RESEARCH ARTICLE

Risk Factors for Endometrial Hyperplasia Concomitant Endometrial Polyps in Pre- and Post-menopausal Women

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Abstract

Purpose: To evaluate the risk factors for endometrial hyperplasia concomitant endometrial polyps in pre- and post-menopausal women. Materials and Methods: A total of 203 patients undergoing endometrial sampling before hysterectomy were evaluated in this retrospective study. Data recorded were age, gravidity, parity, body mass index (BMI: weight(kg)/height(m)^2), endometrial thickness (ET), menopausal status, presence of adenomyosis and diabetes mellitus. Results: Endometrial hyperplasia and polyps were detected in 13 patients. There were statistically significant differences in terms of age, menopausal status, morbid obesity and diabetes mellitus ($p<0.005$). Logistic regression demonstrated that menopausal status and presence of diabetes mellitus were independent risk factors. Conclusions: According to the current study; menopause and diabetes mellitus are strong risk factors for the presence of concomitant endometrial polyps and endometrial hyperplasia.

Keywords: Endometrial hyperplaisa - endometrial polyps - concomitant presence - risk factors

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Introduction

Abnormal uterine bleeding (AUB) is described as bleeding that is excessive or outside the normal menstrual cycle in terms of regularity, volume, frequency, or duration and occurs in the absence of pregnancy (Munro et al., 2011). International Federation of Gynecology and Obstetrics (FIGO) defined a classification system for AUB called as PALM-COEIN (polyp; adenomyosis; leiomyoma; malignancy and hyperplasia; coagulopathy; ovulatory dysfunction; endometrial; iatrogenic; and not yet classified) (Munro et al., 2011).

Endometrial polyp (EP) is one of the most common pathology that is associated with AUB or infertility and may be present in both pre and post-menopausal women (Salim et al., 2011). Endometrial hyperplasia (EH) is the abnormal proliferation of the endometrial glands and stroma and related with risk of increased endometrial carcinoma (Li et al., 2013). Both EP and EH are related with endometrial cancer especially in post-menopausal women (Balik et al., 2013).

In current study, we aimed to evaluate the risk factors for endometrial hyperplasia concomitant endometrial polyp in pre and postmenopausal women.

Materials and Methods

This study was performed according to the standards of Helsinki declaration, and approved by the Ethics Committee of the Institution. In our gynecology clinic, before the hysterectomy operation, the routine preoperative endometrial sampling (ES) has been performing for excluding the probably gynecologic malignancies. The medical records of 2071 patients who underwent hysterectomy operation for benign gynecologic conditions between 2009 and 2014 were evaluated for the study. In 203 of 2071 patients, endometrial polyp was detected in the preoperative pathology examination. These patients with endometrial polyp were enrolled in the study and re-evaluated for the concomitant endometrial hyperplasia in the final pathology examination. ES was performed by sterile carmen cannula injector (Medbar Ltd., Izmir, Turkey) or pipelle (Endocurrette, Midvale, Utah, USA). Clinical data of the patients recorded and evaluated were; age, gravidity, parity, body mass index (BMI), endometrial thickness (ET), menopausal status, presence of adenomyosis and diabetes mellitus and post ES histopathology results.

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Data analyses

The mean and standard deviation (SD) were calculated for continuous variables. Chi-square (χ^2) test and Student's t test evaluated associations between the categorical and continuous variables. Logistic regression method was used to evaluate the risk factors between the groups. Two-sided P values were considered statistically significant at P<0.05. Statistical analyses were carried out by using the statistical packages for SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

EP was obtained in 203 of 2071 patients (9.8%) by the preoperative endometrial sampling. Therefore; the groups were classified according to post-operative histopathological diagnosis (Group 1: patients with EH concomitant EP, n=13 and group 2: patients with EP, n=190). Out of 13 endometrial hyperplasia cases, only in 1 of 13, atypia was detected. 6.4% of the polyps had premalignant lesions. Twelve out of 13 cases had endometrial hyperplasia with no atypia. There were no significant differences between the groups, in terms of gravidity, parity, BMI, obesity, endometrial thickness and adenomyosis (Table 1). The median gravidity of the patients in group 1 and 2 was 5 (range, 2-8) and 4 (range, 0-9), (p=0.052), respectively. The median parity of the patients in group 1 and 2 was 3 (range, 2-5) and 3 (range, 0-6); (p=0.327), respectively. The mean BMI was 30.23±3.95 in group 1 and 30.30±4.23 in group 2 (p=0949). The median ET was 7 mm (5-15) and 7 mm (5-19) in group 1 and 2; respectively (p=0569). There were no significant differences in terms of adenomyosis and obesity (BMI>30) between the groups (p=0.485, p=0.344), respectively. However, a statistically difference was found between groups in terms of morbid obesity (BMI>35) (p=0.017).

Table 1. Demographic And Clinical Parameters in Women with Endometrial Hyperplasia Concomitant Endometrial Polyps

	Polyp and group Endometrial Hyperplasia (n=13) Group 1	Only polyp group (n=190) Group 2	p value
Age (years)	60 (41-69)	49 (40-84)	0.038α
Gravidity	5 (2-8)	4 (0-9)	0.052α
Parity	3 (2-5)	3 (0-6)	0.327[α]
BMI(kg/M2)	30.23±3.95	30.30±4.23	0.949[β]
Obesity			
BMI<30	4 (4.5)	84 (95.5)	0.344[c]
BMI≥30	9 (7.8)	106 (92.2)	
Morbid Obesity			
BMI<35	8 (4.5)	168 (95.5)	0.017[d]
BMI≥35	5 (18.5)	22 (71.5)	
Endometrial thickness (mm)			
	7 (5-15)	7 (5-19)	0.569[α]
Menopause			
Positive (n=102)	10 (9.8)	92 (90.2)	0.047[c]
Negative (n=101)	3 (3.0)	98 (97.0)	
*Adenomyosis			
Positive(n=44)	4 (9.1)	40 (90.9)	0.485[d]
Negative(n=159)	9 (5.7)	150 (94.3)	
DM			
Positive(n=34)	7 (20.6)	27 (79.4)	0.002[d]
Negative(n=169)	6 (36)	163 (96.4)	
HT			
Positive(n=43)	6 (14.0)	37 (86.0)	0.034[d]
Negative(n=160)	7(4.4)	153(95.6)	

Data of variables are expressed as mean±standard deviation (range) or median (min-max) or absolute number and its frequencies .n (%).[α]: Mann Whitney U test. [β]: Student t test.[c]: Chi-square test.[d]: Fischer Exact test *: Pathological diagnosis at the final pathology. DM: Diabetes mellitus. HT: Hypertension

Table 2. Binary Logistic Regression Analysis of Significant Clinical and Pathologic Characteristics in Prediction of Concurrent Endometrial Hyperplasia

	β	SE	Wald	OR	95% CI Upper) (Lower-	P value
DM	-1,645	0.655	6,304	5,183	1.435-18.727	0.012
HT	-1,075	0.688	2,443	2,929	.761-11.270	0.118
Menopause	-1,384	0.725	3,646	3,990	0.964-16.510	0.046
Morbid obesity	-0.817	0.796	1,052	2,263	.475-10.773	0.305

DM: Diabetes mellitus. HT: Hypertension

We found statistically significant differences between two groups in terms of; ages, menopause, DM and HT (p=0.038, p=0.047, p=0.002, p=0034), respectively (Table 1). The median with age of the patients in group 1 was 60 years (range, 41-69 years) and 49 years (range 40-84 years) in group 2 (p<0.05). 9.8% of menopausal women were in Group 1, while 3.0% of the non-menopausal women were in Group 2 (p=0.047). DM and HT were found significantly in higher rate in Group 1 (p=0.002, p=0.034), respectively.

Table 2 summarizes the outcomes of Logistic Regression Models. According to the model DM and menopause were found to be significant risk factor for endometrial hyperplasia concomitant endometrial polyp (p<0.05). The odds ratios (95%CI) found by using Logistic Regression Method were as follows; 5.183 (1.435-18.727), 3.990 (0.964-16.510), respectively.

Discussion

In current study, we evaluated the histopathological results of 203 cases underwent ES before hysterectomy for benign gynecologic conditions. Of all patients; 190 had EP and 13 had EH and EP concomitantly. The demographic and clinical characteristics of the patients showed that age, menopause, morbid obesity, DM and HT were the significant parameters for endometrial hyperplasia concomitant endometrial polyp. We also evaluated the risk factors with logistic regression for the concomitant presence of EP and EH and found that DM and menopause were independent risk factors for this condition.

AUB is one of the most common gynecological

condition that affects all ages of the women (Nicholson et al., 2001). FIGO designed a new classification system for causes of AUB and called as PALM-COEIN (polyp; adenomyosis; leiomyoma; malignancy and hyperplasia; coagulopathy; ovulatory dysfunction; endometrial; iatrogenic; and not yet classified) (Munro et al., 2011).

EP that is generally benign may have base (sessile) or be attached to the uterus by an elongated pedicle. In ultrasound examination, they may be mimic as increased endometrial thickness and especially in postmenopausal women may be misdiagnosed as endometrial cancer (Balik et al., 2013). EH is a clinically important because it may result abnormal uterine bleeding, and can precede, or occur concurrently, with endometrial carcinoma (Kim et al., 2013). Both EP and EH are associated with increased risk of endometrial cancer (Hileeto et al., 2005).

In a study evaluating the presence of premalignant and malignant lesions with EP found that 2.0% of their patients presented premalignant lesions in the polyps, 13 had simple glandular hyperplasia, of which 5 had no atypia, and eight presented with atypia. Eight polyps presented focal area of complex hyperplasia: 4 with atypia and 4 without lesions. In 0.5% of the patients endometrial cancer was found in EP (Lenci et al., 2014). In our study, 13/203 (6.4%) cases with polyps, (twelve with no atypia and 1 with atypia), had premalignant lesions. In another study, postoperative histopathology was more severe than preoperative diagnosis in 5 (6.3%) patients, including 3 preoperative diagnoses of simple hyperplasia without atypia, 1 simple hyperplasia with atypia, and 1 complex hyperplasia without atypia (Kleebkaow et al., 2008). The percentages of premalignant lesions may be seemed difference due to the indefinitive classifications. For example, in a recent study; polyps were classified into benign (endometrial polyps and polyps with nonatypical simple hyperplasia and nonatypical complex hyperplasia), premalignant (polyps with atypical simple hyperplasia or atypical complex hyperplasia), and malignant groups (Costa-Paiva et al., 2011). So; more definitive classifications are needed for the accurately comparisons of the different studies.

Giordano et al. (2007) reported postmenopausal status, hypertension, and obesity as risk factors for the malignant transformation of EP. We did not detect any malignant transformation of EP in our study but we also found that postmenopausal status and obesity were the risk factors for endometrial hyperplasia concomitant endometrial polyp. Drug use; such as; tamoxifen, may also affect endometrial pathologies and increase of the ET and development of the EP (Karimi Zarchi et al., 2009). In our study, there were no women with tamoxifen administration. Therefore, we could not have data about association of tamoxifen used and endometrial polyp.

Acmaz et al. (2014) designed a study and evaluated endometrial precancerous lesions in postmenopausal obese women and found that obesity was higher in EP and EH group in their study. Demographic features and presence of DM and HT were similar between the groups. We also found similar results to this study.

In a recent study, endometrial polyps showed a significantly higher proportion of positive cells in the glands than in the stroma for both estrogen and progesterone receptor (de Carvalho et al., 2011). The molecular differences or variety in the respond of the receptors; may play an important role in the developing of the endometrial pathologies, such as, polyps, hyperplasia or malignancies.

In conclusion, this study shows that; postmenopausal situation and DM may increase premalignant transformation of the endometrial polyps. Therefore, the clinicians have to take care of the evaluation of the postmenopausal diabetic women with endometrial polyp.

References

Acmaz G, Aksoy H, Albayrak E, et al (2014). Evaluation of endometrial precancerous lesions in postmenopausal obese women-a high riskgroup? *Asian Pac J Cancer Prev*, **15**, 195-198.

Balik G, Kagitci M, Ustuner I, et al (2013). Which endometrial pathologies need intraoperative frozen sections? *Asian Pac J Cancer Prev*, **14**, 6121-6125.

Costa-Paiva L, Godoy CE Jr, Antunes A Jr, et al (2011). Risk of malignancy in endometrial polyps in premenopausal andpostmenopausal women according to clinicopathologic characteristics. *Menopause*, **18**, 1278-82.

de Carvalho S, Campaner AB, Lima SM, et al (2011). Differential expression of estrogen and progesterone receptors in endometrial polyps andadjacent endometrium in postmenopausal women. *Anal Quant Cytol Histol*, **33**, 61-67.

Hileeto D, Fadare O, Martel M, et al (2005). Age dependent association of endometrial polyps with increased risk of cancer involvement. *World J Surg Oncol*, **9**, 8.

Giordano G, Gnetti L, Merisio C, et al (2007). Postmenopausal status, hypertension and obesity as risk factors for malignant transformationin endometrial polyps. *Maturitas*, **20**, 190-7.

Karimi Zarchi M, Behtash N, Sekhavat L, et al (2009). Effects of tamoxifen on the cervix and uterus in women with breast cancer: experience with Iranian patients and a literature review. *Asian Pac J Cancer Prev*, **10**, 595-8.

Kim MK, Seong SJ (2013). LNG-IUS treatment of non-atypical endometrial hyperplasia: Can Pipelle endometrial samplingbe an accurate method of follow-up evaluation? *J Gynecol Oncol*, **24**, 103-4.

Kleebkaow P, Maneetab S, Somboonporn W, et al (2008). Preoperative and postoperative agreement of histopathological findings incases of endometrial hyperplasia. *Asian Pac J Cancer Prev*, **9**, 89-91.

Lenci MA, do Nascimento VA, Grandini AB, et al (2014). Premalignant and malignant lesions in endometrial polyps in patients undergoing hysteroscopic polypectomy. *Einstein (Sao Paulo)*, **12**, 16-21.

Li XC, Song WJ (2013). Endometrial intraepithelial neoplasia (EIN) in endometrial biopsy specimens categorized by the1994 World Health Organization classification for endometrial hyperplasia. *Asian Pac J Cancer Prev*, **14**, 5935-9.

Munro MG, Critchley HO, Broder MS, et al (2011). FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. *Int J Gynaecol Obstet*, **113**, 3-13.

Nicholson WK, Ellison SA, Grason H, et al (2001). Patterns of ambulatory care use for gynecologic conditions: A national study. *Am J Obstet Gynecol*, **184**, 523-530

Salim S, Won H, Nesbitt-Hawes E, et al (2011). Diagnosis and management of endometrial polyps: a critical review of the literature. *J Minim Invasive Gynecol*, **18**, 569-81.