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Risk Factors for Abnormal Uterine Bleeding in Women in Perimenopause

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As in all medical practice, the diagnosis of AMC begins with a thorough medical history and physical examination, followed by appropriate laboratory tests and instrumental methods. Diagnosis of abnormal uterine bleeding. General assessment: anamnesis and assessment of the nature of bleeding; physical examination, pelvic examination, and examination using mirrors [1,16,18,23,35,40].

Laboratory tests:

- clinical blood analysis, biochemical analysis (iron content), β-chCG (human chorionic gonadotropin);
- hormonal examination (FSH, LH, anti-Müllerian hormone, estradiol, progesterone), thyroid hormones and prolactin (upon indication);
- concentration of oncomarkers (CA125, HE4, ROMA) in ovarian formations;
- cytological examination of smears from the cervix (RAR smear);
- blood coagulation system examination.

Transvaginal ultrasound examination of pelvic organs: measuring uterine and ovarian dimensions, endometrial thickness:

- color Doppler mapping (according to indications);
- sonohistherography;

Magnetic resonance imaging of pelvic organs (as indicated).

Special studies: endometrial office biopsy and histological examination; endometrial pipette biopsy and histological examination; hysteroscopy and separate diagnostic scraping of the endometrium and cervix with histological examination of the material [2,9,19,27,32,41].

Family history should be included, taking into account the main disorders of the hemostasis system, the use of medicinal or herbal preparations that can provoke bleeding, such as contraceptives, menopausal hormone therapy (MGT), non-steroidal

anti-inflammatory drugs (NSAIDs), warfarin, heparin and their derivatives, ginseng, ginkgo, and arsenic [5, 6]. Physical examination data include symptoms indicating anemia (shortness of breath during physical exertion, dizziness), respiratory rate indicators, heart rate, blood pressure, assessment of body mass index, examination of skin (paleness, hemorrhages, stripes, petechiae), thyroid examination. Gynecological examination: examination using mirrors to differentiate bleeding from the vagina or cervix, bimanual examination of pelvic organs, including the size and contours of the uterus and its appendages [3,10,17,25,34,42].

Laboratory evaluation should include clinical blood analysis and iron testing, as well as a test to detect hemostasis system disorders if they are suspected or indicated. Pregnancy tests and thyroid screening can also be indicated.

Although many women cannot be sure how often and for how long they continue to bleed, it is important to carefully collect the anamnesis of the nature of the bleeding, its frequency and severity to make a diagnosis. For example, cyclic MMCs without MMCs are unlikely to be a consequence of carcinoma or even hyperplasia. The most common cause of irregular bleeding is anovulatory uterine bleeding. Most often, anovulatory bleeding is not associated with anatomical anomalies. In a study involving 443 women who underwent transvaginal ultrasound and sonohisteriography with sodium chloride isotonic solution (SIC) infusion at the first stage of diagnosis, it was reported that 79% of women aged 35 and before menopause with AMC had no anatomical pathology [4,11,20,26,31,39]. In most women with AMC, uterine enlargement and enlargement are observed due to childbirth, the presence of leiomyoma without submucosal growth, or adenomyosis without endometrial abnormalities. Patients with anovulatory bleeding often have endometrial pathology, and therefore, a thorough assessment of endometrial condition is of great importance at the first stage of diagnosis to identify groups with focal or disseminated pathological processes. Historically, dilatation of the cervical canal and scraping of the uterine cavity walls were the primary diagnostic methods for endometrial condition. In fact, this was the most common surgical procedure for women throughout most of the 20th century [5,12,15,28,33,38]. Dilation and separate diagnostic scraping (SDS) are no

longer the standard for initial endometrial assessment. This is a "blind" procedure with a high risk of complications.

Disadvantages of blind endometrial biopsy

After the publication of the research by T. Stovall et al. [8] Endometrial "blind" biopsy using disposable absorbing piston devices has become a standard approach in patients with AMC. T. Stovall performed an outpatient biopsy on 40 patients with carcinoma a week before the hysterectomy. Endometrial carcinoma was confirmed in 39 samples out of 40, which indicates a 97.5% accuracy of the method, and therefore, blind endometrial biopsy quickly became the "gold standard." In a similar study, R. Guido et al. [9] performed a "blind" endometrial biopsy on 65 patients with carcinoma in the operating room immediately before the hysterectomy. In 11 out of 65 cases, malignant tumors were missed (sensitivity only 83%), but after surgery, the authors reported that in cases where cancer occupied more than 50% of the endometrial surface, biopsy accuracy was 100%. Similar research has been conducted by other authors. In women with pre-diagnosed carcinoma, the sensitivity of a "blind" biopsy was only 84% [10, 11], resulting in false negative results of 16 and 32%, respectively [6,13,21,24,30,37]. These studies were conducted using the "blind" biopsy method in women with confirmed carcinoma. To understand why these biopsies are ineffective in uncommon pathologies, it is sufficient to familiarize yourself with the prehysterectomy study by M. Rodriguez et al. [12], where the biopsy device covered an average of 4% of the endometrial surface area (range 0 - 12%).

If abnormal uterine bleeding occurs in patients with ovulatory cycles, progesterone secretion is prolonged; irregular endometrial rejection occurs, likely due to estrogen levels remaining low, close to the threshold level (as in menstrual bleeding). In women with obesity, with high estrogen levels, ovulatory AMC may occur, leading to amenorrhea, alternating with irregular or prolonged bleeding [7,8,14,22,29,36].

The purpose of this study was to study the factors influencing AMC in premenopausal women. Between April 2022 and July 2024, 120 women in premenopause with AMC were included in the observation group, who were diagnosed and treated in the gynecology department of the Urgench branch of the Republican

Specialized Scientific and Practical Medical Center for Emergency Medical Care (RSNPMCEMC). As a control group, women who underwent a planned medical examination in the same department were selected. Indicators such as age, height, and body weight were assessed, according to which the body mass index (BMI) was calculated, menarche age, somatic health, and indicators of laboratory and ultrasound examination of the pelvic organs (OMT). We also assessed the options for prescribed hemostasis, the duration of bleeding and the effectiveness of the treatment, and the length of hospital stay.

Statistical processing of the research results and data visualization were carried out using pandas, numpy, scipy libraries. For quantitative data, a test was conducted for the correspondence of the distribution to the normal (Shapiro-Wilk criterion was used). For normally distributed data, the mean values (M) and standard deviations (SD) were calculated, and the result was presented as M±SD. The comparison of the mean values was carried out using the two-way Student's t-test. For nominal data, absolute frequencies and relative percentages (%) are indicated. To compare categorical data, Fisher's accurate criterion was used, and to assess the size of the observed difference effect, the odds ratio (OR) and its 95% confidence interval (95% CI) were calculated. Differences were considered statistically significant at a level of $p=0.05$.

Excessive menstrual bleeding has been most frequently diagnosed, which negatively affects the physical, emotional, social, and material well-being of women and significantly reduces their quality of life [1,3]. AMC can be acute or chronic, recurring for 3 or more months, often associated with the development of latent iron deficiency or iron deficiency anemia (IDA) [3, 4]. However, about half of women with OMC consider them normal and do not consult a gynecologist with this problem, and most of them are forced to change their lifestyle during this period. All this indicates insufficient attention to the OMC problem from both women and outpatient physicians. Moreover, for a long time, there was no clear nomenclature of AMCs, nor was there a standardized approach to the examination and treatment of women with these disorders. When analyzing the medical histories, special attention was paid to the patient's body weight, considering that obesity and its role in the development of

metabolic syndrome and gynecological pathology are of great importance. Of the 120 women with uterine bleeding, 44.7% had a normal BMI, excess weight was observed in 28.8 patients, obesity - in 26.5% of cases, that is, in 73.5% of women, BMI did not exceed 30 kg/m2. Some authors indicate a high frequency of obesity in women with uterine bleeding in premenopause - up to 73.2% [1,3]. With age, there is an increase in the frequency of obesity and a decrease in normal body weight in patients with AMC.

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