

# Histopathological evaluation of endometrial sampling in different age groups - 1374 cases

## Endometriyal örneklerin farklı yaş gruplarında histopatolojik değerlendirmesi - 1374 olgu

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### ABSTRACT

The aim of this study was to evaluate the relationship between histopathological results and endometrial sampling and to identify specific pathologies in different age groups. The histopathological results of 1374 cases registered in our pathology archives, in whom endometrial sampling was performed in our hospital for various reasons between 2013 and 2014 were evaluated. Biopsy indications included menometrorrhagia (80.5%), postmenopausal bleeding (6.8%), myoma uteri (1.7%), cervical polyp (2.4%), infertility (0.2%), and hyperplasia/malignancy (8.4%). Histopathological diagnoses in order of frequency included endometrial polyp (37.2%), proliferation/secretion/menstrual phase (29.3%), irregular proliferative endometrium (8.4%), insufficient biopsy material (8.4%), endometritis (5.8%), stroma-glandular breakdown (4.2%), endometrial hyperplasia (4%), iatrogenic changes (1.4%), atrophic endometrium (1.2%), and malignancy (0.1%). Endometrial polyps were detected in 14 of 33 patients with cervical polyps. In endometrial samplings performed in patients in whom hysterectomy was planned due to myoma uteri, the most frequent diagnosis was a normal cyclic pattern (50%). In conclusion, in the present study, the most frequent biopsy indications of endometrial sampling were menometrorrhagia, and the most frequent histopathological diagnosis was endometrial polyp. Endometrial polyp was also identified concomitantly in endometrial sampling of 14 out of 33 patients with cervical polyps. Thus, we concluded that in patients with an initial diagnosis of cervical polyp, the endometrium should also be evaluated.

**Keywords:** Endometrial sampling, menometrorrhagia, postmenopausal bleeding, cervical polyp

### Öz

Bu çalışmanın amacı, endometriyal örneklemin histopatolojik sonuçlarla ilişkisini değerlendirmek ve farklı yaş gruplarındaki spesifik patolojileri tanımlamaktır. Hastanemizde 2013-2014 yılları arasında çeşitli nedenlerle endometrial örnekleme yapılan patoloji arşivlerinde yer alan 1374 olgunun histopatolojik sonuçları değerlendirildi. Biyopsi endikasyonları; menometrorrhagia (%80,5), postmenopozal kanama (%6,8), myoma uteri (%1,7), servikal polip (%2,4), infertilite (%0,2) ve hiperplazi-malignite (%8,4) idi. Histopatolojik tanımlar endometrial polip (%37,2), proliferasyon / sekresyon / menstrüel faz (%29,3), düzensiz çoğalma endometriyumu (%8,4), yetersiz biyopsi materyali (%8,4), endometrit (%5,8) (% 4,2), iyatrojenik değişiklikler (%1,4), atrofik endometrium (%1,2), malignite (%0,1) ve endometriyum hiperplazisi (%4) izlendi. Servikal polip bulunan hastalardaki 33 endometriyal küretajın 14'ünde endometrial polip tespit edildi. Myoma uteri nedeniyle histerektomi planlanan olgularda yapılan endometriyal örneklemlerde en sık görülen normal siklik paterni (%50) idi. Çalışmamızda en sık görülen tanı endometrial polip olarak tanımlandı. Servikal polipin ön tanısı konan vakalarda endometriyumun da değerlendirilmesi gerektiği sonucuna varıldı.

**Anahtar kelimeler:** Endometrial örnekleme, menometroraji, postmenopozal kanama, servikal polip

### INTRODUCTION

Endometrial biopsy specimens are among the most common tissue samples sent to the pathology laboratory<sup>1</sup>. Although, the main purpose of sampling is

the exclusion of endometrial malignancies, it is also performed for various reasons, including the identification of the causes of abnormal bleeding and the evaluation of endometrial response to hormonal therapy<sup>2-4</sup>. Endometrial sampling also has therape-

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utic effects in some patients, especially those with abnormal uterine bleeding<sup>3</sup>.

In the literature, the most frequent diagnosis from endometrial sampling is a normal cyclic pattern (proliferation/secretion/menstruation) and endometrial polyp<sup>1,5-10</sup>. However, some authors report different diagnoses from endometrial sampling in different age categories. In a study conducted by Özalp et al.,<sup>11</sup> the patients were classified into either a reproductive age group or a geriatric group; the most frequent diagnoses were proliferative/secretory endometrium in the reproductive age group and malignancy in the geriatric age group. Doraiswami et al.<sup>1</sup> and Soleymani et al.<sup>9</sup> reported that an irregular proliferative pattern is frequently diagnosed in endometrial sampling. While a frequent diagnosis is dysfunctional bleeding due to anovulatory cycles in adolescents, in the perimenopausal group, as well as anovulation, organic lesions such as hyperplasia and polyps and also changes due to exogenous hormone intake become manifest. In the reproductive period, abnormal uterine bleeding due to complications related to pregnancy, endometritis, dysfunctional uterine bleeding, organic lesions, and exogenous hormone intake are observed<sup>2</sup>.

In this study, our aim was to evaluate the relationship of histopathological results of endometrial samplings with indications in different age groups and to identify the specific pathologies.

## **MATERIAL and METHODS**

A total of 1374 consecutive endometrial sampling specimens of women obtained between 2013 and 2014 were evaluated.

Histopathological results of endometrial samplings archived in the pathology database of 1374 patients, in whom the endometrial sampling was performed for various reasons in a state hospital which is the unique referenced hospital for gynecological and obstetrical diseases in the city, were evaluated. Patients were classified into seven groups, in terms of their

ages. The indications for endometrial sampling were classified as abnormal uterine bleeding, menometrorrhagia, postmenopausal bleeding, curettage prior to hysterectomy due to myoma uteri, cervical polyp, infertility, and hyperplasia or malignancy. Remnants of pregnancy and related curettage were excluded from the study. Resected endometrial specimens were placed in a container with 10% formaldehyde and sent to the pathologist for histologic analysis. All specimens were embedded in paraffin, 5 mm-thick slices were cut, and stained with hematoxylin-eosin. All of H&E-stained sections were examined by two pathologists. Histopathological diagnoses were grouped as: proliferation/secretion/menstrual phase endometrium, stromal-glandular breakdown, irregular proliferative endometrium, endometritis, endometrial polyp, iatrogenic changes, atrophic endometrium, endometrial hyperplasia, malignancy, and insufficient material. The results were evaluated according to age, indication and histopathological diagnosis.

Ethics Committee Approval; In this study, the investigation protocol was in accordance with the Helsinki Committee Requirement and was approved by the Institutional Ethical Committee of The General Secretary of State Hospitals (decision no: 91896002/, 2014/12/08).

## **Statistical analysis**

The MedCalc Statistical Software Program version 16.8.4 (MedCalc, Belgium) was used for statistical analysis. In the statistical analysis, quantitative, and qualitative data were expressed as arithmetic mean±standard deviation, and percentage (min-max), respectively.

## **RESULTS**

Mean age of women was 42.4 years (range, 18-95 years) and approximately half of the women (47.2%) were within the 41-50 age group. The most frequent indication for endometrial sampling was menometrorrhagia (80.5%) and the most frequent histopathological diagnosis was endometrial polyp (37.2%). Also,

in 14 out of 33 patients with cervical polyps, endometrial polyp was diagnosed. Other diagnoses were, proliferation/secretion/menstrual phase (29.3%), irregular proliferative endometrium (8.4%), insufficient biopsy material (8.4%), endometritis (5.8%), stroma-glandular breakdown (4.2%), endometrial hyperplasia (4%), iatrogenic changes (1.4%), atrophic endometrium (1.2%), and malignancy (0.1%). The relationship between indications and histopathological diagnoses are presented in Table 1.

As shown in Table 2, the most frequent histopathological diagnosis of the endometrial samplings of the patients who were scheduled for hysterectomy for myoma uteri, normal cyclic pattern (secretion/proliferation/menstruation) (12/24-50%).

Endometritis was reported to be chronic in 78 patients and acute in only 2 patients. Also, the actinomyces infestation was identified in 3 patients with chronic endometritis.

In our study, we observed that from 115 patients insufficient endometrial sampling material had been obtained. In 53 of them, material consisted of cervical mucus and tissue fragments only. In 31 patients, only fibrin and blood were observed in sections of the material. In 20 patients, very small amount of endometrial tissue was observed. In 11 patients, inconclusive diagnosis was made due to routine process problems. Patients whose endometrial sampling material was inadequate to make a definitive diagnosis had menometrorrhagia in 67, and postmenopausal bleeding in 32 patients. Most frequently (34.4%)

**Table 1. The distribution of histopathological diagnoses in terms of the indications.**

	Indications				
	Hyperplasia-Malignancy	infertility	Leiomyoma	Menometrorrhagia	Post-menopausal bleeding
Endometrial polyp	59	1	8	403	27
Secretion/Proliferation/Menstruation	12	2	12	355	13
Irregular proliferation	6	0	2	103	3
Atrophic endometrium	2	0	0	7	5
Endometritis	1	0	0	77	2
Stromal-Glandular breakdown	9	0	0	42	6
Iatrogenic changes	1	0	0	17	0
Hyperplasia	14	0	0	35	5
Malignancy	1	0	0	0	0
Insufficient	10	0	2	67	32
TOTAL	115 (8.4%)	3 (0.2%)	24 (1.7%)	1106 (80.5%)	93 (6.8%)

**Table 2. The distribution of histopathological diagnoses in terms of age.**

	Age Groups							Total n=1374
	18-20	21-30	31-40	41-50	51-60	61-70	71-95	
Secretion/Proliferation/Menstruation	4	32	154	186	27	0	0	403 (29.3%)
Insufficient	3	12	19	36	23	16	6	115 (8.4%)
Endometrial polyp	4	40	167	241	49	8	3	512 (37.2%)
Atrophic Endometrium	0	0	0	5	9	1	1	16 (1.2%)
Irregular Proliferation	1	4	32	71	7	0	0	115 (8.4%)
Stromal-Glandular Breakdown	0	4	9	34	11	0	0	58 (4.2%)
Endometritis	0	13	31	32	3	1	0	80 (5.8%)
Iatrogenic Changes	0	3	4	11	1	0	0	19 (1.4%)
Hyperplasia	0	2	8	32	8	5	0	55 (4%)
Malignancy	0	0	0	0	1	0	0	1 (0.1%)

in postmenopausal patients biopsy material was not adequate to make a definitive diagnosis.

Endometrial hyperplasia was detected in 55 patients with a median age of 47.1 years and the most common indication of endometrial sampling was shown to be menometrorrhagia. The endometrial hyperplasia without atypia in 50, and atypical endometrial hyperplasia in 5 patients were detected.

In our study, no endometrial malignancy was identified. In only one patient, leiomyosarcoma was diagnosed. She was 57 years old and her indication for endometrial sampling was malignancy.

## DISCUSSION

In the present study, the distribution of histopathological diagnoses of endometrial sampling was evaluated according to age groups, and our results showed that the endometrial sampling was most frequently performed in the 41-50 age group, and the most frequent histopathological diagnosis was endometrial polyp. Endometrial polyp was also identified concomitantly with cervical polyp in endometrial sampling of 14 out of 33 patients.

Endometrial polyp is diagnosed in 2%-23% of the patients who underwent endometrial biopsy for abnormal uterine bleeding. It is commonly seen in pre- and postmenopausal women. In biopsies performed for abnormal uterine bleeding, the probability of the existence of a polyp should always be considered<sup>12</sup>. In order to make a histopathological diagnosis of a polyp, polypoid tissues, with their three sides covered with epithelium, stroma different from its surroundings, dilated glands with a cyclic pattern different from their surrounding endometrium, and thick-walled vessel groups should be observed in the sections. In various other studies, the prevalence of endometrial polyp ranged from 1.4% to 21.5%<sup>1,5-10</sup>. In our study, endometrial polyp was diagnosed most frequently in patients operated with the indication of menometrorrhagia at an incidence of 37.2%, and it was most frequently found in the 41-50 age group.

While the diagnosis was definitive in 91.4% of the patients, in 8.6% of the patients, due to fragmented tissues, the diagnosis was reported in the comment section as "suspected polyp." In our study, the high prevalence of endometrial polyp was considered to be associated with the fact that most of the samplings had been performed during the perimenopausal period.

Antunes et al.<sup>12</sup> evaluated the records of 475 patients diagnosed with endometrial polyp, and determined that in 17 patients (2.74%), carcinoma developed on the ground of the polyp. Most of these patients were in the postmenopausal period. Similarly, in different studies, the risk of malignancy in endometrial polyps during the postmenopausal period was greater<sup>13-17</sup>. But in a study by Çakmak et al.,<sup>5</sup> no malignancy was detected in histopathological examination of endometrial polyps. In our study as well, no malignancy was present in endometrial polyps, but in one patient, a focus of atypical endometrial hyperplasia was detected.

In the literature, there are numerous studies questioning the necessity of routine endometrial sampling prior to hysterectomies scheduled for various indications<sup>18-23</sup>. But the main purpose of endometrial sampling is the exclusion of endometrial malignancy<sup>2,4</sup>. Some studies have reported that preoperative endometrial sampling ensured sensitive and accurate diagnosis of endometrial pathologies, particularly tumors<sup>22</sup>. In contrast, other publications defend the view that preoperative endometrial sampling is an unnecessary intervention<sup>5,6,19</sup>. Stock et al.<sup>24</sup> have reported that opening and checking the cavity following excision of the uterus was more valuable than preoperative curettage. Stovall et al.<sup>21</sup> and Bettocchi et al.<sup>23</sup> do not support routine endometrial sampling prior to hysterectomy, and they have suggested that sampling should only be performed in patients above 35 years of age who have abnormal uterine bleeding or in patients with postmenopausal bleeding.

The most common indication for hysterectomy in

gynecological surgery is leiomyoma<sup>25</sup>. In some of the studies, no malignancy was detected in samplings performed for myoma uteri<sup>5,6</sup>. Inal et al.<sup>20</sup> evaluated the endometrial sampling and hysterectomy results of the patients operated on for myoma uteri, and they detected hyperplasia in one of 94 patients preoperatively diagnosed as benign and adenocarcinoma in one of 10 patients preoperatively diagnosed with hyperplasia. In our study, in all patients in whom endometrial sampling was performed with the indication of myoma uteri, no hyperplasia or malignancy was diagnosed. This result was consistent with the results cited in the literature.

Endometritis has commonly been diagnosed in endometrial samplings performed with the indication of menometrorrhagia, and its prevalence has ranged from 2.7% to 8.1%<sup>1,5,6,10</sup>. In a study conducted by Özalp et al.,<sup>11</sup> the incidence rates of endometritis were 8.5% in the reproductive age group and 2% in the geriatric group. In a study by Doraiswami et al.,<sup>1</sup> endometritis was also found to be more frequent in the reproductive period. Our study was also consistent with the literature, and endometritis was detected at a rate of 5.8% in total, more frequently in samplings performed for the indication of menometrorrhagia during the reproductive age group.

Cervical polyp is commonly seen in multigravid women between the fourth and sixth decades of their lives<sup>3,15</sup>. While most patients are asymptomatic, some patients manifest irregular bleeding<sup>3,15-17</sup>. In previous studies, cervical polyp was seen most commonly between the ages of 40 and 60<sup>16,17</sup>. In some studies investigating the endometrial pathologies accompanying cervical polyp its association with cervical and endometrial polyps was determined, particularly in postmenopausal patients<sup>15,16</sup>. Coeman et al.<sup>16</sup> evaluated the association between endocervical and endometrial polyp. In total, 165 patients with cervical polyp were included the study, and 44 of them had endometrial polyp with cervical polyp, all being detected in the perimenopausal group (26.7%). Kucur et al.<sup>6</sup> reported this ratio as 78.6%, while it was 40% in Çakmak et al.'s<sup>5</sup> study. Although different rati-

os have been reported in the literature, in our study, an association of cervical-endometrial polyp was determined in 14 (42.4%) out of 33 patients in whom endometrial sampling was performed with the indication of cervical polyp.

Endometrial hyperplasia usually manifests itself with abnormal uterine bleeding in women with anovulatory cycles during the perimenopausal period. However, it may sometimes be seen in women during their reproductive period, in adolescents with anovulatory cycles, and in postmenopausal women using exogenous estrogen or with increased endogenous estrogen levels<sup>2</sup>. Depending on the atypia of the glands, endometrial hyperplasia is classified as either with atypia or without atypia<sup>27</sup>. In the study of Doraiswami et al.,<sup>1</sup> hyperplasia was detected in 6.1% of the patients, 68% of whom belonged to the 41-50 age group. In most of the studies, hyperplasia was diagnosed in patients who underwent sampling for menometrorrhagia. Previous studies showed that the incidence of hyperplasia detected in endometrial samplings varied between 7.5% and 9.2%<sup>5,6,10</sup>. In our study, consistent with the literature, hyperplasia was most frequently observed in the 41-50 age group, and sampling was performed for indications of menometrorrhagia in 63% of the patients with hyperplasia.

In the literature, the incidence of atrophic endometrium in endometrial samplings ranged from 1.5% to 3.5%, and patients usually belonged to the postmenopausal age group<sup>5,6,10,11</sup>. In our study, the diagnosis of atrophic endometrium most frequently (56%) occurred in the 51-60 age group.

In developed countries, endometrial cancer is the most common malign tumor of the female genital system<sup>3</sup>. It is commonly seen in both pre- and postmenopausal periods, being most common between 55 and 64 years of age. Clinically, it manifests with postmenopausal bleeding and menometrorrhagia<sup>3</sup>. Obesity, a high endogenous estrogen level, exogenous hormone intake, nulliparity, premature menarche, and delayed menopause are considered to be the main predisposing factors. In various studies,

endometrial carcinoma was usually observed in the postmenopausal period, with an incidence of 0.14%-1.75 percent<sup>5,6,10</sup>.

In our study, leiomyosarcoma was diagnosed in only one of 1374 patients, and no tumor of endometrial origin was observed which were suggestively related to high admittance rate of multiparous patients to our hospital and the lower incidence of obesity<sup>28</sup>.

In previous studies, the incidence of obtaining sampling material insufficient to establish a diagnosis has ranged from 0.9 to 7.75 percent<sup>5,6,10</sup>. There are many factors affecting these incidence rates as thin endometrium or inappropriate sampling method. In our study, this incidence rate was 8.4 percent. Most of the samples were histopathologically detected to be blood, fibrin and mucus, and in some others, the observed histopathological findings were described and commented as "insufficient". In our study, 27 (8%) specimens obtained with the indication of postmenopausal bleeding were reported as "insufficient for diagnosis".

In conclusion, endometrial polyp was the most frequent diagnosis determined in our study. In patients admitted for abnormal uterine bleeding, endometrial sampling is suggested to be necessary, in order to exclude organic causes in the reproductive period, and especially in the perimenopausal period. As reported in some studies cited in the literature, in patients with cervical polyp, the endometrium should also be evaluated. Endometrial hyperplasia was more frequently identified in the perimenopausal period. Therefore, in this age group, the patients who have abnormal uterine bleeding, the endometrial sampling should be performed. None of our patients was diagnosed with endometrial cancer and this issue is worth studying, in terms of involving genetic and epigenetic factors.

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