

Relationship Between Endometrial Biopsy Results and Risk Factors in Women with Postmenopausal Bleeding

Postmenopozal Kanama İle Başvuran Kadınların Endometrial Biyopsi Sonuçları ve Risk Faktörleri İlişkisi

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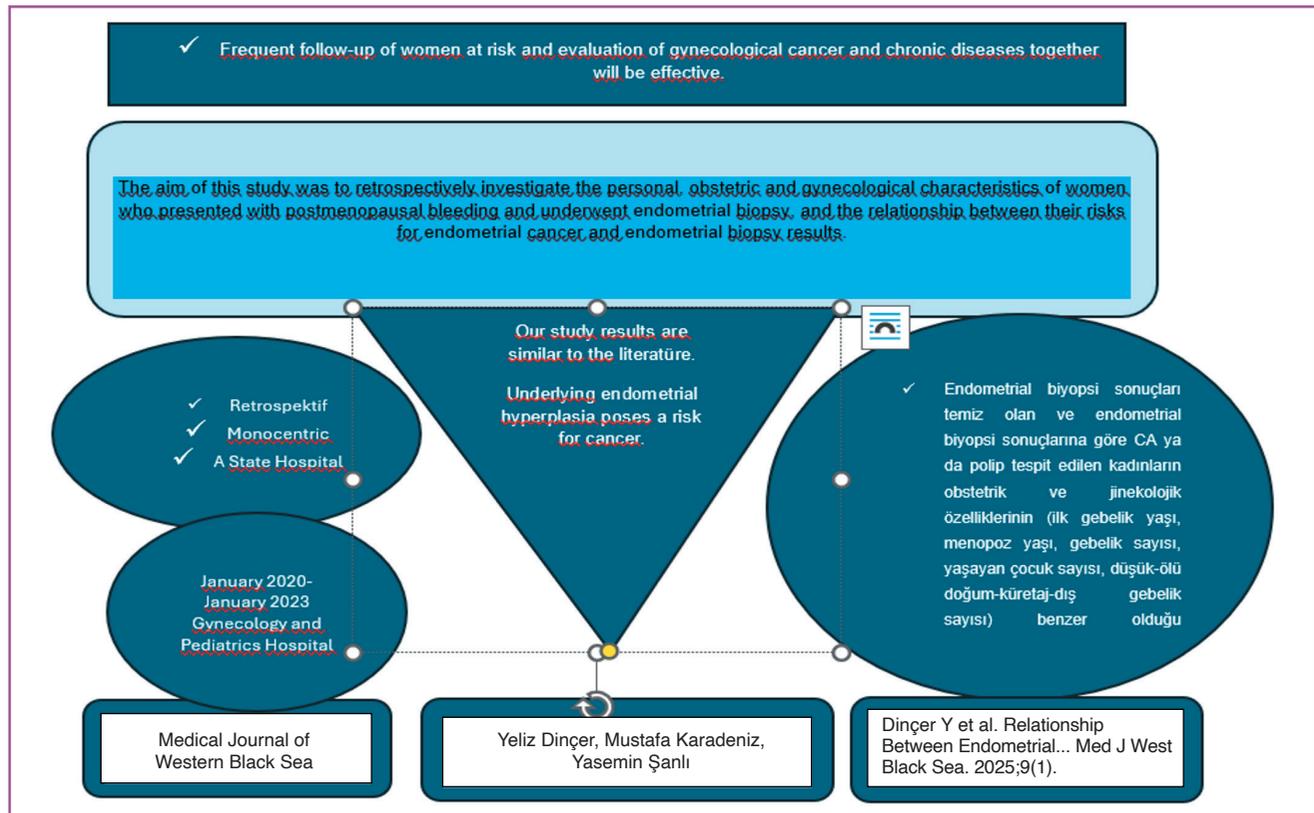
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GRAPHICAL ABSTRACT



ABSTRACT

Aim: This study aims to examine the relationship between the personal, obstetric, and gynecological characteristics of postmenopausal women who have undergone endometrial biopsy and their risks for endometrial cancer, along with their biopsy results.

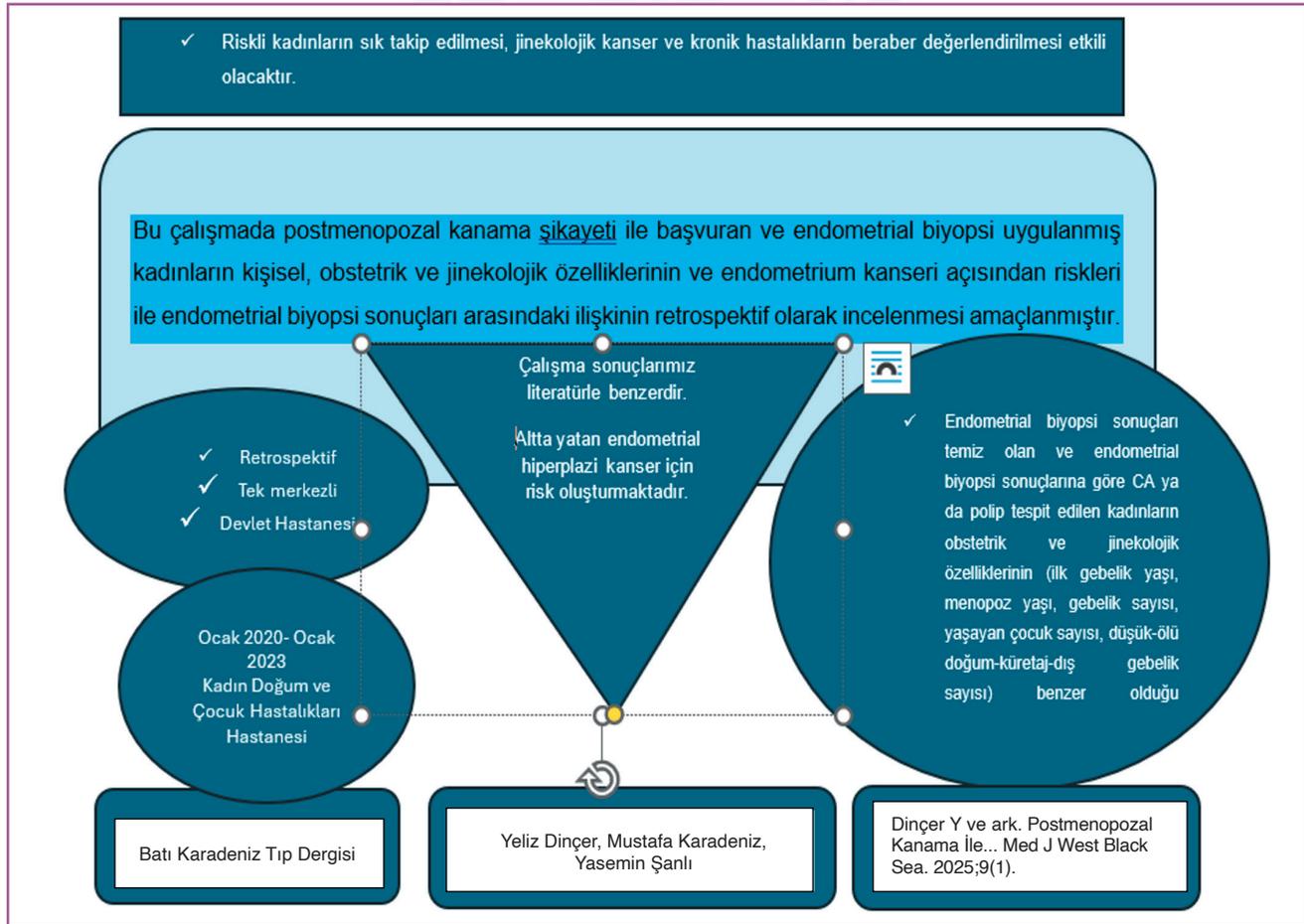
Material and Methods: This study was conducted by retrospectively analyzing the sociodemographic, obstetric, and gynecological characteristics, endometrial cancer risk factors, existing medical conditions, clinical presentations, and biopsy results of 66 women who met the study criteria. According to the study criteria, the data of these women (who applied to the hospital with postmenopausal bleeding and underwent endometrial biopsy in the last three years [January 2020 - January 2023]) were accessed through the hospital's documentation system between February and June 2023.

Results: The mean age of the women included in the study was 54.50 ± 7.99 years, with 63.6% having completed primary education. The most common medical conditions identified were hypertension (19.7%), thyroid disease (12.1%), and diabetes mellitus (9.1%). Endometrial biopsy results indicated that 92.4% of the women had benign findings. Women diagnosed with cancer or polyps were found to have similar characteristics to those with benign outcomes but lower rates of tamoxifen use, alcohol consumption, and smoking.

Conclusion: According to the results of this study, the identified risk factors for endometrial cancer in women included obesity, endometrial hyperplasia, smoking, alcohol consumption, and tamoxifen use. Health professionals working in women's health should develop educational, activity, and awareness programs to promote healthy lifestyle behaviors. Frequent monitoring of high-risk women and the joint evaluation of gynecological cancers and chronic diseases will be effective strategies for managing these patients.

Keywords: Postmenopausal period, women, endometrial biopsy, endometrial cancer

GRAFİKSEL ÖZET



ÖZ

Amaç: Bu çalışmanın amacı, endometrial biyopsi uygulanan postmenopozal kadınların kişisel, obstetrik ve jinekolojik özellikleri ile endometrial kanser riskleri ve biyopsi sonuçları arasındaki ilişkiyi incelemektir.

Gereç ve Yöntemler: Bu çalışma, çalışma kriterlerini karşılayan 66 kadının sosyodemografik, obstetrik ve jinekolojik özelliklerini, endometrial kanser risk faktörlerini, mevcut tıbbi durumlarını, klinik sunumlarını ve biyopsi sonuçlarını retrospektif olarak analiz ederek yürütülmüştür. Çalışma kriterlerine göre bu kadınların (son üç yılda [Ocak 2020 - Ocak 2023] postmenopozal kanama ile hastaneye başvurmuş ve endometrial biyopsi yapılmış olan) verilerine hastanenin dökümantasyon sistemi üzerinden Şubat ve Haziran 2023 tarihleri arasında ulaşılmıştır.

Bulgular: Çalışmaya dahil edilen kadınların ortalama yaşı 54,50±7,99 yıl olup, %63,6'sı ilköğretimi tamamlamıştır. Tanımlanan en yaygın tıbbi durumlar hipertansiyon (%19,7), tiroid hastalığı (%12,1) ve diabetes mellitus (%9,1) idi. Endometrial biyopsi sonuçları kadınların %92,4'ünün iyi huylu bulgulara sahip olduğunu gösterdi. Kanser veya polip teşhisi konulan kadınların iyi huylu sonuçları olanlara benzer özelliklere sahip olduğu ancak daha düşük tamoksifen kullanım oranları, alkol tüketimi ve sigara içme oranlarına sahip olduğu bulunmuştur.

Sonuç: Bu çalışmanın sonuçlarına göre, kadınlarda endometrial kanser için belirlenen risk faktörleri arasında obezite, endometrial hiperplazi, sigara içme, alkol tüketimi ve tamoksifen kullanımı yer aldı. Kadın sağlığı alanında çalışan sağlık profesyonelleri, sağlıklı yaşam tarzı davranışlarını teşvik etmek için eğitim, aktivite ve farkındalık programları geliştirmelidir. Yüksek riskli kadınların sık sık izlenmesi ve jinekolojik kanserler ile kronik hastalıkların ortak değerlendirilmesi, bu hastaların yönetimi için etkili stratejiler olacaktır.

Anahtar Sözcükler: Postmenopozal dönem, kadın, endometrial biyopsi, endometrial kanser

INTRODUCTION

Abnormal uterine bleeding (AUB) is a prevalent and complex issue in women's health, encompassing bleeding outside of the menstrual cycle, excessive menstrual bleeding, or postmenopausal bleeding (1,2). Postmenopausal bleeding (PMB) refers to bleeding that occurs one year after the cessation of menstruation, with the perception of abnormality often being subjective (3,4). Although PMB is frequently attributed to atrophic endometrium, the possibility of malignancy, which accounts for approximately 10% of cases, necessitates thorough evaluation (4-7). Endometrial biopsy is the most commonly used, reliable, and effective method for obtaining histopathological diagnosis during endometrial assessments (5-8). While hyperplasias in women are observed in 1-6% of cases during the premenopausal period, this rate rises to 15% in the postmenopausal period, with bleeding being the primary symptom (8-10).

Globally, the most common cancers in women are breast, cervical, thyroid, and liver cancers, whereas in Turkey, the five most common cancers are breast, thyroid, colorectal, corpus, and lung cancers (11). Endometrial cancer, which originates from the endometrium and is also referred to as corpus or uterine cancer, is the most common gynecological cancer, accounting for 11.1% of cases, particularly among postmenopausal women, both in developed countries and in Turkey (2,5,10-12).

Several risk factors have been identified for endometrial cancer, including nulliparity, early menarche, late menopause, obesity, diabetes mellitus (DM), hormone replacement therapy (HRT), tamoxifen use, familial predisposition, and polycystic ovary syndrome. Estrogen plays a clear role in the development of the disease. Vaginal bleeding is the most frequent clinical presentation (8,12).

Raising awareness among women regarding the factors associated with endometrial cancer and encouraging them to seek medical attention promptly in response to abnormal bodily changes is crucial, as early diagnosis and treatment improve outcomes.

This study aims to retrospectively examine the relationship between the personal, obstetric, and gynecological characteristics of women presenting with postmenopausal bleeding and their risks for endometrial cancer, along with their endometrial biopsy results, over the past three years (January 2020–January 2023).

MATERIALS and METHODS

This study was conducted at Zonguldak Maternity and Child Diseases Hospital between February and June 2023. Permission has been obtained from the director of the institution where this research will be conducted and from the Provincial Health Directorate to which it is affiliated (03.06.2023), and there is ethics committee approval from the ethics committee of Zonguldak Bülent Ecevit Univ Non-Interventional Clinical Research Ethics Board (Number: 2023-02, Date: 25.01.2023). The study population consisted of all women who presented with postmenopausal bleeding and underwent endometrial biopsy at the hospital within the last three years (January 2020–January 2023). The sample included 66 women who met the inclusion criteria and whose data were accessible through the hospital's written records. The sociodemographic information (age, education), obstetric and gynecological history (parity, age at first pregnancy, age at menopause, breastfeeding status), endometrial cancer risk factors [family history, Body Mass Index (BMI), smoking and alcohol use, tamoxifen use, Hormone Replacement Therapy (HRT)], existing medical conditions, clinical presentations, and biopsy results were retrospectively reviewed from the hospital records.

Inclusion Criteria: Women in the postmenopausal period who presented with bleeding and underwent endometrial biopsy and who did not have any mental disabilities or diseases requiring intensive psychiatric treatment.

Exclusion Criteria: Women not in the postmenopausal period, those whose bleeding was of cervical origin, those with insufficient biopsy samples, and women with mental retardation or diseases requiring intensive psychiatric treatment.

Dependent Variables: Risk factors for endometrial cancer in postmenopausal women.

Independent Variables: Endometrial biopsy results of postmenopausal women.

Statistical Analysis

The data obtained in the study were analyzed using SPSS 22 (Statistical Package for the Social Sciences for Windows 22). Descriptive statistics are given with mean and standard deviation or frequency and percent. The conformity of quantitative data to normal distribution was tested with Shapiro-Wilk test and graphical examinations. Independent groups t test was used in comparisons between two groups of quantitative variables showing normal distribution. Statistical significance was accepted as $p < 0.05$.

RESULTS

The demographic and clinical characteristics of the women in the study revealed that the mean age was 54.50 ± 7.99 years, with 63.6% having completed primary education. The most commonly diagnosed conditions were hypertension (19.7%), thyroid disease (12.1%), and diabetes mellitus (9.1%). Among postmenopausal women presenting with endometrial bleeding, 60.7% reported no other complaints, while 25.8% were found to have endometrial thickening. Additionally, 92.4% of the women had benign biopsy results (Table 1). The mean Body Mass Index (BMI) of the women was $30.33 \pm 5.11 \text{ kg/m}^2$.

The average age at first pregnancy for women with benign endometrial biopsy results was 20.20 ± 5.92 years, while their average age at menopause was 50.03 ± 3.74 years. The average number of pregnancies was 2.73 ± 1.52 , with an average of 2.45 ± 1.53 living children. The average number of miscarriages was 0.28 ± 0.66 , stillbirths 0.03 ± 0.18 , and ectopic pregnancies 0.03 ± 0.25 .

When examining the endometrial cancer risk factors in women with benign biopsy results, one had a history of breast cancer, and another had a history of bladder cancer. Neither of these women had a family history of endometrial cancer. Among the six women with a family history of endometrial cancer, five had mothers, and one had a sibling diagnosed with this condition. Regarding other reasons for hospital visits or biopsies aside from bleeding, the most

common reason was endometrial thickening, observed in 16 women (26.7%). In terms of Body Mass Index (BMI), half of the group was classified as obese ($\text{BMI} \geq 30$, $n=31$). Among these, three women were classified as third-degree obese, six as second-degree obese, and 22 as first-degree obese (Table 2).

According to the endometrial biopsy results, women diagnosed with cancer (CA) or polyps had an average age at first pregnancy of 22.66 ± 4.08 years and an average age at menopause of 50.50 ± 2.88 years. The average number of pregnancies was 2.66 ± 0.81 , and the average number of living children was 2.33 ± 1.03 . The average number of miscarriages was 1.00 ± 1.67 .

Table 1: Distribution of Women According to Some Demographic and Disease Characteristics

Findings (n=66)		
Sociodemographic Data		
Age (Year \pm SD)	54.5 \pm 7.99	
BMI (kg/m 2 \pm SD)	30.33 \pm 5.11	
Education Level	n	(%)
Primary School	42	(63.6)
High School	13	(19.7)
No Schooling	6	(9.1)
University and Above	5	(7.6)
Biopsy Results	n	(%)
Benign	61	(92.4)
CA	4	(6.1)
Polyp	1	(1.5)
Reason for Hospital Visit/Biopsy (Other than Bleeding)	n	(%)
No Other Complaint	40	(60.7)
Endometrial Thickening	17	(25.8)
Follow-up	3	(4.5)
Myoma	3	(4.5)
Other	3	(4.5)
Existing Conditions*	n	(%)
Hypertension	13	(19.7)
Thyroid Disease	8	(12.1)
Diabetes Mellitus (DM)	6	(9.1)
Heart Disease	3	(4.5)
Cholesterol	1	(1.5)
Breast Cancer	1	(1.5)
Bladder Cancer	1	(1.5)
Iron Deficiency	1	(1.5)
Rheumatic Disease	1	(1.5)
Psychiatric Disease	1	(1.5)

* Multiple responses were provided.

Table 2: Distribution of Women Characteristics

Women Characteristics	Clear Biopsy Results (n=60)		Diagnosed with CA or Polyps According to Endometrial Biopsy Results (n=6)		P
Obstetric and Gynecological History					
Age at First Pregnancy (year± SD)	20.20±5.92		22.66±4.08		p=0.325*
Age at Menopause (year± SD)	50.03±3.74		50.50±2.88		p=0.768*
Number of Pregnancies (number ± SD)	2.73±1.52		2.66±0.81		p=0.917*
Number of Living Children (number ± SD)	2.45±1.53		2.33± 1.03		p=0.857*
Number of Miscarriages (number ± SD)	0.28±0.66		1.00±1.67		p=0.344*
Number of Stillbirths (number ± SD)	0.03±0.18		-		p=0.656*
Curettage	-		-		
Number of Ectopic Pregnancies (number ± SD)	0.03±0.25		-		p=0.755*
Risk Factors for Endometrial Cancer					
	n	(%)	n	(%)	
Tamoxifen Use	3	(5)	1	(16.7)	p=0.253*
History of HRT Use	3	(5)	0	(0)	p=0.575*
Smoking	6	(10)	1	(16.7)	p=0.613*
Alcohol	6	(10)	1	(16.7)	p=0.613*
Family History	6	(10)	0	(0)	p=0.417*
BMI (kg/m ² ±SD)	30.55±5.18		29.47±4.12		p=0.686*
Reason for Hospital Visit/Biopsy (Other than Bleeding)					
	n	(%)	n	(%)	
No Other Complaint	36	(60)	5	(83.3)	
Endometrial Thickening	16	(26.7)	1	(16.7)	
Follow-up	3	(5)	0	(0)	
Myoma	3	(5)	0	(0)	
Other	3	(5)	0	(0)	

Independent Sample T-test*

* Participants may have met more than one criteria.

When examining the endometrial cancer risk factors in women with biopsy-confirmed CA or polyps, it was noted that 20% (1 woman) used tamoxifen, 16.7% (1 woman) smoked, and 16.7% (1 woman) consumed alcohol. These three risk factors were more prevalent in this group than in women with benign biopsy results. None of these women had a family history of endometrial cancer. Among other reasons for hospital visits or biopsies, the most common was endometrial hyperplasia, identified in 16.7% (1 woman) of the cases. Half of the women in this group were classified as obese (n=3). Among the obese women, two were classified as first-degree obese and one as second-degree obese (Table 2).

According to the findings of the study, when women with clean biopsy results were compared with women diagnosed with cancer or polyps, no statistically significant difference was found in terms of both obstetric and gynecological characteristics and endometrial cancer risk factors. (p<0.05). (Table 2).

DISCUSSION

In this study, data from 66 patients who presented with postmenopausal bleeding and underwent endometrial biopsy within the last three years (2020–2023) were evaluated in terms of endometrial cancer risk factors. The reasons for performing biopsies were identified as complaints of bleeding in 60.7% of the women and endometrial thickening in 25.8%. The biopsy results showed that 92.4% of the women had benign findings, while 6.1% were diagnosed with endometrial cancer. The average age of the patients was 54, and their average BMI was 30. In addition, it was determined that the obstetric and gynecological characteristics (age at first pregnancy, age at menopause, number of pregnancies, number of living children, number of miscarriages, number of stillbirths and ectopic pregnancies) of women with benign biopsy results were similar to those of women with diagnosed CA or polyps, and there was no statistically significant difference between them.

In Zhao et al.'s retrospective study, patients with endometrial hyperplasia were found to have a higher risk of developing endometrial cancer, especially among women over the age of 50, those with a BMI ≥ 25 kg/m², diabetes, hypertension, and advanced hyperplasia. The study emphasized the importance of early diagnosis and treatment in high-risk patients (9). The incidence of endometrial cancer increases with age, peaking in the postmenopausal period (60–70 years). The American College of Obstetricians and Gynecologists (ACOG) has set the age of 45 as the threshold for endometrial cancer screening (13). Our study results align with the literature.

The BMI of all women included in the study who presented with postmenopausal bleeding fell within the obese range, and the BMI characteristics of women with benign and malignant results were similar. Studies have shown that obesity and diabetes are significant risk factors for endometrial cancer (14-16). For every 5 kg/m² increase in BMI, the risk of endometrial cancer increases by 1.6 times (9). Raffone et al. and Garzon et al. demonstrated that obesity increases the risk of death associated with endometrial cancer (17,18). This increased risk is due to adipose tissue being a source of estrogen in the body, leading to the effects of excessive endogenous estrogen on the endometrium, which in turn causes endometrial hyperplasia and cancer (9,17,18). Studies have also found that when insulin resistance is high, the relative risks of endometrial hyperplasia and cancer increase, and when BMI is ≥ 25 kg/m², progesterone treatment becomes less effective and more prone to recurrence (19,20). Therefore, weight control is essential during treatment and follow-up. While simple hypertension does not increase the risk of endometrial cancer, it often leads to complications with obesity and diabetes. Controlling weight, blood sugar and blood pressure early on is crucial, particularly for improving the prognosis of patients (21,22). Although diabetes mellitus (DM) is known to be a risk factor for endometrial cancer, none of the women diagnosed with cancer or polyps in this study had diabetes. However, consistent with the literature, half of the women diagnosed with endometrial cancer were obese and had endometrial hyperplasia.

When examining the risk factors for women diagnosed with endometrial cancer, it was found that 16.7% (1 woman) used tamoxifen, 16.7% (1 woman) smoked, and 16.7% (1 woman) consumed alcohol. These three risk factors were found to be more prevalent among women with endometrial cancer than among women with benign results, but no statistically significant difference was found between them. Several risk factors for endometrial cancer have been identified in epidemiological and retrospective studies, including

nulliparity, late menopause, obesity, smoking, alcohol consumption, diabetes mellitus, unopposed estrogen therapy, tamoxifen use, and polycystic ovary syndrome. Underlying hyperplasia also poses a risk for progression to cancer (8,16,23-25). Our study findings are consistent with the literature.

One of this study's primary limitations is its relatively small sample size due to its retrospective design. Additionally, the data are limited to those obtained from a single state hospital. The information on family history was based solely on patients' self-reported disclosures of endometrial cancer in their families during medical consultations, which may lead to missing data in the system. Furthermore, retrospective data on breastfeeding status were not available, and therefore, no statistical calculations could be made regarding this variable.

The findings of this study indicate that obesity, endometrial hyperplasia, smoking, alcohol consumption, and tamoxifen use are risk factors associated with endometrial cancer in women. Endometrial cancer, similar to trends in developed countries, is the most common gynecological cancer. Women with endometrial cancer typically present with bleeding, which allows for early diagnosis and, consequently, a better prognosis. However, the incidence and mortality rates associated with this disease are rising. Factors contributing to the increasing prevalence of endometrial cancer include rising obesity rates, the absence of an effective screening test, longer life expectancies, late menopause, infrequent routine gynecological exams in asymptomatic women, and the increasing use of tamoxifen, estrogen, smoking, alcohol, and the prevalence of diseases such as diabetes and hypertension.

Identifying these risk factors is crucial for preventing the disease, especially in high-risk women. Accordingly, health-care professionals working in women's health should develop educational, activity-based, and awareness-raising programs to promote healthy lifestyle behaviors. Frequent monitoring of at-risk women and joint evaluation of gynecological cancers and chronic diseases will also be effective in improving outcomes.

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Author Contributions

Concept: **Yeliz Dinçer, Mustafa Karadeniz, Yasemin Şanlı**, Design: **Yeliz Dinçer, Mustafa Karadeniz, Yasemin Şanlı**, Data Collection or Processing: **Yeliz Dinçer, Mustafa Karadeniz**, Analysis or Interpretation: **Yeliz Dinçer, Yasemin Şanlı**, Literature Search: **Yeliz Dinçer, Yasemin Şanlı**, Writing: **Yeliz Dinçer**, Approval: **Yeliz Dinçer**.

Conflicts of Interest

The authors declare no conflict of interest.

Financial Support

The authors declare that they did not receive any financial support during this manuscript's research or writing process.

Ethical Approval

Ethics Committee Approval: This study was conducted following the ethical principles outlined in the Helsinki Declaration. Written approval was obtained from the Zonguldak Bülent Ecevit University Non-Interventional Clinical Research Ethics Board (25.01.2023; 2023-02) and the Provincial Health Directorate (03.06.2023).

Informed Consent Statement

Since this study is a retrospective analysis, patient consent was not obtained.

Data Availability Statement

Data are available for research purposes upon reasonable request to the corresponding author.

Review Process

Externally peer-reviewed.

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