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Risk Factors for the Development of Endometrial Hyperplastic Processes in Women of Late Reproductive Age

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Annotation: Resume. The aim of the study is to determine the risk factors for the development of hyperplastic complications in early reproductive age.

Materials and research methods. To achieve the set goals and objectives, a prospective study was organized, within the framework of which the effectiveness of treatment in 120 women of reproductive age from 30 to 45 years was analyzed. Group 1 included 64 patients from 30 to 45 years with uterine myoma and endometrial hyperplasia. Group 2 consisted of 56 patients from 30 to 45 years with endometrial hyperplasia without uterine myoma.

Conclusion. Despite the successes achieved in the study of the etiopathogenesis, new methods of diagnostics and therapy of GPE, the problem of treating patients with this pathology remains far from being solved. All this dictates the need to optimize the tactics of managing patients with GPE in primary care, which should be aimed not only at creating adequate comprehensive approaches to predicting the development and recurrence of GE, but also developing unified protocols for managing patients with this pathology.

Keywords: hyperestrogenism, proliferation, apoptosis.

Relevance. Endometrial hyperplasia (EH) is a benign pathological process of the uterine mucosa, characterized by proliferation (growth) of glands and an increase in the glandular-stromal ratio (ratio of glandular and stromal cells). The main characteristic feature of the disease is the proliferation of the inner layer of the uterus - the endometrium, leading to thickening and an increase in its volume.

Hyperplastic processes of the endometrium still represent enormous scientific, medical and social significance in terms of frequency of occurrence, disorders of the reproductive system functions and lack of adequate treatment methods [1,2,3]. Abnormal uterine bleeding, which is the most frequent clinical manifestation of endometrial hyperplasia, is the most frequent reason for visiting a gynecologist and is the second most common gynecological problem associated with the referral of a woman for hospitalization [4,5]. The issues of treating patients with endometrial hyperplasia cover a wide range of conservative and surgical methods. However, young women who want to preserve their reproductive function (in the absence of cellular atypia) should consider conservative therapy, among which hormonal therapy occupies a leading place. In this regard, hormonal effects on hyperplastic endometrium have not lost their clinical significance. Endometrial hyperplasia is known to be a consequence of absolute or relative hyperestrogenism and progesterone deficiency, which leads to excessive (uncontrolled) cell division and decreased apoptosis [6,7].

The classical therapy for endometrial hyperplasia (EH) is the administration of progestins to counteract the estrogenic effect. Progesterone has an antiproliferative effect on the mitotic activity of endometrial cells. Progestins reduce the number of estrogen receptors and accelerate their catabolism by stimulating 17-beta-hydroxysteroid dehydrogenase and sulfotransferase, and thus reduce the dominance of estrogens in the hormonal background, leading to endometrial hyperplasia [8].

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At present, based on the analysis of the work of gynecological hospitals, it is important to develop the basis for determining the medical strategy for the treatment of GE in relation to the choice of a conservative method of treating women of reproductive age. In this direction, it seems promising to take into account psychosomatic disorders, the frequency of which ranges from 30% to 57% of the total number of women seeking antenatal care [10,11]. Hyperplastic processes in the endometrium are a large group of histological changes in the glands and stroma of the endometrium, which are the basis for the formation of neoplastic processes in the uterus. One of the most significant factors directly associated with the risk of developing this pathology is the perimenopausal period, when the frequency of hormone-dependent pathology increases. Hyperplastic processes in the endometrium are one of the most common causes of uterine bleeding and hospitalization. The question of the risk of developing malignant transformation of GE remains open [1,2]. According to domestic and foreign studies, the degree of risk of malignancy of various variants of GPE is determined by the morphological state of the endometrium and depends, first of all, on the severity of cellular atypia and, to a lesser extent, on age, the state of the ovaries, concomitant endocrine diseases, and other factors [4]. It has been proven that histopathological and molecular changes reflect the possible risk of transition of GPE to EC.

The complexity of the etiopathogenesis of GPE creates significant difficulties in choosing treatment methods. This can explain the lack of uniform recommendations for the choice of a drug, dose and optimal duration of its use, which is often inadequate, and therefore, we have to deal with relapses of GPE [5]. Recurrent uterine bleeding, oncological alertness in long-term proliferative processes against the background of concomitant pathology, dictate the need to use more active tactics for managing this contingent of patients [6]. Thus, despite the successes achieved in the study of the etiopathogenesis, new methods of diagnosis and therapy of GPE, the problem of treating patients with this pathology remains far from being solved. All this dictates the need to optimize the tactics of managing patients with GPE in primary care, which should be aimed not only at creating adequate comprehensive approaches to predicting the development and recurrence of GPE, but also developing uniform protocols for managing patients with this pathology.

The aim of the studywas the definition of risk factors for the development of hyperplastic complications in early reproductive age.

Materials and research methods. To achieve the set goals and objectives, a prospective study was organized, within the framework of which the effectiveness of treatment in 120 women of reproductive age from 30 to 45 years was analyzed.

Group 1included 64 patients aged 30 to 45 years with uterine myoma and endometrial hyperplasia. In patients of this group, despite the presence of uterine myoma, the development of endometrial hyperplasia is not directly related to the presence of myoma.

Group 2consisted of 56 patients aged 30 to 45 years with endometrial hyperplasia without uterine myoma. In these patients, the absence of myoma allowed us to evaluate hyperplastic processes in the endometrium without the influence of this factor.

Control groupincluded 20 healthy women aged 30 to 45 years, in whom ultrasound examination did not reveal hyperplastic processes or organic changes in the endometrium, such as uterine myoma, polyps or adenomyosis. These women served as a control group for comparison with patients in the first two groups in order to identify characteristic changes associated with endometrial pathology (Table 1).

The study was conducted at the Tashkent City Hospital No. 4 in the gynecology department from 2021 to 2023. Before starting the treatment course, all participants were carefully assessed for clinical manifestations of the disease, and their hormonal status was analyzed. In particular, the levels of

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hormones such as estradiol, progesterone, lutropin (LH), follitropin (FSH) and prolactin in the blood serum were measured.

The following inclusion criteria were taken into account when hospitalizing women to participate in the study:

- Absence of oncological diseases according to the initial examination results.
- The absence of endocrine pathology, including diabetes mellitus, hypo- and hyperthyroidism, obesity, which allows us to exclude the influence of these conditions on the hormonal background and treatment results.
- Age from 30 to 45 years, corresponding to the late reproductive period.
- The absence of acute inflammatory processes in the pelvic organs ensures the absence of external inflammatory effects on the results of the study.
- Informed voluntary consent to participate in the study and to undergo all necessary medical and diagnostic procedures, guaranteeing the legal and ethical correctness of the study.

These criteria ensure the reliability and objectivity of the data obtained, eliminating possible distortion of the results.

Table 1. Distribution of patients by age (n=120)

Age	30-35 years old	36-40 years old	41-45 years old	Total
Group 1	16 (25%)	22 (34.4%)	26 (40.6%)	64 (100%)
Group 2	11 (19.6%)	20 (35.7%)	25 (44.7%)	56 (100%)
Control group	6 (30%)	8 (40%)	6 (30%)	20 (100%)

In Group 1, there were 16 patients (25%) in the 30-35 age range, 22 patients (34.4%) in the 36-40 age range, and 26 patients (40.6%) in the 41-45 age range. In Group 2, there were 11 patients (19.6%) in the 30-35 age category, 20 patients (35.7%) in the 36-40 age category, and 25 patients (44.7%) in the 41-45 age category. In the control group, there were 6 patients (30%) in the 30-35 age range, 8 patients (40%) in the 36-40 age range, and 6 patients (30%) in the 41-45 age range.

The majority of patients in both groups lived in urban areas: 65.6% in group 1 and 67.9% in group 2. Rural residence was less common, accounting for 34.4% in group 1 and 32.1% in group 2.

In both groups, the largest percentage is made up of working women: 50.0% in Group 1 and 50.0% in Group 2. Housewives make up 31.3% in Group 1 and 32.1% in Group 2. Female students are a minority, making up 18.8% in Group 1 and 17.9% in Group 2.

Table 2 shows the main reasons for hospitalization of patients included in the study.

Table 2. Main indications for hospitalization of patients included in the study (n=120)

Indications for hospitalization	1 group (n=64)	%	Group 2 (n=56)	%	r
Uterine bleeding	50	78.1	42	75.0	>0.05
Endometrial changes according to ultrasound data	14	21.9	14	25.0	>0.05

In the main group, consisting of 64 patients, uterine bleeding was observed in 50 women (78.1%), and endometrial changes according to ultrasound data were observed in 14 patients (21.9%). In the comparison group, which included 56 patients, uterine bleeding was recorded in 42 women (75.0%), and endometrial changes were observed in 14 patients (25.0%). The differences between the groups were not statistically significant (p> 0.05).

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According to the study data, patients in Group 1, which included women with uterine myoma, more often complained of heavy (62.5%) and prolonged (50.0%) menstruation, which was also often irregular (46.9%). A significant number of women in this group had a combination of two or more complaints, indicating more pronounced clinical manifestations of the disease. The duration of clinical symptoms in patients in Group 1 ranged from 1 to 6 years, which is logical, given the presence of uterine myoma, which is often accompanied by such symptoms.

In group 2, which included women without uterine myoma, menstrual cycle disorders such as menorrhagia were observed in 23.2% of cases, and metrorrhagia in 51.8% of cases, while menstruation remained irregular in 21.4% of patients. The duration of the disease in women from group 2 ranged from 2 months to 1 year. A combination of two or more complaints was observed in 25.0% of women in group 2, indicating less pronounced, but still significant clinical manifestations (Table 3).

Table 3. Main complaints of the examined patients (n=120)

Complaints	Main group (n=64)	%	Comparison group (n=56)	%	r
Heavy menstruation	40	62.5	29	51.8	>0.05
Long periods	32	50.0	13	23.2	<0.05
Irregularity of menstruation	30	46.9	12	21.4	<0.05
General weakness, increased fatigue	12	18.8	10	17.9	>0.05
Acyclic bleeding	6	9.4	5	8.9	>0.05
Bloody discharge after and/or before menstruation	3	4.7	4	7.1	>0.05
No complaints were filed	9	14.1	12	21.4	>0.05

Thus, it should be noted that patients in group 1 with uterine myoma had earlier and more pronounced clinical symptoms of the disease compared to group 2.

During the analysis of the family history of the study participants, it was found that in close relatives of women from the second group, where uterine fibroids were not observed, 47.1% of cases were benign tumors and tumor-like diseases of the reproductive organs, including their combinations. In the first group, where the participants suffered from uterine fibroids, such diseases were much less common - only in 22.8% of cases ($p<0.0001$).

Regarding malignant diseases of the reproductive organs, they were registered in 8.7% of cases among relatives of women from the second group, while among relatives of the first group this figure was 7.6%, and no statistically significant differences were observed ($p>0.05$).

These results indicate that women in the first group, where uterine fibroids were more common, had a lower risk of developing malignant neoplasms, in contrast to the second group, where fibroids were absent, but family history showed an increased risk of both benign and malignant diseases (Table 4).

Table 4. Hereditary burden of the examined women (n=120)

Hereditary factors	Group 1 (n=64)	%	Group 2 (n=56)	%
Benign diseases of the reproductive system (isolated or in combination):				
- Uterine fibroids	30	46.9	13	23.2
- Endometrial hyperplasia	12	18.8	10	17.9
- Adenomyosis	9	14.1	5	8.9
- Dyshormonal pathology of the	11	17.2	8	14.3

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mammary glands				
Malignant diseases of the reproductive system:				
- Endometrial cancer	4	6.3	4	7.1
- Cervical cancer	2	3.1	1	1.8
- Ovarian cancer	1	1.6	1	1.8
- Breast cancer	2	3.1	2	3.6
- Others	2	3.1	2	3.6

Table 4 shows the distribution of hereditary burden among the examined women in group 1 (with uterine myoma) and group 2 (without uterine myoma). In group 1, benign diseases such as uterine myoma (46.9%) and endometrial hyperplasia (18.8%) were more common, which is logical for this category of patients. In group 2, where there was no myoma, benign pathologies were also noted, but with a lower frequency. Malignant diseases such as endometrial cancer and breast cancer were observed in both groups with comparable frequency.

Table 5. Structure of the main extragenital diseases in the examined women (n=120)

Extragenital diseases	Group 1 (n=64)	%	Group 2 (n=56)	%
Diseases of the gastrointestinal tract and hepatobiliary complex	43	67.2	19	33.9
Cardiovascular diseases	35	54.7	20	35.7
Obesity I-II degree	32	50.0	17	30.4
Chronic inflammatory diseases of the upper respiratory tract	15	23.4	9	16.1
Urinary tract infections	13	20.3	10	17.9
Functional disorders of the nervous system	11	17.2	12	21.4
Dyshormonal pathology of mammary glands	15	23.4	12	21.4

The analysis showed that childhood infectious and inflammatory diseases such as chickenpox, scarlet fever, measles and rubella were common among participants in both study groups. The results showed no statistically significant effect of these childhood diseases on the development of endometrial hyperplastic processes in women in Group 1 with uterine myoma and Group 2 without myoma ($p>0.05$).

The presence of extragenital diseases in women was also studied. In the first group, 80.9% of women had two or more extragenital diseases, which was higher than 77.4% in the second group. Among the most common diseases in women in the first group, gastrointestinal tract and hepatobiliary system diseases were identified: chronic gastritis in 26.6% of patients, cholecystitis in 18.9%, peptic ulcer in 7.4%, and spastic enterocolitis in 15.8%. In the second group, these diseases were less common, occurring in 33.7% of participants, with chronic gastritis in 19.7%, spastic colitis in 4.7%, and cholecystitis in 14.2%.

Cardiovascular diseases were also observed more frequently in women with uterine fibroids in the first group (54.5%) compared to the second group (35.7%), with conditions such as vegetative-vascular dystonia, hypertension, coronary heart disease, angina pectoris and varicose veins of the lower extremities, and the differences were statistically significant ($p<0.001$).

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