Published online 2023 January 25 **Original Article**

Histopathological Evaluation of Endometrial Biopsies in Different Age Groups: A Tertiary Care Experience in Turkey

Begum Kurt[1], Tulay Koc[2], Serkan Celikgun[3] and Caglar Yildiz[4]

[1]Assistant Professor, Department of Obstetrics and Gynecology, Faculty of Medicine, Sivas Cumhuriyet University, Sivas, Turkey
[2]Assistant Professor, Department of Medical Pathology, Faculty of Medicine, Sivas Cumhuriyet University, Sivas, Turkey
[3]Ph.D. Student, Department of Public Health, Institute of Health Sciences, Dokuz Eylul University, Izmir, Turkey
[4]Associate Professor, Department of Obstetrics and Gynecology, Faculty of Medicine, Sivas Cumhuriyet University, Sivas, Turkey

*** *Corresponding author:*** Begum Kurt, Department of Obstetrics and Gynecology, Faculty of Medicine, Sivas Cumhuriyet University, Sivas, Turkey. Email: begumkurt@cumhuriyet.edu.tr

Received 2022 April 09; **Revised** 2022 May 06; **Accepted** 2023 January 18.

Abstract

Background: An endometrial biopsy primarily aims to determine endometrial cancer and hyperplasia with atypia at an early stage.
Objectives: This study aims to evaluate the indications, histopathological diagnoses, and the number of endometrial biopsies performed in our clinic, according to the age groups of patients, in light of the literature.
Methods: A retrospective review was conducted on the file data of 4,965 patients who underwent endometrial biopsy for non-obstetric reasons between 2014-2021. The patients were divided into five groups, according to their age. Pathology diagnoses were classified as benign endometrial pathology, premalignant-malignant pathology, and insufficient for diagnosis.
Results: The most common biopsy indication was abnormal uterine bleeding (61.9%), while the most common histopathological result was benign endometrial pathologies (75.3%). Endometrial cancer was also detected in 3% of the patients. The highest diagnosis of benign endometrial pathology among age groups was 96.6% in those below 35. The comparison of age groups in the diagnosis of premalignant-malignant pathology revealed that the highest diagnosis rate was 32.1% in those 65 years and over. Furthermore, the evaluation of the relationship between indications and material adequacy showed that the highest rate of insufficient for diagnosis pathology was in the postmenopausal patient group (34.0%). Moreover, insufficient for diagnosis and endometrial surface epithelium results were highest in patients over 65 (46.7%).
Conclusion: Patients aged 55-64 and those over 65 had the highest rate of endometrial cancer and insufficient for diagnosis biopsy results. Therefore, dilation and curettage may be recommended while taking a biopsy from patients in this age group.

Keywords: Abnormal uterine bleeding, Dilation and curettage, Endometrial biopsy, Insufficient for diagnosis

1. Background

Abnormal uterine bleeding (AUB) is prolonged bleeding that occurs at irregular intervals, excluding menstrual bleeding. It affects 10%-35% of women of reproductive age and approximately 50% of perimenopausal women, and it is one of the most common reasons for referring to the gynecology outpatient clinic (1-3). Perimenopause is the transition period in women's lives from regular bleeding to irregular menstrual periods and finally, to anovulation cycles (4). It usually starts 2-8 years before menopause and ends a year later (5). Approximately 90% of patients with endometrial hyperplasia or endometrial carcinoma have AUB as the predominant symptom (6-8). However, in most premenopausal women, the etiology of bleeding may also result from a structural cause, such as myoma uteri, adenomyosis, and endometrial or cervical polyps (9). Transvaginal ultrasound is the first-choice imaging technique for diagnosing endometrial pathology due to its accessibility and low cost. In postmenopausal women, the endometrial thickness of below 3-5 mm seems to have a very high negative predictive value for endometrial cancer (10,11). However, there is no established consensus or standardized limit for endometrial thickness in premenopausal women (12,13). There is also no age limit for endometrial biopsy to determine atypia**,** hyperplasia, and cancer in women with premenopausal AUB. The primary purpose of an endometrial biopsy is to determine endometrial cancer and hyperplasia with atypia at an early stage. Endometrial cancer is the most common gynecological cancer (14), and thus the detection of this cancer and surgical treatment is essential to prolong survival. Hyperplasia with atypia detected in an endometrial biopsy sample may be accompanied by endometrial carcinoma at a rate of 15%-45% (15,16).

2. Objectives

Considering the high rate of insufficient samples and endometrial pathologies in elderly patients, this study aimed to evaluate the indications and histopathological diagnoses of endometrial biopsies performed in our clinic in different age groups.

3. Methods

This retrospective study included 4,965 patients

who were referred to the Sivas Cumhuriyet University Department of Obstetrics and Gynecology and underwent endometrial biopsy for non-obstetric reasons between 30.06.2014 and 30.06.2021. The study was approved by the Non-Interventional Clinical Research Ethics Committee of the Sivas Cumhuriyet University [registry No: 2021-11/14]. Pathology reports of endometrial biopsies were obtained from the pathology department, and the patients' files were analyzed.

During the statistical evaluation, the patients were divided into five age groups: under 35, 35-44, 45-54, 55-64, and over 65.

Histopathological results were classified as benign endometrial pathology (proliferative-secretory endometrium, endometrial polyp, endometritis, and atrophic endometrium), premalignant-malignant (endometrial hyperplasia, endometrial hyperplasia with atypia, and endometrial cancer), and insufficient (insufficient for diagnosis and endometrial surface epithelium). Regarding biopsy indications, AUB was determined as the preoperative evaluation of myoma uteri and postmenopausal patients (bleeding-thickness increase).

3.1. Statistical Analysis

Data were analyzed using the SPSS software (version 22; SPSS INC, Chicago, IL, USA). The primary dependent variable of the study was the pathology diagnoses, and the independent variables were age, indication, and date range. The quantitative variables were presented as mean±SD (minimum-maximum), and the qualitative ones were described by frequency and percentage. A Chi-squared test was run to compare the adequacy and type of lesion in age groups and indications. Data were compared between the pre-Covid-19 pandemic and during the Covid-19 pandemic using an independent samples t-test. A P-value of <0.05 was considered statistically significant.

4. Results

The mean age of the patients participating in the study was 45±10.68 years, with the lowest being 17 and the highest 94. When the age variable was categorized, 1,861 participants (37.5%) were 45-54. A total of 61.9% of the indications were evaluated as AUB. While 3,737 (75.3%) of the samples sent to pathology were benign endometrial pathologies, 149 (3.0%) were diagnosed with endometrial cancer (Table 1).

In total, 827 (16.7%) of the biopsies sent to the pathology laboratory were reported as insufficient, and 142 (46.7%) of the biopsies performed on patients aged 65 and over were considered inadequate. Additionally, the insufficiency rate of biopsies performed on patients aged 55-64 was 207 (43.9%). The evaluation of the relationship between indications and material adequacy revealed that the highest rate of insufficient for diagnosis results was in the postmenopausal patient group, with 494 (34.0%). The failure rate in biopsies performed on patients with AUB complaints was 270 (8.8%). These obtained data were statistically significant (P<0.001) (Table 2).

Table 1. Demographic and disease characteristics of the patients

n=4,965	n (%)
Age groups	
<35	634 (12.8%)
35-44	1,694 (34.1%)
45-54	1,861 (37.5%)
55-64	472 (9.5%)
≥65	304 (6.1%)
Indications	
Abnormal uterine bleeding	3,073 (61.9%)
Pre-operative evaluation	441 (8.9%)
Post-menopausal patient	1,451 (29.2%)
Pathological diagnosis	
Proliferative-secretory endometrium	2,825 (56.9%)
Endometrial polyp	797 (16.1%)
Endometritis	96 (1.9%)
Atrophic endometrium	19 (0.4%)
Endometrial hyperplasia	228 (4.6%)
Endometrial hyperplasia with atypia	24 (0.5%)
Endometrium cancer	149 (3.0%)
Endometrium surface epithelium	384 (7.7%)
Insufficient for diagnosis	443 (8.9%)
Pathological diagnosis code	
Benign	3,737 (75.3%)
Pre-Malignant	252 (5.1%)
Malignant	149 (3.0%)
Insufficient	827 (16.7%)

The highest diagnosis of benign endometrial pathology among age groups was 588 (96.6%) in those under 35 years. The age group with the lowest diagnosis of benign endometrial pathology was 65 years and older with 110 (67.9%). The comparison of age groups and premalignant-malignant diagnoses showed that the highest diagnosis rate was in the 65 years and over group, with 52 (32.1%). The incidence of benign endometrial pathology in patients with AUB complaints was 2,603 (92.9%), and the rate of premalignant-malignant pathology was 200 (7.1%). Furthermore, the highest rate of premalignant-malignant pathology diagnosis was in the postmenopausal patient group. These data were statistically significant (P<0.001) (Table 3).

On March 11, 2020, the first Covid-19 case was detected in Turkey. Before the Covid-19 pandemic, endometrial biopsies were obtained from 486 patients in 2014, 485 patients in 2015, 559 patients in 2016, 640 patients in 2017, 685 patients in 2018, and 788 patients in 2019. During the Covid-19 pandemic, 714 patients in 2020 and 608 patients in 2021 underwent endometrial biopsies. The evaluation of the number of patients who underwent endometrial biopsy in our department between 2015 and 2021 by years indicated an

Table 2. Distribution of material adequacy by age and indication

Age groups	Sufficient	Insufficient	Total	P-value
	n (%)	n (%)	n (%)	
<35	609 (96.1%)	25 (3.9%)	634 (100%)	<0.001
35-44	1,556 (91.9%)	138 (8.1%)	1,694 (100%)	
45-54	1,546 (83.1%)	315 (16.9%)	1,861 (100%)	
55-64	265 (6.1%)	207 (43.9%)	472 (100%)	
≥65	162 (53.3%)	142 (46.7%)	304 (100%)	
Total	4,138 (83.3%)	827 (16.7%)	4965 (100%)	
Indications				
Abnormal uterine bleeding	2,803 (91.2%)	270 (8.8%)	3,073 (100%)	<0.001
Pre-operative evaluation	378 (85.7%)	63 (14.3%)	441 (100%)	
Post-menopausal patient	957 (66%)	494 (34.0%)	1,451 (100%)	
Total	4138	827 (16.7%)	4,965 (100%)	

Table 3. Distribution of pathology diagnoses by age and indication

Age Groups	Benign	Premalignant-malignant	Total	P-value
	n (%)	n (%)	n (%)	
<35	588 (96.6%)	21 (3.4%)	609 (100%)	<0.001
35-44	1,443 (92.7%)	113 (7.3%)	1,556 (100%)	
45-54	1,398 (90.4%)	148 (9.6%)	1,546 (100%)	
55-64	198 (74.7%)	67 (25.3%)	265 (100%)	
≥65	110 (67.9%)	52 (32.1%)	162 (100%)	
Total	3,737 (100%)	401 (100%)	4,138 (100%)	
Indications				
Abnormal uterine bleeding	2,603 (92.9%)	200 (7.1%)	2,803 (100%)	<0.001
Pre-operative evaluation	341 (90.2%)	37 (9.8%)	378 (100%)	
Post-menopausal patient	793 (82.9)	164 (17.1%)	957 (100%)	
Total	3,737 (90.3%)	401 (9.7%)	4,138 (100%)	

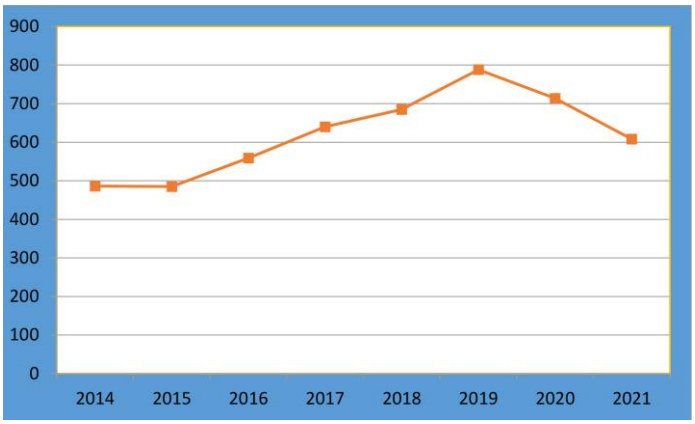

Figure 1. Distribution of the number of patients who underwent endometrial biopsy between 2014-2021

increase from 2016 to 2020 and a decrease from 2020 to 2021 (Figure 1).

5. Discussion

According to the results of this study, patients aged 55 and over had the highest rate of insufficient for diagnosis biopsy results. Considering that the same age group is also at an increased risk of endometrial cancer, endometrial biopsy adequacy is highly crucial for early diagnosis and treatment.

Many women enter natural menopause between the ages of 45-55 (17). In developed countries, the age of menopause is approximately 51 (18); however, the mean age of menopause in Turkey has not yet been clearly stated. Age and endometrial pathologies have a strong relationship, so age has become an essential determinant in the endometrial evaluation decision (19,20). This study aimed to evaluate endometrial biopsies in different age groups. The limiting age to perform the endometrial biopsy in cases of AUB remains a subject of debate and varies widely among guidelines worldwide. The inconsistency between guidelines is due to the lack of prospective, comprehensive studies on the threshold age for sampling the endometrium (19). In this study, the most biopsied age group was the 45-54 one (37.5%), followed by the 35-44 age group (34.1%). In total, 71.6% of the performed biopsies were in the 35-54 age range. American College of Obstetricians and Gynecologists recommends biopsy in all women with AUB over the age of 45 and in those under 45 with a history of unopposed estrogen exposure (polycystic ovary syndrome or obesity). In addition,

endometrial biopsy is recommended in cases with persistent AUB who do not respond to medical treatment (21). The Canadian Association of Obstetricians and Gynecologists recommends endometrial biopsy for patients with AUB over 40 years old (22).

Due to benign indications, pre-hysterectomy endometrial biopsy has become a routine procedure for most clinicians (14). Tosun et al. stated in their study that this biopsy procedure might cause the loss of workforce, infection, or bleeding (23). The present study determined the rate of premalignant-malignant pathology at 9.8% in the performed biopsies with the indication of preoperative evaluation. Based on this finding, endometrial sampling is recommended for preoperative evaluations due to myoma uteri.

In a study by Azatçam et al., which evaluated 1,374 endometrial biopsies, the most common diagnosis was an endometrial polyp, with a rate of 37.2% (24). In the present study, although the rate of polyps was 16.1%, which was higher than other pathology results, the highest rate was the proliferative-secretory endometrium (56.9%).

Endometrial biopsy performed in outpatient settings is the first step in evaluating patients with suspected endometrial pathology or AUB. The diagnostic accuracy of biopsy is 90%-98%, compared to subsequent hysterectomy or dilation and curettage (D&C) findings (25-28). In the present study, 46.7% of the biopsies performed on patients aged 65 and over were evaluated as insufficient biopsies. The insufficiency rate of biopsies performed on patients aged 55-64 was also 43.9%. The evaluation of the relationship between indications and material adequacy showed that the highest rate of inadequate biopsy was in the postmenopausal patient group, with 34.0%, which is higher than previous study results (29, 30). Insufficient biopsy results are affected by factors such as the experience of the people who perform the biopsy and evaluate the result, the quality of the equipment used, and the amount of atrophic tissue. However, D&C may be recommended to diagnose a possible endometrial cancer. The reason is many patients who learn that the biopsy result is insufficient do not want to have the biopsy again or may want to wait for a while before having it again, which may lead to the loss of time for diagnosis.

Esmer et al., in their study examining 2,516 premenopausal patients and investigating the threshold age for biopsy, stated that instead of using a standard age limit for performing the endometrial biopsy, each patient's risk factors for endometrial malignancy should be evaluated individually (19). İnal et al., in their study, claimed that endometrial evaluation should be performed in postmenopausal patients. Still, a routine endometrial biopsy may increase the cost in premenopausal patients with other indications (31). Postmenopausal patients require endometrial biopsy following endometrial evaluation. In premenopausal patients, a biopsy should be decided by considering other risk factors (such as nulliparity, infertility, and obesity) due to the high rate of benign pathology (32,33).

The evaluation of the number of patients who underwent endometrial biopsy in our clinic in terms of years highlighted an increase from 2016 to 2020 and a decrease from 2020 to 2021. This decrease might be because many people postponed their health checks due to the Covid-19 pandemic (34). It is thus worrying that the diagnosis of early-stage cancer has decreased due to the Covid-19 pandemic worldwide and that cancer-related deaths may increase (35).

The present study suggests that premenopausal patients should be evaluated clinically regarding the risk factors, and histopathological biopsies should be performed. Women with postmenopausal bleeding and asymptomatic postmenopausal women with endometrial thickness are at the highest risk of endometrial cancer. Therefore, further endometrial evaluation is necessary for these women.

This is a cross-sectional and retrospective study, and its limitation is the lack of data on endometrial cancer and other risk factors for endometrial hyperplasia. On the other hand, the sample size is the strength of this study. It may be appropriate to determine an age limit for endometrial biopsy with comprehensive prospective studies evaluating risk factors together in the coming years. Moreover, a different and more effective method can be developed to reduce the number of biopsy results insufficient for diagnosis.

6. Conclusion

The patients in this study were aged 55-64. Those over 65 years had the highest rate of endometrial cancer and insufficient for diagnosis biopsy results. Therefore, D&C should be recommended instead of endometrial biopsy when the biopsy is taken from patients in this age group.

Acknowledgments

This study was presented at the 2nd International Cancer Days in Sivas, Turkey, as a preliminary study.

Footnotes

Conflicts of Interest: None to declare.
Authors' contributions: Conceptualization and methodology: BK, TK, SC, and CY
Data collection: BK, TK, and SC
Data analysis and interpretation: BK and SC
Drafting the article: BK, TK, SC, and CY

Revising and the final approval of the manuscript: BK, TK, SC, and CY

Funding/Support: None.

Ethical statements: Non-Interventional Clinical Research Ethics Committee of the Sivas Cumhuriyet University approval was received for this study [registry No: 2021-11/14].

References

1. Cote I, Jacobs P, Cumming DC. Use of health services associated with increased menstrual loss in the United States. *Am J Obstet Gynecol.* 2003;**188**(2):343-8. doi: 10.1067/mob.2003.92. [PubMed: 12592237].
2. Santer M, Warner P, Wyke S. A Scottish postal survey suggested that the prevailing clinical preoccupation with heavy periods does not reflect the epidemiology of reported symptoms and problems. *J Clin Epidemiol.* 2005;**58**(11):1206-10. doi: 10.1016/j.jclinepi.2005.02.026. [PubMed: 16223665].
3. Shapley M, Jordan K, Croft PR. An epidemiological survey of symptoms of menstrual loss in the community. *Br J Gen Pract.* 2004;**54**(502):359-63. [PubMed: 15113519].
4. Goldstein SR, Lumsden MA. Abnormal uterine bleeding in perimenopause. *Climacteric*. 2017;**20**(20):414-20. doi: 10.1080/13697137.2017.1358921. [PubMed: 28780893].
5. Nicula R, Diculescu D, Lencu CC, Ciortea R, Bucuri CE, Oltean IA, et al. Accuracy of transvaginal ultrasonography compared to endometrial biopsy for the etiological diagnosis of abnormal perimenopausal bleeding. *Clujul Med.* 2017;**90**(1):33-9. doi: 10.15386/cjmed-670. [PubMed: 28246495].
6. Saccardi C, Vitagliano A, Marchetti M, Lo Turco A, Tosatto S, Palumbo M, et al. Endometrial cancer risk prediction according to indication of diagnostic hysteroscopy in post-menopausal women. *Diagnostics*. 2020;**10**(5):257. doi: 10.3390/diagnostics10050257. [PubMed: 32349386].
7. Espindola D, Kennedy KA, Fischer EG. Management of abnormal uterine bleeding and the pathology of endometrial hyperplasia. *Obstet Gynecol Clin North Am*. 2007;**34**(4):717-37. doi: 10.1016/j.ogc.2007.09.001. [PubMed: 18061866].
8. Early detection, diagnosis and staging of endometrial cancer. 2020. Available from:https://www.cancer.org/cancer/endometrial-cancer/detection-diagnosis-staging/signs and-symptoms.html.
9. Munro MG, Critchley HO, Broder MS, Fraser IS, Disorders FWGoM. FIGO classification system (PALMCOEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. *Int J Gynaecol Obstet.* 2011;**113**(1):3-13. doi: 10.1016/j.ijgo.2010.11.011. [PubMed: 21345435].
10. Timmermans A, Opmeer BC, Khan KS, Bachmann LM, Epstein E, Clark TJ, et al. Endometrial thickness measurement for detecting endometrial cancer in women with postmenopausal bleeding: a systematic review and meta-analysis. *Obstet Gynecol.* 2010;**116**(1):160-7. doi: 10.1097/AOG.0b013e3181e3e7e8. [PubMed: 20567183].
11. Gupta JK, Chien PF, Voit D, Clark TJ, Khan KS. Ultrasonographic endometrial thickness for diagnosing endometrial pathology in women with postmenopausal bleeding: a meta-analysis. *Acta Obstet Gynecol Scand.* 2002;**81**(9):799-816. doi: 10.1034/j.1600-0412.2001.810902.x. [PubMed: 12225294].
12. Getpook C, Wattanakumtornkul S. Endometrial thickness screening in premenopausal women with abnormal uterine bleeding. *J Obstet Gynaecol Res*. 2006;**32**(6):588-92.
13. Park YR, Lee SW, Kim Y, Bae IY, Kim HK, Choe J, et al. Endometrial thickness cut-off value by transvaginal ultrasonography for screening of endometrial pathology in premenopausal and postmenopausal women. *Obstet Gynecol Sci*. 2019;**62**(6):445-53. doi: 10.5468/ogs.2019.62.6.445. [PubMed: 31777741].
14. Siegal R, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. *CA Cancer J Clin.* 2021;**71**(1):7-33. doi: 10.3322/caac.21654. [PubMed: 33433946].
15. Trimble CL, Kauderer J, Zaino R, Silverberg S, Lim PC, Burke JJ, et al. Concurrent endometrial carcinoma in women with biopsy diagnosis of atypical endometrial hyperplasia: a Gynecologic Oncology Group study. *Cancer*. 2006;**106**(4):812-9. doi: 10.1002/cncr.21650. [PubMed: 16400639].
16. Kadirogullari P, Atalay CR, Ozdemir O, Sari ME. Prevalence of Co-existing Endometrial Carcinoma in Patients with Preoperative Diagnosis of Endometrial Hyperplasia. *J Clin Diagn Res*. 2015;**9**(10):10-4. doi: 10.7860/JCDR/2015/12484.6618. [PubMed: 26557570].
17. Gunes, G. Determination of Menopause and Related Factors in Women aged 35 and over in Malatya City Center. *Medical Sciences*. 2009; **4**(3):59-66.
18. Iram S, Musonda P, Ewies AA: Premenopausal bleeding: when should the endometrium be investigated? – A retrospective non-comparative study of 3,006 women. *Eur J Obstet Gynecol Reprod Biol.* 2010;**148**(1):86–9. doi: 10.1016/j.ejogrb.2009.09.023. [PubMed: 19853362].
19. Esmer AC, Akbayir O, Goksedef BP, Gunduz N, Kisacık S, Dagdeviren H, et al. Is there an appropriate cutoff age for sampling the endometrium in premenopausal bleeding? *Gynecol Obstet Invest*. 2014;**77**(1):40-4. doi: 10.1159/000356959. [PubMed: 24334971].
20. Doraiswami S, Johnson T, Rao S, Rajkumar A, Vijayaraghavan J, Panicker VK. Study of endometrial pathology in abnormal uterine bleeding. *J Obstet Gynecol India*. 2011;**61**(4):426-30. doi: 10.1007/s13224-011-0047-2. [PubMed: 22851826].
21. ACOG . diagnosis of abnormal uterine bleeding in reproductive-aged women. *Obstet Gynecol.* 2012;**120**(1):197-206. doi: 10.1097/AOG.0b013e318262e320. [PubMed: 22914421].
22. Vilos G, Lefebvre G, Graves G. Guidelines for the management of abnormal uterine bleeding. *J Obstet Gynaecol Can.* 2001;**23**(8):704–9.
23. Tosun AK, Tosun I, Suer N, Güzin K. The necessity of endometrial sampling in preoperative benign indications. *Abant Med J*. 2014; **3**:156-60. doi: 10.5505/abantmedj.2014.87004.
24. Azatçam M, Altun E, Usta A. Histopathological evaluation of endometrial sampling in different age groups -1374 cases. *Medeniyet Med J*. 2017; **32**(1): 26-32.
25. Yasmin F, Farrukh R, Kamal F. Efficacy of Pipelle As A Tool For Endometrial Biopsy. *Biomedica*. 2007;**23**:12–5.
26. Saadia A, Mubarik A, Zubair A, Jamal S, Zafar A. Diagnostic accuracy of endometrial curettage in endometrial pathology. *J Ayub Med Coll Abbottabad*. 2011;**23**(1):129–31.
27. Dijkhuizen FPH, Mol BW, Brolmann HA. The accuracy of endometrial sampling in the diagnosis of patients with endometrial carcinoma and hyperplasia: a meta-analysis. Cancer 2000;**89**(8):1765–72. [PubMed: 22830167].
28. Turan G, Bahat PY, Çetin BA, Selçuki NFT. How Compatible are Hysterectomy Pathology Results with Endometrial Biopsy in Abnormal Uterine Bleeding Women? *Kafkas J Med Sci*. 2020;**10**(2):104–9 doi: 10.5505/kjms.2020.80148.
29. Sargın MA, Yassa M, Somay A, Ergun E, Orhan E, Tuğ N. Clinical outcomes of postmenopausal patients with insufficient sample from endometrial biopsy. *Bosphorus Med J*. 2016;**3**(2):54-59.
30. Çakır A. Öz İ, Ün B. Endometrial Sampling Results: Analysis of 365 Cases. *Bozok Medical Journal*. 2020; 10.16919/bozoktip.539875.
31. Inal ZO, Inal HA, Kucukosmanoglu I, Kucukkendirci H. H. Assessment of Endometrial Sampling and Histopathological Results: Analysis of 4,247 Cases. Eurasian J Med. 2017 **49**(1), 44–47. doi: 10.5152/eurasianjmed.2017.16269 [PMID: 28416932]
32. Constantine GD, Kessler G, Graham S, Goldstein SR. Increased incidence of endometrial cancer following the women's health initiative: an assessment of risk factors. *J Womens Health (Larchmt).* 2019;**28**(2):237–43. doi: 10.1089/jwh.2018.6956. [PubMed: 30484734].
33. Cote ML, Ruterbusch JJ, Olson SH, Lu K, Ali-Fehmi R. The growing burden of endometrial cancer: a major racial disparity affecting black women. *Cancer Epidemiol Biomarkers Prev.* 2015;**24**(9):1407–15. doi: 10.1158/1055-9965.EPI-15-0316. [PubMed: 26290568].
34. Riera R, Bagattini ÂM, Pacheco RL, Pachito DV, Roitberg F,

Ilbawi A. Delays and disruptions in cancer health care due to COVID-19 pandemic: systematic review. *JCO Glob Oncol.* 2021;**7**(1):311-23. doi: 10.1200/GO.20.00639. [PubMed: 33617304].

35. Lai AG, Pasea L, Banerjee A, Denaxas S, Katsoulis M, Chang WH, et al. Estimating excess mortality in people with cancer and multimorbidity in the COVID-19 emergency. *BMJ Open*. 2020;**10**:e043828. doi: 10.1101/2020.05.27.20083287.