

## THE ENDOMETRIUM IN PATIENTS WITH METABOLIC SYNDROME

\* Özgül ÖZGAN ÇELİKEL, \* \*Y. Özlem BARAK SERKANT

\*Yıldırım Beyazıt University, Yenimahalle Training and Research Hospital, Gynecology and Obstetrics Clinic, Ankara/TURKEY. e-mail: drozgulozgan@gmail.com

\*\*Yıldırım Beyazıt University, Yenimahalle Training and Research Hospital, Department of Internal Medicine, Ankara/TURKEY e-mail: oybarak@yahoo.com

### ABSTRACT

**Introduction:** Metabolic disorders can increase the risk of endometrial diseases and endometrial cancer. Patients with metabolic syndrome are at risk for endometrial pathologies. Advising routine gynecological examination even to the patients with metabolic syndrome having no gynecological complaints may be helpful in early diagnosis.

**Materials and Method:** 120 patients diagnosed with metabolic syndrome in the Internal Diseases Outpatient Clinic were examined for endometrial diseases in the Gynecology Clinic. Data were analyzed using SPSS 16 statistical software, and Chi-square test was performed.  $p < 0.05$  was considered as statistically significant.

**Results:** 36 patients had undergone a diagnostic curettage. There was no endometrial cancer in any patient. The rate of endometrial hyperplasia without atypia was found significantly increased in the patient group with abnormal uterine bleeding when compared to the patient group with menopause having postmenopausal bleeding and an increased endometrial thickness ( $p = 0.001$ ).

**Conclusion:** Endometrial pathology was diagnosed in 15% of the patients with metabolic syndrome. It was concluded that the question of whether routine gynecological examination of metabolic syndrome patients is required in clinical practice could be answered by further studies including larger patient groups.

**Key Words:** Metabolic syndrome, probe curettage, Endometrial polyp

### ÖZET

**Giriş:** Metabolik hastalıklar endometrial hastalıklar ve endometrium kanseri riskini artırabilmektedir. Metabolik sendromlu hastalar endometrial patolojiler açısından risk altındadırlar. Tanı alan hastaları

jinekolojik yakınması olmasa bile rutin olarak jinekolojik muayeneye yönlendirmek erken tanı için faydalı olabilir.

**Materyal Metod:** Dahiliye polikliniğinde metabolik sendrom tanısı alan 120 hasta jinekoloji polikliniğinde endometrial hastalıklar açısından değerlendirilmiştir. Veriler SPSS 16 istatistik programında analiz edilmiş Ki kare(chisquare) testi uygulanmıştır.  $P<0.05$  istatistiksel olarak anlamlı kabul edilmiştir.

**Bulgular:** 36 hastaya probe küretaj yapılmıştır. Endometrial kansere rastlanmamıştır. Atipisiz endometrial hiperplazi anlamlı olarak anormal uterin kanaması olan grupta; postmenopozal kanama ve endometrial kalınlığı bulunan menopozlu hasta grubuna göre daha fazla bulunmuştur ( $p=0.001$ ).

**Sonuç:** Metabolik sendromlu hastaların %15’de endometrial patoloji tesbit edilmiştir. Hasta sayısı artırılarak yapılan çalışmalarla klinik pratikte metabolik sendromlu hastaların jinekolojik muayenelerinin rutin olarak yapılıp yapılmamasının tesbit edilebileceği kanaatine varılmıştır.

## Introduction

Metabolic syndrome is a fatal endocrinopathy that begins with insulin resistance and continues with the addition of other systemic disorders such as abdominal obesity, glucose intolerance, dyslipidemia, hypertension, and coronary artery diseases. The prevalence of metabolic syndrome is increased by age, and its incidence is 28% in males and 40% females in Turkey (1).

Metabolic disorders can increase the risk of endometrial diseases and endometrial cancer (2,3). Particularly, hyperinsulinemia is a risk factor in the development of endometrial cancer (4). The levels of estrogen, testosterone, and insulin are frequently elevated in patients with metabolic syndrome. The FSH level decreases and the LH level increases as a response to the elevated insulin level, resulting in an increased LH/FSH ratio. The reduction of the levels of

FSH and progesterone initiates the pathological changes in the endometrium (5), and the formation of an endometrial polyp is triggered (6). Estrogen has been known to play a role in the etiopathogenesis of endometrial cancer; however, most of the endometrial cancer cases are encountered in the postmenopausal period. Not only the levels of ovarian estrogens but also the levels of endogenous androgens are reduced in the postmenopausal period (1,2). It has been demonstrated that elevated free estrogen and testosterone levels increase the risk of endometrial cancer development in postmenopausal patients (7). Furthermore, it is known that endometrial cancer risk is also increased in patients with a high body mass index (8).

Being overweight is a major risk factor for endometrial cancer development (9). The biological mechanism of this is the increased estrogen and decreased progesterone levels due to obesity, estrogen increasing the mitotic activity of endometrial cells, resulting in increased endometrial thickness and endometrial cancer development (9,10). The increased insulin level and diabetes mellitus play important roles in endometrial cancer development (11,12) whereas the other components of metabolic syndrome such as hypertension, increased glucose level, and altered lipid profile play small roles.

Based on the previous studies, it can be asserted that the risk of endometrial cancer development and mortality can be reduced by administering antihypertensive agents and also medications for regulation of lipid profile in patients with metabolic syndrome (13).

In this study, we aimed to diagnose the endometrial pathologies of metabolic syndrome patients by questioning medical history, and performing a physical examination, ultrasonography together with endometrial sampling, if necessary. We also planned to assess whether gynecological examination of every metabolic syndrome patient is useful in

clinical practice or not; in this context, we might be able to avoid development of endometrial hyperplasia, polyp, and endometrial cancer by preventing metabolic syndrome development, eliminating risk factors and treating the disease.

## **Materials and Method**

120 patients who were admitted to the Internal Diseases Outpatient Clinic of Yenimahalle Research and Training Hospital and were diagnosed with metabolic syndrome were included in the study group. Based on their complaints, the patients were assessed as with abnormal uterine bleeding (AUB), postmenopausal bleeding (PMB), and no complaint. Body mass index, waist circumference, lipid profile, insulin resistance, fasting blood glucose (FBG), postprandial blood glucose (PBG) were measured, and the patients were investigated in terms of hypertension and diabetes mellitus. The patients were consulted with the Gynecology Department regarding the presence of clinical findings that might be related to endometrial pathologies. Their gynecological examination findings and results of their pelvic ultrasonographic investigations were recorded. A diagnostic curettage was performed in patients when it was indicated. The results of the pathology report were recorded. The data were analyzed by using SPSS 16 software, a Chi-square test was performed, and  $p < 0.05$  was considered as statistically significant.

The endometrial thickness was measured by transvaginal ultrasonography during the routine gynecological examination. A Voluson 739 (General Electric) device was used in ultrasonographic examinations. Probe curettage (PC) and endometrial sampling were performed in patients with an endometrial thickness exceeding 5 mm, together with patients having AUB or PMB. The results of the pathology report were recorded. The

patients were divided into three groups according to their complaints as AUB, PMB, and patients with no complaint in whom diagnostic curettage was performed with the indication of an endometrial thickness more than 5mm. Multiple comparisons were made, and the distinctive results were summarized in tables at the 1% significance level.  $P < 0.05$  was considered as statistically significant.

## Results

The mean age was calculated as  $54.1 \pm 0.81$ . 38 patients (31.66%) were in the menopausal period while the remaining 82 patients (68.33%) were not. 36 (30%) of 120 patients who were admitted to the Gynecology Department had an indication for performing PC, and the endometrial sampling was performed. The patients without menopause were determined to be within the AUB group, whereas the patients with menopause were within the PMB group or the group having an endometrial thickness over 5 mm. A diagnostic curettage was performed in 16, 8 and 12 patients with the indications of AUB, PMB, and increased endometrial thickness with no complaint, respectively (Table 1). One patient without any complaint but having increased endometrial thickness refused undergoing a probe curettage. The DC rate was found to be higher in the AUB group. (Table 1,  $p = 0.000$ )

Table 1: The status of diagnostic curettage according to the complaints ( $p = 0.000$ )

Complaint	PC (+)	PC (-)	Total
AUB	16	0	16
PMB	8	1	9
Endometrial thickness > 5mm	12	83	95

Menopausal status of DC patients was shown in table 2.

Table 2: The menopausal status according to the complaints (p=0.000)

Complaint	Menopausal	Non-menopausal	Total
AUB	0	16	16
PMB	8	0	8
endometrial thickness>5 mm	9	4(1 patient PC was not made)	13

Table 3: Pathology results according to the complaints (p=0.001)

Complaint	Normal	Endometrial Polyp	non-atypical endometrial hyperplasia	Total
AUK	2	9	4	16
PMK	7	1	0	8
endometrial thickness>5mm	9	3	0	12
Toplam	18	13	4	36

The presence of an endometrial polyp and endometrial hyperplasia without atypia were found to be significantly higher in the AUB group. No endometrial hyperplasia was reported as the PC pathology result in patients with no complaint but increased endometrial thickness, whereas endometrial polyp was present in three (1.2%) patients in (Table 3, p=0.001).

We did not encounter any case with endometrial cancer, and endometrial hyperplasia without atypia was diagnosed in four patients with abnormal uterine bleeding. 12 out of 13 menopausal patients with increased endometrial thickness had undergone diagnostic

curettage, and three patients were diagnosed with endometrial polyp whereas the pathology reports of the remaining nine patients revealed normal results ( $p=0.001$ ,  $p<0.05$ ).

## **Discussion**

In a study conducted in Brazil in 2016, it was reported that the rates of dyslipidemia, high BMI, diabetes mellitus, and hyperglycemia were increased in 132 menopausal patients with endometrial polyp ( $p=0.0001$ ) (14). In our study, a substantial number of patients with metabolic syndrome, 36 (30%) out of 120, had an indication for diagnostic curettage. In a study conducted in China in the year of 2010, it was indicated that metabolic syndrome frequently accompanied endometrioid uterine carcinoma and that diagnosing metabolic syndrome may be useful in screening, preventing and treating endometrioid uterine carcinoma (15). There are studies indicating that the rate of endometrial carcinoma is elevated with increased BMI and thus, BMI (16,17,18) can adversely affect prognosis in this disease (19,20). In another study conducted in both Mexico and Canada, it was reported that metabolic syndrome components are related to the increased endometrial cancer risk (18).

In a study performed in Düzce, Turkey, in 2012, it was reported that there were no significant relationships between the endometrial thickness and the levels of sex steroids as well as metabolic parameters (21).

In another study conducted in Turkey in 2015, it was reported that impairment of metabolic parameters was present in patients in whom diagnostic curettage was performed due to abnormal uterine bleeding, in cases with hyperplasia and cancer; however, no significant difference was observed between post-menopausal and pre-menopausal patients (22). In our study, PC was performed in menopausal patients with PMB or with endometrial

thickness above 5mm; endometrial hyperplasia was not observed in any patient while endometrial polyp was observed in four patients. In the pre-menopausal patient group, endometrial hyperplasia without atypia was observed in four patients, and an endometrial polyp was observed in nine patients. The difference between the two groups was significant in terms of these findings ( $p=0.001$ , Table 3).

As a conclusion, PC was performed in 30% of patients with metabolic syndrome consulted with the Gynecology Department and the pathology examination revealed that 50% of these patients were normal while the remaining 50% were reported as having an endometrial polyp and endometrial hyperplasia. In our study, the incidence of endometrial pathologies in patients with metabolic syndrome was calculated as 15%. We suggest that further studies including larger number of patients are required to determine whether routine gynecological examination of patients with metabolic syndrome is necessary or not.

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