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FREQUENCY AND CLINICAL AND ANAMNESTIC FEATURES OF PATIENTS WITH ADENOMYOSIS

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A comprehensive clinical, laboratory, and instrumental prospective examination of 224 female patients aged 30 to 50 years (mean age, 42.0 ± 1.8 years) with adenomyosis was performed. These patients constituted the main examination group. The patients of the main group were divided into 2 subgroups depending on the form of adenomyosis (group 1 – diffuse form (106 women), group 2 – nodular form (118 women)). The control group consisted of 84 women of relatively healthy reproductive age, with regular ovulatory menstrual cycle and no history of gynecologic diseases. Cohort examinations were prospective in nature. Inclusion criteria for the study: patients diagnosed with adenomyosis; age – from 30 to 50 years; obtaining written consent of the patient to participate in the examinations. Exclusion criteria: detection of malignant pathological process in the organs of the reproductive system or other localization; presence of hormone-synthesizing ovarian tumors; pregnancy and lactation; patients younger than 30 years and older than 50 years; refusal to participate in the study.

Keywords: adenomyosis, diagnosis, hysterectomy, uterus, differential diagnosis.

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ЧАСТОТА І КЛІНІКО-АНАМНЕСТИЧНІ ОСОБЛИВОСТІ ПАЦІЄНТОК З АДЕНОМІОЗОМ

Проведено комплексне клініко-лабораторне та інструментальне проспективне обстеження 224 пацієнток віком від 30 до 50 років (середній вік – $42,0 \pm 1,8$ років) з аденоміозом. Ці пацієнтки становили основну групу обстеження. Хворі основної групи були поділені на 2 підгрупи залежно від форми аденоміозу (1 група – дифузна форма (106 жінок), 2 група – вузлова форма (118 жінок)). Групу контролю склали 84 відносно здорових жінки репродуктивного віку, з регулярним овуляторним менструальним циклом та без гінекологічних захворювань в анамнезі. Когортні обстеження мають проспективний характер. Критерії включення у дослідження: пацієнтки з діагнозом аденоміоз; вік – від 30 до 50 років; отримання письмової згоди пацієнта щодо участі в обстеженнях. Критерії виключення із дослідження: виявлення злоякісного патологічного процесу в органах репродуктивної системи чи іншої локалізації; наявність гормонсинтезуючих пухлин яєчників; вагітність та лактація; пацієнтки віком до 30 років і старше 50 років; відмова від участі у дослідженні.

Ключові слова: аденоміоз, діагностика, гістеректомія, матка, диференційна діагностика.

The presence of endometrial-like epithelial and stromal tissue in the myometrium and enlargement of the uterus are signs of a benign condition known as uterine adenomyosis [3, 5]. In modern gynecology, adenomyosis (AM) ranks third after uterine fibroids and inflammatory diseases and is one of the most common problems [1, 2]. Its prevalence is about 1 %, and the frequency of occurrence is 29 cases per 10,000 person-years [6]. Adenomyosis, like endometriosis and leiomyoma, is most often diagnosed in 7.4–53 % of women aged 41–45 years [3, 4, 5, 7]. First of all, the variety of criteria used to diagnose adenomyosis is responsible for a wide range of differences in the frequency of occurrence [9, 10]. In addition to the fact that the disease is very common, the study of adenomyosis is of great importance due to its complexity and variety of clinical manifestations. Most women suffering from pelvic pain suffer from persistent menstrual disorders such as menometrorrhagia and/or dysmenorrhea, or reproductive functions such as infertility or miscarriage. They also undergo a variety of diagnostic procedures, surgical interventions and long courses of medication and physiotherapy procedures that do not always work [12, 13]. Severe menstrual bleeding and dysmenorrhea are signs of adenomyosis, which often indicate hysterectomy in women of late reproductive age.

Currently, this problem remains relevant, despite some successes in the study of individual elements of the pathogenesis, diagnosis and treatment of various types of adenomyosis. Not only obstetricians and gynecologists, but also doctors of other specialties are paying increasing attention to adenomyosis. International experts agree that adenomyosis is a poorly understood disease, since the etiology and pathogenesis of the disease are still unknown [15]. Despite numerous proposed theories, including Muller residues, stem cell metaplasia, genetic mutations, and endometrial invagination into the myometrium, the exact cause of adenomyosis and its effect on reproductive function is still unknown [8, 11]. Along with this, there is very little data on the analysis of gynecological morbidity and extragenital pathology in patients with adenomyosis.

The purpose of the study was to establish the incidence and clinical and anamnestic characteristics of patients with adenomyosis.

Materials and methods of research. A comprehensive clinical, laboratory and instrumental prospective examination of 224 patients aged 30 to 50 years (average age – 42.0 ± 1.8 years) with adenomyosis was performed. These patients made up the main examination group. The patients of the main group were

divided into 2 subgroups depending on the form of adenomyosis (group 1 – diffuse form - 106 women, group 2 – nodular form – 118 women). The control group consisted of relatively healthy 84 women of reproductive age, with a regular ovulatory menstrual cycle and without a history of gynecological diseases. Cohort surveys are promising. Criteria for inclusion in the study: patients diagnosed with adenomyosis; age of patients from 30 to 50 years; obtaining written consent of the patient to participate in examinations. Exclusion criteria from the study: detection of a malignant pathological process in the organs of the reproductive system or other localization; the presence of hormone-synthesizing ovarian tumors; pregnancy and lactation; patients younger than 30 years and older than 50 years; refusal to participate in the study.

The clinical characteristics of the examined women were based on the study of complaints, obstetric-gynecological and somatic anamnesis. The data of general and gynecological anamnesis, peculiarities of menstrual function were studied in all patients. Special attention was paid to the inflammatory diseases of the genital organs, spontaneous abortions in the anamnesis, premature pregnancies, antenatal fetal death, the course of pregnancy, as well as their results. The statistical significance of the differences was calculated on a personal computer using Microsoft Office Excel software applications, using the Student's t-test and the nonparametric Wilcoxon-Mann-Whitney U-test based on modern recommendations [14]. The statistical difference was considered significant at a value of $p < 0.05$.

Results of the study and their discussion. As a result of the analysis, it was found that during the observation period from 2020 to 2022 in Baku, the prevalence of adenomyosis (AM) was 12.0 % (Fig. 1.).

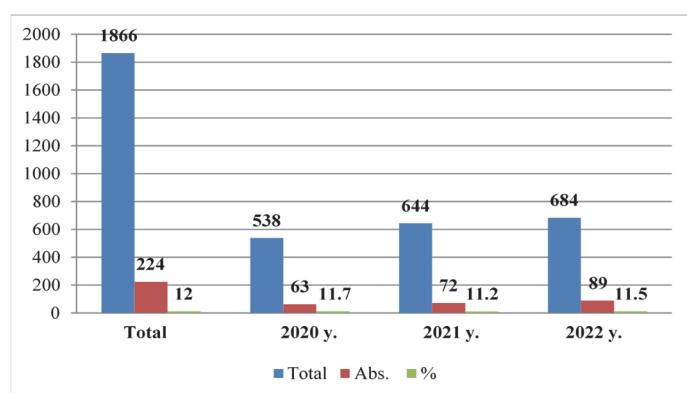


Fig.1. Indices of adenomyosis incidence in women of reproductive age in Baku (2020–2022)

A total of 1,866 women of reproductive age aged 30 to 50 years (mean age – 42.0 ± 1.8 years) were examined during this period and 224 patients with uterine adenomyosis were identified. If in 2020 63 women (11.7 %) with AM were identified in Baku during the examination of 538 patients, then in 2021 72 (11.2 %) patients with AM were identified in Baku during the examination of 644 women. In 2022, the number of identified women with AM increased slightly compared to 2020 and amounted to 79 cases (11.5 %) when 684 women were examined. When studying the analysis of gynecological morbidity and

extragenital pathology in the examined patients, it was found that gynecological diseases in the anamnesis were observed in all examined women with various forms of adenomyosis. The distribution of gynecological morbidity by nosology is shown in Table 1.

Table 1

Gynecological diseases in the anamnesis in patients with adenomyosis

Indices	Group 1 (n=106)		Group 2 (n=118)		Total (n=224)		Control group (n=84)		χ^2 1-2	p
	Abs.	%	Abs.	%	Abs.	%	Abs.	%		
Pathology of the cervix	58	54.71 ± 4.8	56	47.45 ± 4.6	114	50.89 ± 3.3	-	-	1.18	0.2779
Uterine fibroids	60	56.60 ± 4.8	53	44.93 ± 4.6	113	50.45 ± 3.4	-	-	3.05	0.0806
PID	47	44.33 ± 4.8	66	55.13 ± 4.6	113	50.45 ± 3.4	6	7.1 ± 2.8	3.00	0.0832
PCOS	39	36.79 ± 4.6	34	28.81 ± 4.2	73	32.58 ± 3.1	2	2.38	1.62	0.2033
External genital endometriosis	37	34.9 ± 4.6	33	27.9 ± 4.1	70	31.25 ± 3.1	-	-	1.25	0.2632
Bacterial vaginosis	32	31.94 ± 4.5	32	27.1 ± 4.1	64	28.57 ± 3.0	-	-	0.26	0.6116
Vaginitis	28	26.4 ± 4.3	28	23.7 ± 3.9	56	25.27 ± 2.8	-	-	0.21	0.6430
Tumor-like formations (cysts) ovaries	18	16.24 ± 3.6	12	10.16 ± 2.8	30	13.39 ± 2.3	2	2.38	2.23	0.1350
Prolapse of the walls of the vagina and uterus	9	8.49 ± 2.7	8	6.78 ± 3.3	17	7.58 ± 1.8	-	-	0.23	0.6293
Chronic inflammatory diseases of the uterine appendages	14	13.20 ± 3.3	7	5.93 ± 2.1	21	9.37 ± 4.0	-	-	3.48	0.0622
Genitourinary infections	24	22.64 ± 4.1	21	17.79 ± 3.5	45	20.08 ± 2.6	9	10.7 ± 3.4	0.82	0.3662

These data show that patients with various forms of the disease had the most common pathology of the cervix – 50.89 ± 3.3 % (114 women), uterine fibroids – 50.45 ± 3.4 % (113 women) and pelvic inflammatory diseases (PID)- 50.45 ± 3.4 % (113 women). These diseases occurred in almost every second patient. Accordingly, the following was noted by groups: in women with diffuse adenomyosis, cervical pathology was observed on average in 54.71 ± 4.8 % of patients (58 women). Uterine fibroids and PID were observed in 56.60 ± 4.8 % of patients (60 women) and 44.33 ± 4.8 % of patients (47 women), respectively in women with

nodular adenomyosis, cervical pathology was observed on average in 47.45 ± 4.6 % of patients (56 women). Uterine fibroids and PID were observed, respectively, in 44.93 ± 4.6 % of patients (53 women) and 55.13 ± 4.6 % of patients (66 women), respectively, polycystic ovary syndrome (PCOS) was observed in 32.58 ± 3.1 % of patients (73 women), respectively, by groups: in group 1 – 36.79 ± 4.6 % (39 women), in group 2 – 28.81 ± 4.2 % (34 women). Symptoms of PCOS were more often observed in patients with pathological endometrial processes. External genital endometriosis was noted somewhat less frequently – in 31.25 ± 3.1 % of patients (70 women), respectively, by groups: in group 1 – 34.9 ± 4.6 % (37 women), in group 2 – 27.9 ± 4.1 % (33 women). Bacterial vaginosis was also observed in women – 28.57 ± 3.0 % (64 women) and vaginitis – 25.27 ± 2.8 % (56 women). Tumor-like formations (cysts) were noted somewhat less frequently ovaries (13.39 ± 2.3 %, 30 women) and genitourinary infections (20.08 ± 2.6 %, 45 women). Sexually transmitted infections (STD) had a history of approximately an equal percentage of cases in all study groups. In the control group, the following diseases were noted: PID – 7.1 ± 2.8 % (6 women), PCOS – 2.38 % (2 women), tumor-like formations (cysts) ovaries – 2.38 % (2 women), genitourinary infections – 10.7 ± 3.4 % (9 women).

Thus, gynecological morbidity was detected in all patients with adenomyosis (100 %) and in 19 patients of the comparison group (22.61 ± 4.6 %). In the anamnesis, among the surgical interventions, one in ten patients had a cystectomy, less often a tubectomy (Table 2).

Table 2

History of surgical interventions in patients with adenomyosis

Surgical interventions	Group 1 (n=106)		Group 2 (n=118)		Total (n=224)		χ^2	p
	Abs.	%	Abs.	%	Abs.	%		
Cystectomy	14	13.20 ± 3.3	12	10.16 ± 2.8	26	11.61 ± 2.2	0.50	0.478
Tubectomy	9	8.49 ± 2.7	8	6.78 ± 2.3	17	7.59 ± 1.8	0.23	0.629
Total	23	21.69 ± 4.0	20	16.95 ± 3.5	43	19.20 ± 2.6	0.81	0.368

In women with diffuse adenomyosis, cystectomy was performed in 13.20 ± 3.3 % of cases (14 women), and tubectomy – in 8.49 ± 2.7 % of patients (9 women). In women with nodular adenomyosis, cystectomy was performed in 10.16 ± 2.8 % of cases (12 women), and tubectomy in 6.78 ± 2.3 % (8 women). This indicates the development of adenomyosis after undergoing surgery and may be involved as a criterion for inducing the development of a nodular form of adenomyosis.

Of the extragenital pathology, chronic diseases of the gastrointestinal tract (gastritis, cholecystitis) were most often recorded – in 40.62 ± 3.3 % of cases (91 women), diseases of the nervous system – in 35.71 ± 3.2 % of cases (88 women), chronic diseases of the nasopharynx – 35.29 ± 3.2 % of cases (79 women). Endocrine diseases were less common (24.55 ± 2.8 %, 55 women) and diseases of the cardiovascular system (22.32 ± 2.8 %, 50 women). Diseases of the skin (20.98 ± 2.7 %, 47 women) and the genitourinary system (14.73 ± 2.4 %, 33 women) also occurred. Mastopathy was detected in 25 patients with various forms of adenomyosis, which amounted to 11.16 ± 2.2 %, among the patients of the control group there was no mastopathy. There were no statistically significant differences in extragenital pathology among groups with different forms of adenomyosis. We analyzed the frequency of extragenital pathology by groups.

Our studies have shown that in patients with diffuse adenomyosis from extragenital pathological conditions, diseases of the gastrointestinal tract – 42.38 ± 4.8 % (48 women), diseases of the nervous system – 43.39 ± 4.8 % (46 women) and chronic nasopharyngeal diseases – 38.67 ± 4.7 % (41 women) were most common. In patients with nodular adenomyosis, diseases of the gastrointestinal tract – 36.44 ± 4.4 % (43 women), diseases of the nervous system – 35.59 ± 4.4 % (42 women) and chronic nasopharyngeal diseases – 32.20 ± 4.3 % (38 women) were also most common from extragenital pathological conditions.

Thus, a comparative analysis did not reveal a clear relationship between gynecological and extragenital diseases observed in patients with various forms of adenomyosis. Concomitant somatic pathology was present in all the examined women. However, it is important to note that all women had a combination of several concomitant diseases. It was also noted that the majority of patients were diagnosed with 2 or more different diseases, mainly combined with dys hormonal pathologies, which coincides with the opinion of most scientists about the etiopathogenesis of endometrial pathology [12, 13, 15].

The study revealed an increase in the frequency of infectious diseases in the examined women, which may indicate a high infectious index characteristic of these patients. However, there were no statistically significant differences in the incidence of infectious diseases.

In patients with diffuse adenomyosis, the most common infectious diseases were influenza (46.23 ± 4.8 %, 97 women), ARVI (46.23 ± 4.8 %, 49 women), chickenpox (42.45 ± 4.8 %, 33 women), rubella (31.13 ± 4.5 %, 33 women). In patients with nodular adenomyosis, the most common infectious diseases were influenza (92.37 ± 2.3 %, 109 women), ARVI (48.31 ± 4.6 %, 48 women), chickenpox (45.76 ± 4.6 %, 54 women), rubella (29.66 ± 4.2 %, 35 women).

A detailed analysis of the frequency of concomitant and transferred diseases in the studied patients was also carried out.

It was found that in patients with diffuse adenomyosis, obesity of the 2nd degree was most often noted – the body mass index (BMI) was 35–39.99 in 35.84±4.6 % of cases (38 women). At the 1st degree of obesity, 16.98±3.6 % of patients (18 women) had a BMI (30–34.99). Overweight BMI of 25–29.99 was observed in 14 women (13.20±3.3 %). In general, obesity with a BMI of 30 or more was observed in 58 women (54.71±4.8 %). In patients with nodular adenomyosis, obesity of the 2nd degree of severity was also most often noted (BMI (35–39.99) in 33.38±4.4 % of cases (40 women). The 1st degree of obesity (BMI 30–34.99) was registered in 20.34±3.7 % of patients (24 women). A BMI of 25–29.99 was observed in 19 women (16.10±3.4 %). Obesity with a BMI of 30 or more was observed in 67 women (56.78±4.6 %). A total of 125 women (55.80±3.3 %) with various forms of adenomyosis were obese with a BMI of 30 or more. Overweight BMI of 25–29.99 was observed in 33 women (14.73±1.3 %).

As can be seen, in patients with diffuse adenomyosis, hypertension (13.20±3.3 %, 14 women), varicose veins (9.43±2.8 %, 10 women) and diffuse nontoxic goiter (7.55±2.7 %, 8 women) were the most common of the concomitant pathological conditions. In patients with nodular adenomyosis, hypertension (10.16±2.8 %, 12 women) and varicose veins (6.78±2.3 %, 8 women) were the most common of the concomitant pathological conditions. Thus, the somatic status of all patients was burdened by a combination of serious concomitant diseases.

The study of body mass index indices in the examined women showed that overweight and obese patients are more likely to suffer from various types of adenomyosis. This indicates that obesity plays a statistically significant role in the development of various forms of adenomyosis, since the lower limit of the 95 % confidence interval is higher than 1. The relative risk index in patients in the first group was 5.38 ($p<0.05$), and patients in the second group had a steady tendency to obesity. Constant eating behavior in premenopausal age leads to an age-related decrease in the intensity of metabolic processes. This leads to an increase in body mass index and the potential development of signs of perimenopausal metabolic syndrome. The main factor determining the likelihood of developing adenomyosis or endometrial hyperplasia in perimenopausal women is body mass index. It is important to note that endocrine diseases, cardiovascular diseases and obesity are risk factors for hyperplastic and malignant endometrial processes.

In addition, adipose tissue is able to secrete leptin, interleukin-6 and tumor necrosis factor, as well as participate in the conversion of androgens to estrogens (androstenedione to estrone), which is the basis for hyperplastic endometrium. We found that a high incidence of endocrine and metabolic disorders is the pathogenetic basis of endometrial hyperplasia and adenomyosis in women of reproductive age and perimenopause. The data obtained are consistent with the results of the work of a number of authors published earlier [1–3].

Conclusion

Cervical pathology, uterine fibroids and pelvic inflammatory diseases were the most common in patients with various forms of the disease. Of the extragenital pathology, such diseases as chronic diseases of the gastrointestinal tract (gastritis, cholecystitis), diseases of the nervous system, and chronic diseases of the nasopharynx were most often recorded. Endocrine diseases and diseases of the cardiovascular system were less common. Our results showed that the high frequency of endocrine and metabolic disorders indicates the pathogenetic basis for the occurrence of endometrial hyperplasia and adenomyosis in women of reproductive age and perimenopause.

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CHANGES IN THE DIASTOLIC FUNCTION OF THE HEART AND TUMOR NECROSIS FACTOR-ALPHA IN PATIENTS WITH COMBINED PATHOLOGY: ARTERIAL HYPERTENSION WITH TYPE 2 DIABETES AND OBESITY

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The purpose of the work was to study the features of the diastolic function of the left ventricle and the tumor necrosis factor- α level in patients with combined pathology: arterial hypertension with type 2 diabetes and obesity. Disorders of the diastolic function of the left ventricle were established to be more often registered in patients with arterial hypertension with type 2 diabetes and obesity, compared to the group of patients with arterial hypertension and type 2 diabetes with normal body weight. A significant increase in the content of tumor necrosis factor- α was determined in the group of patients with arterial hypertension with type 2 diabetes and obesity compared to the group with arterial hypertension and type 2 diabetes with normal body weight.

Key words: arterial hypertension, type 2 diabetes, diastolic dysfunction, tumor necrosis factor- α .

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ЗМІНИ ДІАСТОЛІЧНОЇ ФУНКЦІЇ СЕРЦЯ ТА ФАКТОРУ НЕКРОЗУ ПУХЛИНИ-АЛЬФА У ПАЦІЄНТІВ З АРТЕРІАЛЬНОЮ ГІПЕРТЕНЗІЄЮ, ПОЄДНАНОЮ З ЦУКРОВИМ ДІАБЕТОМ 2 ТИПУ ТА ОЖИРІННЯМ

Метою роботи було вивчення особливостей стану діастолічної функції лівого шлуночка та фактору некрозу пухлин- α у пацієнтів з поєднаною патологією артеріальна гіпертензія з цукровим діабетом 2 типу та ожирінням. Встановлено, що у пацієнтів з артеріальною гіпертензією з цукровим діабетом 2 типу та ожирінням порівняно з групою пацієнтів з артеріальною гіпертензією і цукровим діабетом 2 типу з нормальною масою тіла частіше реєстрували порушення діастолічної функції лівого шлуночка. Визначено достовірне підвищення вмісту фактору некрозу пухлин- α у групі пацієнтів з артеріальною гіпертензією з цукровим діабетом 2 типу та ожирінням у порівнянні з групою з артеріальною гіпертензією та цукровим діабетом 2 типу з нормальною масою тіла.

Ключові слова: діастолічна дисфункція, фактор некрозу пухлин – альфа, артеріальна гіпертензія, цукровий діабет 2 типу.

The work is a fragment of the research project “To determine the features of immunocytokine imbalance in comorbid patients with arterial hypertension and type 2 diabetes and cardiovascular and renal complications”, state registration No. 0123U101711.

The trend today is to increase arterial hypertension (AH) in combination with type 2 diabetes mellitus (DM type 2) [5]. The combination of AH and DM type 2 leads to a mutual influence on the course of diseases, nature and severity of complications. Often such a combination complicates the diagnosis, and also determines the peculiarities of the choice of drug therapy. Thus, among patients with DM type 2, hypertension is found in 60–80 % [9]. On the other hand, DM type 2 is one of the risk factors for the development of cardiovascular diseases [14]. It has been demonstrated that the combination of