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RESEARCH ARTICLE

The Relationship Between Endometrial Biopsy Results and Covid-19 in Postmenopausal Women

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Abstract

Introductıon: To investigate the impact of Covid-19 infection on postmenopausal bleeding and endometrial sampling results in postmenopausal women.

Methods: Our study is a retrospective study, and it compares the demographic data, transvaginal ultrasound findings, and histopathological results of endometrial biopsies in postmenopausal women who had postmenopausal bleeding or underwent endometrial sampling due to asymptomatic endometrial thickness increase of the groups of those who had and had not experienced Covid-19 at Ankara City Hospital between October and December 2020.

Results: Among the 274 patients included in our study, it was observed that biopsies were taken from 173 (63.13%) due to postmenopausal bleeding (PMB), and from 101 (31.86%) asymptomatic women due to increased endometrial thickness. It was determined that 60 (21.89%) of the women had experienced Covid-19 infection. The mean endometrial thickness in patients who underwent biopsy was 8.93±6.42mm, and no significant difference was observed between the measured endometrial thickness in the groups who had and had not experienced Covid-19 (7.98±4.80 vs 9.20±6.79; p=0.17). It was observed that 37 of the 173 patients (21.39%) who had samples taken due to PMB had experienced Covid-19. In both groups of patients who had and had not experienced Covid-19, no significant difference was observed in the rates of postmenopausal bleeding and in the benign and malignant pathology results from the histopathological examination ($p > 0.05$).

Conclusion: In terms of our study in postmenopausal women, it was observed that Covid-19 infection did not affect the rates of postmenopausal bleeding and endometrial biopsy results.

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Introduction

The Covid-19 infection, which emerged in China by the end of 2019 and quickly led to a global pandemic, has caused illness and death in millions of people.[1,2] While most of the disease's effects primarily result from respiratory involvement, it has also been shown to have long-term effects on other systems.[2,3] From the start of the pandemic until the present, numerous studies have investigated the effects of the pandemic on the female reproductive system.[3-5] The most widely studied pathogenetic mechanism being the virus causing genetic expression changes in endometrial cells.[4,6,7]

Endometrial cancer is the most common gynecological cancer in women in developed countries, and its incidence is steadily increasing.[8,9] Approximately 80% of patients are in the postmenopausal period, and vaginal bleeding is present in 90% of patients.[8,10] In postmenopausal women, the likelihood of developing endometrial cancer increases with the presence of obesity, diabetes, hypertension and endometrial hyperplasia.[8,11] Histopathological examination is strongly recommended in women with postmenopausal bleeding, especially if the endometrial thickness is >5 mm.[12,13] While the exact threshold for endometrial thickness is not clear for asymptomatic women, especially with the presence of risk factors, sampling at 8 mm and above is important for early diagnosis of endometrial cancer.[8,11]

Previous studies have shown the effect of Covid-19 infection on the female reproductive system and endometrial cells. It is stated that especially endometrial Angiotensin II (ACE 2) and inflammatory mechanisms are effective in pathogenesis.[4,6,7] In addition to these studies, there are also studies stating that endometrial tissue becomes thinner and reproductive functions are negatively affected due to hormonal changes caused by infection.[14,15]

The aim of our study is to assess the impact of Covid-19 infection on postmenopausal bleeding and endometrial biopsy results in postmenopausal women who underwent endometrial sampling due to postmenopausal bleeding and increased endometrial thickness.

Material and Methods

Our study is a retrospective cohort study, with the necessary ethical approval for the research obtained from the Ankara Yıldırım Beyazıt University Health Sciences Institute ethics committee (decision no: 2022-650). The files of patients who underwent endometrial sampling during the postmenopausal period throughout the 3-month period covering October to December 2020 were included in our research. The files of patients who had postmenopausal bleeding and of those who underwent procedures due to asymptomatic postmenopausal endometrial thickness increase were scanned. Demographic data, indications for endometrial sampling, endometrial thickness in transvaginal ultrasound, Covid-19 infection status, body mass indices (BMI), pathology results, and the patients' comorbidities were recorded. Patients using tamoxifen, patients with chronic conditions posing a risk (hypertension, diabetes mellitus), those with known gynecological precancerous diseases and patients under the age of 40 who entered menopause were not included in the study. In our clinic, endometrial sampling is performed on women with postmenopausal bleeding and asymptomatic postmenopausal women with an endometrial thickness ≥ 8 mm, regardless of risk factors. The files related to our research were collected before the introduction of the vaccine. Percentages and frequencies were used in the statistical analysis of our study, and for continuous variables mean-median, SS and min-max values were employed. Differences between the group that experienced Covid-19 and the group that did not were assessed using t-tests and Mann-Whitney U tests. The Chi-squared test was used for categorical variables. The significance level was taken as $p<0.05$.

Results

In our study, we accessed 352 files of endometrial biopsies performed within the defined period of the postmenopausal stage. After applying exclusion criteria, 274 patient files were included in our study. The mean age of the patients included in the study was 59.93±8.01 (min-max: 44-83), with a median gravida of 3 (range: 1-13) and a median parity of 3 (range: 0-12). It was determined that biopsies were taken from 173 (63.13%) of the women due to postmenopausal bleeding (PMB) and from 101 (36.86%) who were asymptomatic but underwent biopsy due to an increase in endometrial thickness. It was determined that 60 (21.89%) of the women had experienced Covid-19 infection, while 214 (78.61%) had not. Out of the 173 patients who had samples taken due to PMB, it was observed that 136 (78.61%) had not experienced Covid-19, while 37 (21.39%) of them had. 19 (6.93%) patients had malignant pat-

hology results. In terms of postmenopausal bleeding rates and histopathological examination, no significant difference was observed between the group that had experienced Covid-19 and the group that had not ($p > 0.05$). The data is summarized in Table 1.

In the group of patients who underwent endometrial sampling and had experienced Covid-19, the mean age was determined to be 56.96±6.32. The mean age of the group that had experienced Covid-19 was significantly lower than that of the group that had not experienced Covid-19 (p=0.001). The average endometrial thickness in patients who underwent biopsy was 8.93±6.42 mm, and there was no significant difference in the measured endometrial thickness between the group that had experienced Covid-19 and the group that had not (7.98±4.80 vs. 9.20±6.79; p=0.17). In the group that underwent biopsy due to PMB, the mean endometrial thickness in the group that had not experienced Covid-19 was 7.67±5.07 mm, while it was 9.11±7.58 mm in the group that had experienced Covid-19, and there was no statistically significant difference between the two groups in terms of mean endometrial thickness (p=0.45). In asymptomatic women who underwent biopsy, the endometrial thickness was 8.47±4.39 in the group that had experienced Covid-19, and 9.37±5.16 in the group that had not. Similarly, there was no statistically significant difference between the two groups in terms of endometrial thickness (p=0.27). The data is summarized in Table 1.

Table 1

		Covid-19		
	Total	Had	Never had	*P*
Age (years)	59.93±8.01	56.96 ±6.32	60.77±8.25	0.001*
Gravida	3.97±2.05	3.51±1.40	4.09±2.18	0.068*
Parity	3.22±1.56	3.05±1.17	3.26±1.64	0.27*
BMI (kg/m²)	32.06±6.12	33.36±2.97	31.75±6.67	0.045*
Endometrial thickness (mm)	8.93±6.42	7.98±4.80	9.20±6.79	0.17*
PMB	8.80±4.67	9.11± 7.58	7.67 ± 5.07	0.45*
Asymptomatic thickness increase	9.16±4.99	8.47 ± 4.39	9.37± 5.16	0.27*
Histopathological examination	255(93.07)	56 (21.96)	199 (78.04)	0.92ª
Benign	19 (6.93)	4 (21.06)	15 (78.94)	
Malign				
Postmenopausal bleeding				
Present	173	37 (21.39)	136 (78.61)	0.78ª
None	101	23 (22.78)	78 (77.22)	

Table 1: Comparison of groups based on Covid-19 infection status (PMB: Postmenopausal bleeding, BMI: Body Mass Index, *; Student T-test, a; Chi-squared test)

There was no significant difference in the average age between the patients who were grouped in either of the two categories, malign and benign, of histopathological diagnosis (p=0.23). The endometrial thickness was determined as 13.48±10.03 in the malign group, while it was 8.57±5.93 in the benign group, and a statistically significant difference was observed between both groups (p=0.004). It was observed that in 16 out of the 19 patients with a malignancy in the pathology result (84.25%), biopsy was performed due to PMB. However, malignancy was detected in 3 out of the 101 patients who underwent biopsy due to asymptomatic endometrial thickness increase (2.97%). The data is summarized in Table 2.

Table 2

		Histopathological diagnosis		
	Total	Malign (n=19)	Benign (n=255)	*P*
Age	59.93±8.01	62.05±7.23	59.78±8.06	0.23*
BMI	32.06±6.12	31.68±5.27	27.67±3.63	0.01*
Endometrial thickness		13.84±10.03	8.57±5.93	0.004*
PMB	173	14.81±10.64	8.19±6.41	0.001*
Asymptomatic thickness increase	101	8.66±2.88	9.18±5.05	0.48*
PMB				
Present	173	16 (9.25)	157 (90.75)	0.04ª
None	101	3 (2.97)	98 (97.03)	

Table 2: Comparison of histopathological diagnosis data (BMI: Body Mass Index, *; Student T-test, a; Chi-squared test)

Discussion

Endometrial cancer is the fourth most common cancer among women both worldwide and in our country, and it is the most frequently occurring malignancy among gynecological cancers.[9,16] The risk of developing endometrial cancer over the course of a woman's lifetime is 2.8%.[12] The average age of women diagnosed with endometrial cancer is 63 and more than 90% of endometrial cancer cases are diagnosed after the age of 50.[17] In our study also, the average age was found to be 62, which is consistent with the literature. It was observed that women who had experienced Covid were of a younger age, however, any relationship between having experienced Covid and endometrial cancer was not determined. In accordance with the literature, 84% of patients in our study who had been diagnosed endometrial cancer had postmenopausal bleeding.[8,17] Among the patients who were asymptomatic and underwent biopsy due to endometrial thickness, 2.97% were found to have endometrial cancer, which is also consistent with the literature.[8,11]

Studies have shown that the Covid-19 pandemic has affected the menstrual cycle.[5,18] Primarily in the pathogenesis, it has been reported that endometrial Angiotensin II (ACE 2) and inflammatory mechanisms are effective. During Covid-19 infection, a decrease in ACE2 expression has been demonstrated

in both in vivo and in vitro.[6,7] ACE2 also increases the proliferation of endometrial epithelial cells and stromal cells and affects their regeneration.[19-21] In addition to these studies, there are also studies indicating that the endometrial tissue becomes thinner and reproductive functions are adversely affected due to hormonal changes caused by the infection.[14,15] The impact of Covid-19 on postmenopausal bleeding has been mainly studied in the context of vaccines, and secondary to vaccination, it has been reported that there has been an increase in postmenopausal bleeding.[22,23] In our study, we observed that in the group that had experienced Covid-19 there was no significant difference in endometrial thickness compared to the group that had not experienced Covid-19, both in those with and without postmenopausal bleeding. Similarly, no significant difference was observed in the rates of postmenopausal bleeding between the group that had experienced Covid-19 and the group that had not.

It has been shown that Covid-19 infection has a negative impact on the prognosis of endometrial cancer.[6] However, the effect of decreased ACE2 expression due to viral infection on malignant transformation in normal endometrial cells is not known. In our study, no significant difference was observed in terms of the detection of malignancy in the histopathological examination between patients who had experienced Covid-19 and those who had not.

Independent of having experienced Covid-19 infection, patients with a malignancy in the pathology result exhibited a significant difference in endometrial thickness compared to benign women, with an probability of cancer increasing as endometrial thickness increases. This finding is consistent with the results of previous studies.[8,11] Additionally, the BMI was higher in the malignancy group than it was in the benign group, and obesity is a well-known risk factor for endometrial cancers.[12]

According to the results of our study, in the samples taken from postmenopausal women, the main risk factor for obtaining a malignant result was PMB. Having experienced Covid-19 did not show a significant relationship with the rate of PMB and endometrial cancers in our study population. The limitation of our study was the lack of data on factors that could affect the prognosis, such as the severity of Covid clinical manifestations and the type of endometrial cancer. Additionally, our study had a limited number of cases due to being highly selective in its criteria. However, it is important because it is one of the few studies regarding the impact of Covid-19 infection on postmenopausal bleeding and endometrial histopathological diagnoses, especially among the unvaccinated population. More comprehensive research is needed to determine the long-term relationship between endometrial cancer and postmenopausal bleeding and to understand their etiopathogenesis.

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