whereas the number of individuals who breastfed for 6–12 months (34.7%) was the greatest in the study group. The mean duration of breastfeeding in the study group was significantly shorter than that in the control group ($p < 0.05$) (Table 2).

Table 3
Comparison of total and mean breastfeeding durations in the study group according to cytology results

Breastfeeding Smear	< 6 months (n = 31)		6–12 months (n = 34)		13–36 months (n = 24)		> 36 months (n = 9)		Statistical analysis* Probability
	n	%	n	%	n	%	n	%	
ASCUS	13	42.0	23	67.6	18	75.0	7	77.8	$\chi^2 = 11.115$
LSIL	9	29.0	8	23.6	3	12.5	2	22.2	p = 0.085
HSIL	9	29.0	3	8.8	3	12.5	-	-	

	n	Duration of breastfeeding (months)		Statistical analysis* Probability
		$\bar{X} \pm S.S.$	Median [Min–Max]	
ASCUS (1)	61	13.02 ± 1.33	11.0 [7.0–80.0]	$\chi^2 = 16.105$
LSIL (3)	22	5.91 ± 0.98	6.0 [3.0–15.0]	[1–2,3]
HSIL (2)	15	5.60 ± 0.83	5.0 [2.0–14.0]	p < 0.001

Although not statistically significant, the majority of the ASCUS group breastfed for 6–12 months, whereas most of the LSIL and HSIL groups had a total breastfeeding duration of < 6 months. When the mean breastfeeding duration was evaluated, the highest mean duration was observed in the ASCUS subgroup, and the lowest duration was reported in the HSIL subgroup; this difference was statistically significant ($p < 0.05$) (Table 3).

Table 4
Logistic regression model based on abnormal cytology status

Variable	B	S.H.	Wald	Sd	p	OR	95% Confidence Interval (OR)	
							Lower	Upper
HPV	3.272	0.514	40.541	1	**0.001**	26.369	9.631	72.200
Breastfeeding (> 36 months)			11.475	3	**0.009**			
Breastfeeding (< 6 months)	1.686	0.578	8.520	1	**0.004**	5.399	1.740	16.747
Breastfeeding (6– 12 months)	0.754	0.534	1.997	1	0.158	2.126	0.747	6.049
Breastfeeding (13– 36 months)	0.315	0.559	0.318	1	0.573	1.371	0.458	4.097
Constant	-1.925	0.481	15.992	1	0.001	0.146		
CCR = 78.6% $\chi^2_{(8)}$ = 2.850; p = 0.943								

According to logistic regression analysis in Table 4, total breastfeeding duration and HPV positivity were the most significant factors affecting abnormal cytology ($p < 0.05$); women who breastfed for < 6 months had a 5.399-fold greater risk of abnormal cytology than those who breastfed for 36 months (OR = 5.399), and HPV-positive women had a 26.369-fold greater risk than HPV-negative women did (OR = 26.369) (Table 4).

DISCUSSION

Despite the presence of effective screening programs, cervical cancer—the fourth most common cancer in women worldwide—remains among the leading causes of mortality among gynecological cancers. Cervical intraepithelial neoplasia, which is diagnosed through cervical biopsy and histological examination, is a premalignant squamous lesion of the uterine cervix; its early detection is crucial for preventing prolonged and costly treatments, as well as for reducing the incidence of invasive cervical cancer cases (1). Breastfeeding, known for its numerous benefits to maternal health, may play a potential role in the regeneration of the cervical epithelium through its immunomodulatory and cellular immunity-enhancing effects. The present study was conducted to investigate the effect of breastfeeding on cervical dysplasia, and the results revealed that the study group had a significantly shorter mean duration of breastfeeding, with the control group predominantly breastfeeding for 13–36 months rather than for 6–12 months. Within the study group, the lowest mean breastfeeding duration was noted in the HSIL subgroup. Moreover, total breastfeeding duration was identified as a significant factor influencing the risk of abnormal cytology, with women who breastfed for < 6 months showing a 5.399-fold greater risk than those who breastfed > 36 months.

Breastfeeding provides innumerable benefits to both mothers and infants (4). The WHO recommends exclusive breastfeeding for the first 6 months and continuing breastfeeding with complementary foods for at least 2 years. (5) WHO has a target of %50 for the first 6 month of exclusive breastfeeding (6). According to the 2018 Turkey Demographic and Health Survey data, the rates of exclusive breastfeeding during the first 6 months increased from 10.4% in 1993 to 40.7% in 2018; however, these rates remain substantially lower than those reported in developed countries.

In addition to its numerous benefits for maternal health, breastfeeding is also recognized for its protective effects against several cancers. The preventive effect of breastfeeding against breast and ovarian tumors has been well documented in the literature (3). Chowdhury et al. (2015), in their systematic review and meta-analysis investigating the effects of breastfeeding on maternal health, concluded that in patients with a total breastfeeding duration > 2 months, the risk of breast cancer was reduced by 26% and that of ovarian cancer was reduced by 37%. (3) Palmer et al. (2014), while examining the impact of parity and breastfeeding on breast cancer, reported an increased incidence of estrogen receptor-negative breast tumors among parous women who did not breastfeed, emphasizing that the protective effect is more attributable to breastfeeding than to parity and that encouraging mothers to breastfeed is an important strategy in reducing breast cancer-related mortality. (7) In their meta-analysis on the effect of breastfeeding on endometrial cancer risk, Zhan et al. (2015) reported a linear relationship between breastfeeding and endometrial cancer risk, with each month of breastfeeding reducing the risk by 1.2%, highlighting the significant protective effect of long-term breastfeeding against endometrial cancer.(8) Similarly, Ma et al. (2018), in their meta-analysis of studies examining the association between breastfeeding and endometrial cancer, reported that breastfeeding consistently exerts a protective effect, with a 7% reduction in risk for every 6 months of breastfeeding, emphasizing the importance of encouraging women to breastfeed for prolonged periods. (9) Furthermore, in a meta-analysis incorporating five cohort studies and 35 case—control studies examining the relationship between breastfeeding and ovarian cancer, breastfeeding was associated with a 30% reduction in ovarian cancer risk, and the degree of risk reduction increased with the total duration of breastfeeding: 15% for < 6 months, 27% for 6–12 months, and 36% for > 12 months (10).

In the present study, the mean total breastfeeding duration was 14.11 ± 2.96 months in the study group and 23.60 ± 3.35 months in the control group, with the control group exhibiting a significantly longer duration. A statistically significant difference in total breastfeeding duration was detected between the groups. The number of individuals who breastfed for 13–36 months (35.1%) was the greatest in the control group, whereas the number of individuals who breastfed for 6–12 months (34.7%) was the greatest in the study group. In addition, total breastfeeding duration was found to be an important parameter affecting the risk of abnormal cytology; women who breastfed for < 6 months had a 5.399-fold greater risk of abnormal cytology than those who breastfed for > 36 months. When the study group was analyzed separately, the majority of the ASCUS subgroup had a total breastfeeding duration of 6–12 months, whereas most of the LSIL and HSIL subgroups had a duration of < 6 months. Moreover, the highest mean breastfeeding duration was observed in the ASCUS subgroup, whereas the lowest duration was found in the HSIL subgroup. Although the protective effects of breastfeeding on breast, endometrial,

and ovarian cancers have been extensively documented, studies investigating its impact on cervical dysplasia and cervical cancer are limited. Jin et al. (2021) conducted a secondary analysis of data from the Korean Genome and Epidemiology Study, including 113,944 women aged ≥ 40 years from 2004–2013, to examine the relationship between breastfeeding and the incidence of breast, thyroid, and cervical cancers among Korean women. They reported that the prevalence of cervical cancer in the nonbreastfeeding group was 1.37 times greater than that in the breastfeeding group and that increasing total breastfeeding duration was associated with a decrease in cancer incidence. The authors concluded that breastfeeding and longer breastfeeding durations significantly reduced the incidence of breast, thyroid, and cervical cancers. (11) In a study conducted by Mekonen et al. (2024) in four sub-Saharan African countries aimed at determining the prevalence of cervical cancer screening and its associated factors, the results revealed that breastfeeding women were 25% less likely to undergo cervical cancer screening than nonbreastfeeding women were, which the authors attributed to the prevailing notion that breastfeeding and prolonged breastfeeding duration reduce the risk of developing cervical cancer (12).

Like the breast and endometrium, the cervix is highly sensitive to hormones, and hormones are known to play a significant role in the pathogenesis of cervical cancer. (13) Yu et al. (2018), in their systematic review on the protective effects of reduced estrogen receptor alpha (ER-α) expression in cervical cancer, concluded that targeting reduced ER-α expression in cervical cancer patients could serve as a potential therapeutic approach, particularly for patients who do not wish to undergo surgical treatment. Furthermore, in their systematic review investigating the relationship between estrogen and cervical cancer, Chung et al. (2010) highlighted that, on the basis of the plateau pattern of cervical cancer incidence in postmenopausal women, estrogen plays a crucial role in cervical carcinogenesis by increasing the expression of the E6 and E7 oncogenes—key drivers in the development of cervical cancer—and by significantly influencing HPV gene expression. (14)

Collectively, these findings suggest that the reduction in estrogen levels during breastfeeding due to the suppression of pituitary and ovarian hormones may decrease endometrial stimulation and exert significant effects on the cervix (15). In the present study, the lowest total breastfeeding durations were observed in the LSIL and HSIL subgroups, and total breastfeeding duration was identified as a critical factor affecting abnormal cervical cytology. These results support the notion that breastfeeding has a positive effect on the cervix. Despite the extensive documentation of the protective effects of breastfeeding against estrogen-related cancers such as breast and endometrial cancer, the literature on cervical cancer and cervical dysplasia—conditions in which estrogen also plays an important role—is limited. This underscores the necessity for further research focused on this area.

The limitations of the present study include the relatively small number of patients, the reliance on self-reported breastfeeding histories (which may introduce recall bias in the estimation of total breastfeeding duration), and the homogeneous nature of the study population. Nonetheless, we believe that our prospective study, which examines the effect of breastfeeding on cervical precancerous lesions, is noteworthy, given that the protective effects of breastfeeding, although well established in many other

cancer types, have not been adequately addressed in the context of cervical precancerous lesions and cervical cancer.

In conclusion, early detection of cervical intraepithelial lesions is crucial in patients with cervical cancer—the first cancer type that could be eradicated through a comprehensive screening and control strategy. Given the innumerable benefits of breastfeeding for women's health, as well as its ability to prevent gynecological cancers, we advocate for extensive, multicenter, prospective, randomized controlled trials on breastfeeding and for the adoption of effective policies aimed at increasing breastfeeding rates.

Declarations

Ethics approval: Ethical approval for the study was obtained from the ethics committee of the Department of Obstetrics and Gynecology, Health Sciences University Ankara Ataturk Sanatoryum Training and Research Hospital, Ankara, Turkey, on August 23, 2023 (Approval Number: 2012-KAEK-15/2772). The universal principles of the Helsinki Declaration were applied and informed consent was obtained from all participants.

Consent for publication: Obtained

Availability of data and material: All data is provided within the manuscript. Additional information can be accessed through the electronic health records of the hospital where the study was conducted. However, the data is not available via a publicity accessible link.

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Authors Contributions:

HKG- wrote the main manuscript text

TT- All authors reviewed the manuscript

CBC- All authors reviewed the manuscript

LA- All authors reviewed the manuscript

EY- All authors reviewed the manuscript

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