

ABNORMAL UTERINE BLEEDING AS A PREDICTOR FOR ENDOMETRIAL ABNORMALITIES, QUICK DIAGNOSIS OF PREMALIGNANT AND MALIGNANT STATES AND THE IMPACT OF VARIOUS RISK FACTORS

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Abstract

Approximately 30% of women will experience abnormal uterine bleeding (AUB) during their lifetime. It is a common medical problem, with a direct influence on women's quality of life, utilization of health care resources, and costs.

The aim of this study was to analyze the histopathological findings of the samples from dilatation and curettage (D&C) in patients with abnormal uterine bleeding and to determine the presence of certain risk factors (age, obesity, hypertension, diabetes, parity) in the examined groups.

This was a prospective study including a total of 77 patients from the Department of Gynecology and Obstetrics in PHI General Hospital Gevgelija, who underwent D&C in 2021. Data were collected through interviews and analysis of findings from histopathological analyses of samples obtained by D&C. The following anamnestic data were analyzed: age, parity, history of hypertension and diabetes. Weight and height were measured in all patients.

The most common pathological change of the endometrium was endometrial polyp. The second most common histopathological diagnosis in premenopausal women was anovulatory bleeding vs. menopausal women who were secondly frequent diagnosed with endometrial hyperplasia. Gynecological cancers were more common in menopausal age. Various anamnestic factors were differently related to various histopathological diagnoses.

All patients that report abnormal uterine bleeding are diagnosed with endometrial abnormalities by TVUS and should undergo D&C for quick diagnosis of premalignant and malignant states of the genital tract. By reducing body weight, regulating hypertension and diabetes, the risk of the most severe pathological diagnosis is reduced.

Keywords: abnormal uterine bleeding, dilatation and curettage, transvaginal ultrasound, risk factors

Introduction

A normal menstrual cycle has a frequency of 24 to 38 days, lasts 7 to 9 days, with 5 to 80 milliliters of blood loss. Variations in any of these 4 parameters constitute abnormal uterine bleeding^[1]. Approximately 30% of women will experience abnormal uterine bleeding (AUB) during their lifetime. It is a common medical problem, with a direct influence on women's quality of life, utilization of health care resources, and costs. AUB in women older

than 40 years and especially in postmenopausal women requires a prompt and efficient evaluation, mainly to exclude the presence of malignant or premalignant lesions of the endometrium^[2]. According to the new nomenclature of FIGO (International Federation of Gynecology and Obstetrics), abnormal uterine bleeding is classified under the acronym PALM-COEIN, which includes structural (PALM) and functional (COEIN) etiological causes of abnormal uterine bleeding^[3]. Endometrial polyps cause abnormal bleeding, usually as a result of vascular fragility, chronic inflammation, or superficial erosions. Bleeding is usually scanty and intermenstrual. Adenomyosis is a disorder characterized by migration of the endometrial glands and stroma in the myometrium. The uterus is generally enlarged and is a very common cause of menorrhagia although the pathogenetic mechanisms are not well understood, yet^[4]. Submucosal and large intramural fibroids are thought to cause stretching of the endometrium. Due to compression and trauma during intracavitary friction, focal chronic inflammation occurs, resulting in bleeding^[5]. Malignancy or hyperplasia is a common cause of vaginal bleeding and it is of particular concern in postmenopausal women. Hyperplasia occurs due to chronic estrogen stimulation. It can be simple or complex with or without atypia. If left untreated, 10-30% of hyperplasia with atypia progresses to adenocarcinoma and is therefore considered a precancerous lesion^[6]. Coagulation or bleeding defects should be considered in adolescents with a short menstrual history who report heavy, regular, cyclical, and long periods^[7]. Ovulatory dysfunction refers to anovulation that results from a number of endocrine disorders that indirectly or directly involve the hypothalamus-pituitary-ovarian axis, thyroid disease, hyperprolactinemia, PCOS, or hypothalamic disorders that can cause systemic or non-systemic disorders^[8]. Endometrial causes refer to chronic endometritis, which occurs postpartum and is usually characterized by heavy menstrual bleeding. It also occurs in patients with subclinical chlamydia infection, pelvic tuberculosis, and pelvic inflammatory disease^[9]. Iatrogenic causes refer to various drugs that predispose to abnormal bleeding, due to the effect on the amount of hormones or interference with hemostasis. These include hormonal contraceptives, postmenopausal hormone-replacement therapy, anticoagulants, and anticonvulsants^[10]. Not classified elsewhere abnormal uterine bleeding usually refers to chronic endometritis or abnormal bleeding due to arteriovenous malformations^[11].

To analyze the histopathological findings of the samples from dilatation and curettage (D&C) in patients with abnormal uterine bleeding and to determine the presence of certain risk factors (age, obesity, hypertension, diabetes, parity) in the examined groups.

Materials and methods

This was a prospective study including a total of 77 patients from the Department of Gynecology and Obstetrics in PHI General Hospital Gevgelija, who underwent D&C in 2021. Informed consent was obtained from every participant in the study. The group A comprised 55 patients in whom D&C was preformed, due to abnormal uterine bleeding, and group B comprised 22 patients in whom D&C was preformed due to endometrial abnormality diagnosed by transvaginal ultrasound. Patients were divided into four subgroups: 27 in group A postmenopausal age and 28 in group A premenopausal age, 14 in group B postmenopausal age and 8 in group B premenopausal age. Data were collected through interviews and analysis of findings from histopathological analyses of samples obtained by D&C. D&C was performed under intravenous anesthesia, taking samples from the endocervix and from the endometrium. Samples were immediately fixed in 10% formalin and sent to a histopathological laboratory. The obtained histopathological findings and their distribution in the four examined groups were analyzed. The following anamnestic data were analyzed: age, parity, history of hypertension and diabetes. Weight and height were measured in all patients. The Body Mass Index (BMI) was calculated according to the following formula: body weight

(kg)/body height (m²)^[12]. Histopathological analyses were performed at the Institute of Pathology at the Faculty of Medicine, Ss. Cyril and Methodius University in Skopje.

Results

The most common pathological change of the endometrium in both groups, A and B, was endometrial polyp, 55.56% and 57.14%, respectively. The frequencies of the histopathological diagnoses are shown in Table 1.

Table 1. Frequencies of the histopathological diagnoses

Histopathological diagnoses	Group A		Group B		TOTAL	
	N	Number of histopathological diagnoses	Number of	histopathological diagnoses		
Anovulatory uterine bleeding	12	22.22%			12	16.00%
Cervical carcinoma	2	3.70%			2	2.67%
Endometrial carcinoma	2	3.70%			2	2.67%
Chronic cervicitis	2	3.70%			2	2.67%
Cervical intraepithelial neoplasia III	1	1.85%			1	1.33%
Hyperplasia simplex	2	3.70%	7	33.33%	9	12.00%
Myoma submucosum	1	1.85%	1	4.76%	2	2.67%
Polypus canalis cervicalis	2	3.70%	1	4.76%	3	4.00%
Polypus endometrii	30	55.56%	12	57.14%	42	56.00%
TOTAL	54	100.00%	21	100.00%	75	100.00%

Cervical and endometrial cancer were diagnosed only in group A, with a representation of 3.70% each. Of all the patients with endometrial polyp, 29 were in menopause and 13 in premenopause. Twenty (75%) of them in menopause and 10 (25%) of them in premenopause had abnormal uterine bleeding, compared to control group B of whom 9 (75%) in menopause and 3 (25%) in premenopause did not have bleeding.

Of all the patients with endometrial polyp, 4 (9.52%) were nulliparous, and 38 (90.48%) had given birth at least once in their life. Three (10%) nulliparous women reported abnormal uterine bleeding, and 1 (8.33%) did not report abnormal uterine bleeding. Parous women who reported uterine bleeding were 27 (90%), and without bleeding 11 (91.67%). There were 4 (9.52%) nulliparous women diagnosed with endometrial polyp, and 38 (90.48%) were parous.

Out of 42 patients with endometrial polyp, 6 (14.29%) had diabetes, and 36 (85.71%) did not have diabetes. Of those with diabetes, 3 (10%) had abnormal uterine bleeding and 3 (25%) did not have. Twenty-two (52.38%) patients had hypertension. Thirteen (43.33%) of them reported abnormal vaginal bleeding, and 9 (75%) of them did not report abnormal vaginal bleeding. Seventeen (23.82%) patients with endometrial polyp with normal body weight reported abnormal uterine bleeding, and 7 (23.87%) were without abnormal uterine bleeding. There were 4 (32.55%) obese patients with endometrial polyp with abnormal uterine bleeding, and 1 (33.30%) was without abnormal uterine bleeding. Overweight patients with endometrial polyp and abnormal uterine bleeding were 9 (26.67%), and without abnormal uterine bleeding were 4 (27.48%). These data are shown in Figures 1 and 2.

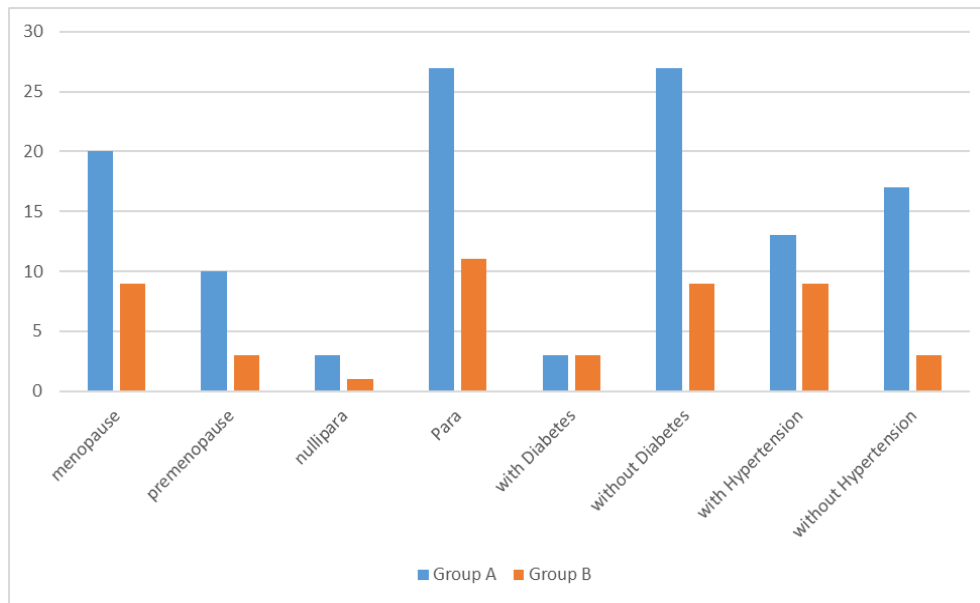


Fig. 1. Menstrual status, parity and presence of additional risk factors in patients from group A and B, with diagnosed endometrial polyp

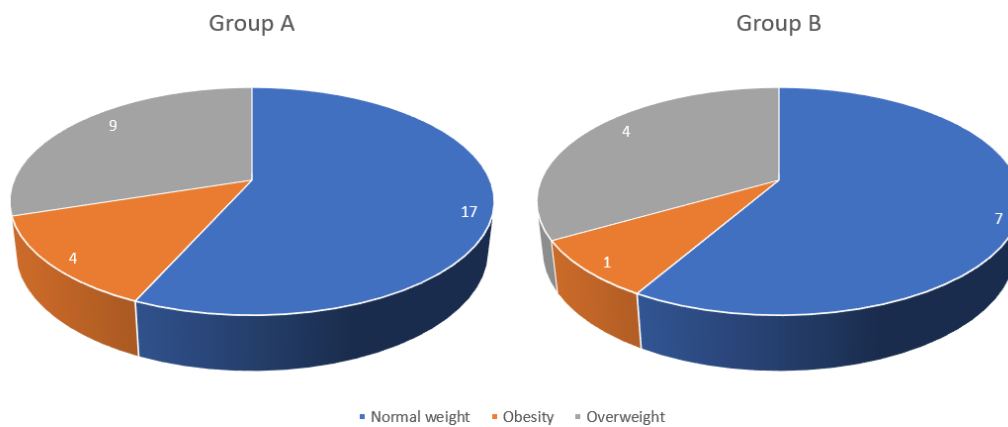


Fig. 2. Body mass index categories of group A and B patients with diagnosed endometrial polyp

There were 12 patients with anovulatory uterine bleeding in group A. None of them had diabetes, 5 (41.67%) had hypertension, and 7 (58.33%) did not have hypertension. Of all the patients with abnormal uterine bleeding, there were 7 (58.33%) with normal body weight, 3 (25%) were overweight, 1 (8.33%) was obese, and 1 (8.33%) was underweight.

In total, there were 9 patients diagnosed with simple hyperplasia of the endometrium. Of them, 4 (44.44%) were in menopause, and 5 (55.56%) were in premenopause. One (25%) patient with simple hyperplasia reported abnormal uterine bleeding and was in menopause, and 3 (75%) patients did not report bleeding. One (20%) premenopausal patient reported abnormal uterine bleeding due to simple endometrial hyperplasia, and 4 (80%) patients did not report abnormal uterine bleeding. Out of 9 patients with simple endometrial hyperplasia, 4 (44.44%) had hypertension, only 1 reported abnormal uterine bleeding (25%), and 3 were asymptomatic (75%). Only 2 patients reported abnormal uterine bleeding due to simple endometrial hyperplasia and they were in the group of overweight patients, while of those who did not report symptoms, 3 (42.86%) had normal body weight, 2 (28.57%) were in the group with preobesity, 1 (14.28%) was obese and 1 (14.28%) was underweight.

Cervical cancer patients had a normal BMI; all had given birth, all had hypertension, 50% had diabetes and all were in menopause.

The mean BMI of patients with endometrial cancer was 28.75; they all had given birth, 50% had diabetes and hypertension and all were in menopause.

Discussion

Abnormal uterine bleeding is one of the most common gynecological problems, which can occur at any age. Endometrial polyps are the most common abnormalities and their frequency increases with age^[12,13]. In our study, they were most commonly diagnosed in menopausal women. However, abnormal uterine bleeding is not a specific symptom of an endometrial polyp. Parity is not associated with abnormal uterine bleeding due to an endometrial polyp, but it is associated with endometrial polyps. Nevertheless, patients who have given birth are more likely to be diagnosed with an endometrial polyp during their lifetime compared to nulliparous women.

Diabetes and hypertension are not associated with endometrial polyps and abnormal uterine bleeding due to endometrial polyps. In obese patients with a higher BMI, endometrial polyps are more common, but the abnormal uterine bleeding due to endometrial polyp is not associated with obesity. The average BMI value in both groups, A and B, was 25.8, which means that most of the patients diagnosed with endometrial polyp were included in the group of obese women. Obesity is an independent risk factor for the development of endometrial polyps^[14,15].

Anovulatory bleeding is the result of estrogen withdrawal, which occurs due to a decrease of estrogen levels as a result of follicular cohort regression. Anovulatory bleeding is a very common cause of bleeding in adolescent and perimenopausal women, but it does not spare the women of reproductive age^[16,17]. Chung *et al.* (2021) claimed that hypertension may be associated with subsequent risk of irregular uterine bleeding. According to our findings, hypertension was not associated with abnormal anovulatory uterine bleeding and it occurred more often in patients with normal body weight^[18].

Endometrial hyperplasia occurs due to prolonged exposure to unopposed estrogen and is a premalignant condition that can lead to the development of endometrial cancer. It is not well known how long it takes for a cancer to develop, but a study by Lacey *et al.* found an average time of 6 years for cancer to develop, in all types of hyperplasia^[19]. The most common symptom of endometrial hyperplasia is abnormal uterine bleeding, but according to our study menopausal and premenopausal patients with simple endometrial hyperplasia were usually asymptomatic and did not report abnormal uterine bleeding. Hypertension is not associated with simple hyperplasia of the endometrium and most often patients are asymptomatic, i.e., they do not report abnormal uterine bleeding. The mean value of BMI in patients diagnosed with endometrial hyperplasia was 24.46 and most of them had a normal body weight. However, there are a lot of studies proving the positive correlation between BMI higher than 30 and endometrial thickness^[20].

Cervical carcinoma is probably not related to obesity, hypertension and diabetes, although it is more often encountered in women who have given birth and are in menopause. High parity is positively associated with cervical cancer and its incidence rises with the age and the duration of menopause^[21].

Endometrial cancer is also associated with excessive estrogen exposure, high blood pressure, and diabetes^[22]. In our study, the mean BMI of patients diagnosed with endometrial cancer was 28.4; half of them had diabetes and hypertension and all of them were in menopause and had given births.

Conclusion

All patients that report abnormal uterine bleeding or are diagnosed with endometrial abnormalities by TVUS should undergo D&C for quick diagnosis of premalignant and

malignant states of the genital tract. Particular importance is given to patients in postmenopausal age when no bleeding should occur and when organic causes of abnormal bleeding are more common, especially cancer as the most severe pathology. By reducing body weight, regulating hypertension and diabetes, the risk of the most severe pathological diagnosis is reduced.

Conflict of interest statement. None declared.

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