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ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

CLINICAL, MORPHOFUNCTIONAL FEATURES OF ENDOMETRIAL HYPERPLASIA IN POSTMENOPAUSAL WOMEN WITH DERIVATIVES OF REPRODUCTIVE ORGANS

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GENERAL CHARACTERISTICS OF THE DISSERTATION

The relevance of the problem. The time in a woman's life following the end of her ovaries' functional activity is known as the postmenopausal period. Due to the lengthened lifespan of women under modern conditions, postmenopausal phase has been extended to 30-60 years[1]. It is determined that by 2030, every fifth person in the world will be 65 years old based on demographic forecasts. It is defined that European nations and Russia are among those with a significant demographic aging rate, which leads to problems such as the frequency of postmenopausal diseases, treatment and prevention of their course characteristics.

It has been determined that the frequency of diseases in the early elderly (60-74 years old) increases by 2 times, and in the late elderly (aged over 75 years) by 6 times. It further demonstrates the presence of challenges in provision of medical care[2].

Based on the results of scientific research carried out in Azerbaijan, it was recorded that the frequency of women over 55 years old with osteoporosis in the postmenopausal period comprises 52.8%. The frequency of elderly women without osteoporosis in the postmenopausal period is 55.9%[3].

According to scientific research done in Baku in 2014 on the long-term postmenopausal period, 66.7% of women were aged 55-65 years, 21.3% were aged 65-75 years, and 12% were over 76 years old. The average duration of the postmenopausal period was 14.18±1.08 years and varied between 8 and 30 years[4].

It should be mentioned that an increase in the hyperplastic processes of the reproductive organs is seen during the

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[1]Буянова С.Н., Пучкова Н.В., Гитинова Э.М. Диагностика и тактика ведения больных с гиперпластическим процессом в эндометрии в постменопаузальном периоде // Российский вестник акушера-гинеколога, – 2009, №5, – с. 46-49.

[2]Ковалькова И.В. Профилактика и лечение эстрогендефицитных состояний у женщин в постменопаузе / Автореф. дис. к.м.н. / – М., 2010, – 32 с.

[3] Əliyeva E.M., Əsədova Ş.Ş. Postmenopauzal osteoporoz /– Bakı, – 2006, – 103 s.

[4] Şərifova J.R., Əliyeva E.M. Postmenopauzal dövrdə olan qadınlarda reproduktiv orqpnlarında qedən atrofik proseslərin ultrasəs müayinəsinin xüsusiyyətləri // Sağlamlıq, – 2012, №2, – s. 99-103.

postmenopausal period as a result of hormonal changes. According to various authors, the frequency of polyps of the endometrium in this period comprises 39.2-69.3%, the thickness of atrophic processes in the endometrium is 16.7-47.4%, hyperplasia of the endometrium without atypia is 3.3-4.9%, the frequency of atypical hyperplasia is 0.5-5.2%, adenocarcinoma 0.5-14%, uterine submycosis myoma 3.6-8.5%, intrauterine synechiae 4.8-7.9%[5].

Accumulation of intrauterine fluid (serometra) in the postmenopausal period is determined with a frequency of 35.2%. It was defined that the frequency of endometrial hyperplasia in women with serometra is 55.1%. The thickness of the uterine cavity in these women varies from 1 to 24 mm. It has been determined that the thickness of the uterine cavity increases by 1-6 mm in simple hyperplasia, and by 3-24 mm in endometrial cancer. The authors claim that in 92% of cases, the presence of fluid in the uterine cavity has pathological prognostic value[6].

Anita S.Y. and co-author have substantiated in their study (2016)[7] that an increase in the body weight index, the use of hormone replacement drugs, the age of woman, the presence of sexual intercourse, the presence of fibromatous nodes in childhood for a long time, the length of the postmenopausal period, and the presence of a hypertensive condition are the main causes of endometrial thickening in the postmenopausal period up to 1-32 mm.

Exogenous (hormone replacement drugs) and endogenous (obesity) factors both have a major role in endometrial hyperplasia, according to the authors. It should be noted that there is limited scientific data available on the diagnosis and morphofunctional

[5] Raouf S.A., Gupta P., Papaioannou S. [et al.] Endometrial thickness for invasive investigations in women with postmenopausal bleeding / // Am. J. Climacteric, – 2011, vol. 14, №1, – p. 117-120.

[6]Гарашова М.А., Алиева Э.М. Диагностическая значимость гормональных, биохимических и эхографических методов исследования при раке эндометрия в постменопаузальном периоде // Ж.Акушерство, Гинекология и Репродукция, – 2019, том 13, №3, – с.189-196.

[7]Anita S.Y., Francesmary M., Lyndon M. Transvaginal Ultrasound Measurement of Endometrial Thickness as a Biomarker for Estrogen Exposure // Am.Association for Cancer Research, – 2016, vol. 25, №1, – p. 340-345.

features of endometrial hyperplasia in the context of reproductive organs in the postmenopausal period.

The object and subject of the study. The object of the study was the clinical-anamnestic, laboratory, and instrumental diagnostic aspects of 130 patients who were treated for various localized derivatives of the genitals in the postmenopausal period at the Oncology and Teaching Surgery clinics of Azerbaijan Medical University in Baku during the years 2016-2019. The subject of the study was the clinical and morphofunctional features of endometrial hyperplasia during the derivation of reproductive organs in the postmenopausal period.

The purpose of the study. The purpose is the study of the morpho-functional features of endometrial hyperplasia in women with reproductive organ derivatives in the postmenopausal period.

Objectives of the study:

1. Study of the occurrence frequency of derivatives of reproductive organs and subjective symptoms in the postmenopausal period.
2. Evaluation of the state of the hypothalamic-pituitary-adrenal-ovarian system in derivatives of the reproductive organs in the postmenopausal period and determination of the characteristics of hormonal changes.
3. Determination of informativeness of Estriol and Cytomegalovirus IgG of the oncomarker CA-125 (CA-125) in postmenopausal women with derivatives of the reproductive organs.
4. Study of the features of changes in the thickness of the endometrium in various derivatives of the reproductive organs in the postmenopausal period based on ultrasound scan.
5. Studying the degree of spread of neoplastic processes of the pelvic organs in the postmenopausal period by the method of Magnetic Resonance Imaging (Computed Tomography).
6. Evaluation of the state of the endometrium in the derivatives of the reproductive organs in the postmenopausal period by the electron-microscopy method.

Research methods. To achieve the objectives set, the patients were examined by the following methods:

- clinical and anamnestic
- physical and gynecological examination
- methods of laboratory blood tests
- radiological examinations
- preoperative surgical diagnosis
- histological examination
- statistical analysis

The principal propositions to be defended:

1. There are determined myoma in 30%, endometrial hyperplasia in 17.7%, ovarian tumor-like derivatives in 13.1%, endometrial cancer in 15.4%, uterine sarcoma in 12.3%, cervical cancer in 6.2%, and ovarian cancer in 5.4% of postmenopausal women with various derivatives.

2. In the neoplastic processes of various derivatives of the genital organs in the postmenopausal period, there are noted hyperprolactinemia, adrenal hyperandrogenism, and hyperestrogenism caused by a high estrone level.

3. Ultrasound scan detects that the thickness of the endometrium is 15,580 ± 1.53 mm in postmenopausal women, this figure increases significantly to 22.74 ± 1.75 mm in women with uterine sarcoma, but decreases by 11.1 ± 1.64 mm in tumor-like derivatives of the ovaries and 7.98±2.48 mm in ovarian cancer.

4. Magnetic resonance imaging in the postmenopausal period allows you to detect the thickness of the uterus, ovaries, endometrium, the size of regional lymph nodes, the degree of metastasis and to choose the extent of surgical intervention.

5. Electron microscopy reveals degenerative and chronic inflammatory changes in the context of simple and complex endometrial hyperplasia in postmenopausal women with various reproductive derivatives.

Scientific novelty of the study: As a result of the study, the frequency of occurrence of derivatives of reproductive organs in the postmenopausal period was determined. It was found out that benign (36.8%), invasive (34%) and preinvasive (21.7%) diseases of the uterus predominate in the postmenopausal period. In this period, 26.2% of women have asymptomatic progression of derivatives of

reproductive organs, and 73.8% have a high frequency of various subjective symptoms. It was determined that bleeding is observed in 34.6%, and spotting in 17.7% of cases among the clinical symptoms in postmenopausal women with reproductive derivatives.

In the tumor processes of the reproductive organs during the postmenopausal period, there are noted hyperprolactinemia, adrenal hyperandrogenism caused by a rise of androgens, and hyperestrogenism due to a high estrone (E1) level.

Based on the study, it was found that endometrial hyperplasia in the postmenopausal period is defined as an independent nosological form in the presentation of its benign, preinvasive and invasive derivatives, and magnetic resonance imaging is mandatory for this group of women.

During the tumor processes of the reproductive organs in the postmenopausal period, the morphofunctional features of the endometrium were studied using an electron microscope. It was determined that hyperplasia of the endometrium, observed with degenerative and chronic inflammatory changes, was also detected in women with various localized genital warts.

Theoretical and practical significance of the study: Aparılan tədqiqat nəticəsində müəyyən edilmişdir ki postmenaopauzal dövrdə yumurtalıqların aktivliyinin sönməsi fonunda reproduktiv orqanların törəmələrinin rastgəlmə tezliyi artması ehtimalı yüksəkdir. Bu tezliyin artmasına səbəb olaraq ekstragenital patalogiya, endokrin metabolik pozulmalar fonunda baş verir. Ginekoloji xəstəliklərdən reproduktiv dövrdə yüksək tezliklə rast gəlməsi postmenopauzada reproduktiv orqanların neoplaziyalarının ehtimalını artırır.

The study also reveals that hyperprolactinemia, hyperandrogenemia, and hyperestrogenemia are observed in benign, preinvasive, and invasive derivatives of reproductive organs.

Regardless of the course of the reproductive cycle in the postmenopausal period, it is advisable to conduct ultrasound scan as a screening method for all women. Magnetic resonance imaging is of high diagnostic importance when determining derivatives in this period. Clinical, echographic, hormonal, functional and radiological studies allow to determine the characteristics of benign and malignant

tumors of the reproductive organs in the postmenopausal period, as well as to define the morpho-functional features of the endometrium, the criteria for their early diagnosis and the correct determination of treatment strategies.

Approval of the dissertation. The principal propositions of the dissertation were presented at the republican conference "Actual approach to some problems of Obstetrics and Gynecology in Azerbaijan" (Baku, 2019), at the scientific conference "Actual problems of medicine" dedicated to the 90th anniversary of Azerbaijan Medical University (Baku, 2020). The preliminary discussion of the dissertation took place at the joint meeting of the 1st and 2nd departments of Obstetrics and Gynecology of Azerbaijan Medical University (12.02.2022, protocol No.4). The approval of the dissertation was held at the Scientific seminar of the Dissertation Council ED 2.06 under Azerbaijan Medical University (23.06.2022, protocol No. 16).

Overall, 12 scientific works have been published on the subject of the dissertation. 7 of them are articles, 5 are theses and conference materials. Besides, 2 of the articles and 2 of the theses have been published in foreign publishing houses.

The main consequences of the study are applied at the Teaching Surgery Clinic of Azerbaijan Medical University.

The scope and structure of the dissertation. The dissertation is written on 170 pages printed on a computer, consisting of 42 tables, 6 diagrams and 16 figures. The list of references covers 229 sources. The volume of the dissertation consists of 197,783 characters, including the introduction – 10,383, chapter I – 93,939, chapter II – 8,716, chapter III – 53,144, conclusions – 27,882, consequences – 2,887, practical recommendations - 832 characters.

CONTENT OF THE DISSERTATION

Materials and methods of the study. 130 postmenopausal women with the derivatives of the reproductive organs have been examined to fulfill the intended aim. All patients were examined and taken appropriate treatment at the Oncology Clinic of Azerbaijan

Medical University (Baku).

Participation criteria:

1. Postmenopausal period lasting more than 2 years;
2. Various localized tumors of the genital organs verified by clinical and radiological examination techniques. The patients examined have given their consent in advance for operative treatment and participation in scientific research.

The average age of the examined women was 60.03±0.69 years and varies between (48-79) years. The women, along with clinical examination, have undergone functional, hormonal, radiological, morphological, and biochemical examinations. The clinical and anamnestic methods of the study included the analysis of patients' complaints (mainly whether there is a bloody secretion or not), gynecological and extragenital diseases, menstruation, the state of sexual and reproductive functions. The occurance of climacteric syndrome in patients was assessed using the Kuperman scale. The degrees of climacteric syndrome have been measured. According to the Ferriman-Gallway scale the presence and degree of hirsutism has been determined.

The patients involved in the study definitely underwent transvaginal ultrasound scanning. The ultrasound parameters of the uterus were measured, including the anterior-posterior size, length, and width, as well as the length, width and thickness of the ovaries. As per USS indicators, the dimensions of the tumor and the thickness of endometrium were evaluated. An analogy was applied using J.R. Sharifova's (2013) and V.V. Rahimova's (2019) results for the assessment of the echographic (ultrasonic) indicators of the uterus and ovaries. The examination methods as Magnetic Resonance Tomography and Computer Tomography are also included in the radiological examinations.

The amount of the follicle-stimulating hormone (FSH), luteinizing hormone (LH), Prolactin (Prl), Progesterone (P), Dehydroepiondesterone-sulfate (DHEA-S), Testosterone (T), Estradiol (E_2), and Estriol (E_3) in the blood serum of the postmenopausal women involved in the study was determined during

the hormonal examinations.

By the biochemical tests, there was identified the titer of alanine aminotransferase (ALT), aspartate aminotransferase (ALT), glucose, creatinine, carbamide, residual nitrogen and total protein in the blood serum.

CA (Cancer antigen 125) was prescribed for all the women. The form of Cytomegalovirus (SMV G) was determined in the examined women. In the conducted study, women with the derivatives of the reproductive organs in the postmenopausal period underwent ultrasound, hormonal, biochemical, computed tomography, histological, and electron-microscopic examinations.

The morphological study included the histological examination of the endometrium before and after the surgical operation. Samples taken from the endometrium of patients with genital warts of various localizations were examined by electron microscopy. Electron microscope allows examination of 1 nm-10 μm thick sections of the endometrium with 1000-10000 times magnification. In order to take images with electron microscopy there is used a special magnetic lens guided by the movement of electrons.

The obtained results were statistically processed using the "Statgraph" program. Group indicators are placed on the variation scale. The arithmetic mean of the average (m), the standard deviation of the average ( ), its standard error (Se), as well as the minimum (min) and maximum (max) values of the series were calculated for each group.

RESULTS OF PERSONAL RESEARCH

This study has investigated the frequency of occurrence of various derivatives in 130 postmenopausal women. The results obtained are shown in Figure 1.

As can be seen from Figure 1, the diagnoses set for postmenopausal women are: 30% (39) myoma, 17.7% (23) endometrial hyperplasia, 15.4% (20) endometrial cancer, 13.1% (17) ovarian tumor-like derivatives, 12.3% (16) uterine sarcoma, 6.2% (8) cervical cancer, and 5.4% (7) ovarian cancer. The study has revealed that benign tumors and tumor-like derivatives of

reproductive organs are 60.8%, and the frequency of malignant tumors is 39.3%.

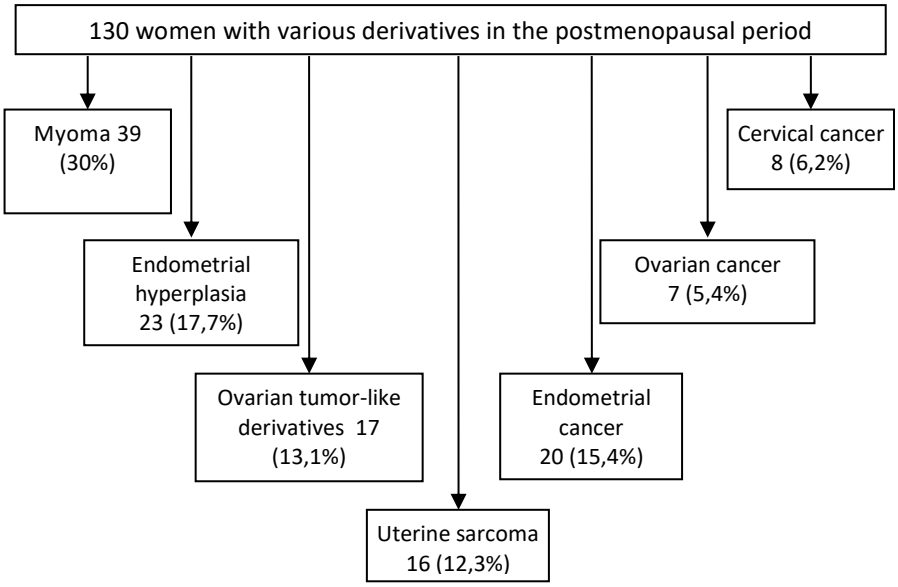

Figure 1. The frequency of occurrence of various derivatives of the reproductive organs in the postmenopausal period

When studying the frequency of occurrence of uterine derivatives in the postmenopausal period, it was determined that 36.8% frequency was myoma, 21.7% endometrial hyperplasia, 18.9% endometrial cancer, 15.1% uterine sarcoma. Meantime, ovarian tumor-like derivatives were detected in 70.8% cases, and ovarian cancer in 29.2%.

It should be noted that benign tumors of the cervix uteri are not identified in postmenopause, and 7.5% of malignant tumors are diagnosed as cervical cancer. There were detected ovarian tumors in 70.8% cases and ovarian cancer in 29.2% in the postmenopausal period.

Based on the anamnestic data, it was defined that postmenopausal women with reproductive organs had a high frequency of chronic inflammatory processes during the

reproductive period (51.1%), background lesions and precancerous diseases (displasia) of the cervix uteri (6.2%), tumor-like ovarian tumors (6.6%), uterine fibroids (5.2%), and relatively less frequency of pathology of the mammary glands (3%).

When examining women with reproductive organs in the postmenopausal period, it was found that the duration of the postmenopausal period was 9.55±0.74 (2-31) years. This reflects the wide range of postmenopausal women examined.

As a result of the research, there were identified subjective symptoms of the patients and it was detected that 34 (26.2%) women with benign preinvasive and invasive tumors had no complaints, and 96 (73.8%) women had multiple complaints with various frequencies.

It was determined that 77 of 130 patients (59.2%) had pains of various localization and intensity, 80 women (61.5%) had bloody discharge from the uterus, 96 (100%) had dysuric symptoms, 92 (70.8%) %) nervous tension, 89 (68.5%) anxiety, 76 (58.5%) fatigue, 76 (58.5%) sleep disorders, 46 (35.4%) pain during intercourse, 49 (37.4%) body hair growth, 45 (34.6%) bleeding, 42 (32.3%) body weight loss, 56 (43.1%) loss of appetite, 40 (30.8%) hair loss, 36 (27.7%) increased intra-abdominal volume, 31 (23.8%) shortness of breath, 23 (17.7%) pain and tension in the mammary glands, 16 (12.3%) changes in voice timbre, 23 (17.7%) the presence of bloody discharge, 8 (6.2%) postcoital bleeding, 28 (21.5%) increased heart rate.

The condition of the hypothalamic-pituitary-adrenal ovarian system in postmenopausal women with derivatives of reproductive organs. The study conducted has investigated the condition of the hypothalamic-pituitary-adrenal-ovarian system of postmenopausal women with various derivatives of reproductive organs. The amount of follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin (Prl), estradiol (E_2), estrone (E_1), dehydroepiandesterone sulfate (DHEA-S), and testosterone (T) was determined in the blood serum of all patients by immunoenzymatic techniques. The obtained results were compared with V.V. Rahomova's (2018) hormonal parameters of

women who had experienced the postmenopausal period without complications.

The level of hormones in women with various derivatives of reproductive organs in the postmenopausal period is described in Table 1.

Table 1.

Hormonal indicators in postmenopausal women with various derivatives of reproductive organs (M±Se)

Indicators	Postmenopausal women with various derivatives	Postmenopausal women without complications	P
FSH, mIU/ml	43,95±2,82 (2,82-134,7)	51,21±2,4	>0,05
LH, mIU/ml	29,0±2,1 (1,79-79,62)	21,91±1,92	>0,05
Prl, ng/ml	756,1±83,37 (31,01-3380)	116,86±3,99	<0,05
E_2, pg/ml	13,91±1,41 (0,07-69,29)	40,41±2,1	<0,05
P, ng/ml	0,29±0,04 (0,005-2,5)	0,54±0,99	<0,05
DHEA-S, ng/dl	125,83±10,80 (10,72-545,81)	1,3±0,03	<0,05
T, ng/dl	0,17±0,01 (0,025-0,64)	1,81±0,005	<0,05
E_1, pg/ml	97,0±2,89 (25,0-190,0)	9,5±0,52 (8-11,5)	<0,05

As can be seen from the Table, there is detected a statistically significant increase in Prl and DHEA-S, and a considerable decrease in E_2, P, T in postmenopausal women with various derivatives. $P<0.05$

There was determined uterine myoma in 39 (30%) of 130 postmenopausal women with benign preinvasive and invasive derivatives of reproductive organs in the postmenopausal period. The average age of those women was 58.29±1.18 (48-79) years. As a result of the detection of hormones, it was found that FSH, E_2, T are at a statistically noticeably low level, and Prl, DHEA-S, E_1 are at a high level in postmenopausal women with fibromyoma.

In the study, there was detected endometrial hyperplasia in 23 (17.7%) women in the postmenopausal period. The average age of women with endometrial hyperplasia was 62.06±1.27 (52-72) years. Decrease of E_2 by 19.89±4.85 pg/ml, P by 0.26±0.06 ng/ml,

T by 0.16±0.03 ng/dl, and increase of Prl by 722.4±122.6 ng/ml, DHEA-S by 98.58±19.1 ng/ml, and E_1 by 97.12±3.12 pg/ml were observed in women with endometrial hyperplasia.

In the study conducted, uterine sarcoma was found in 16 (12.3%) women. The age of those women was 62.67±1.68 (54-75) years. The level of hormones in the blood serum of patients included in this group was studied and it was determined that their Prl (544.69±55.37 ng/ml), DHEAS (135.58±37.26 mg/ml), E_1 (107.31±4.25 pg/ml) indicators were increased, and E_2 (22.46±5.19 pg/ml), T (0.22±0.037 ng/dl) were decreased (P <0.05).

20 (15.4%) of 130 postmenopausal women were diagnosed with endometrial cancer. The average age of women with endometrial cancer was 63.2±1.79 (58-75) years. While studying the level of hormones in the blood serum of this group of patients it was observed that LH (27.39±0.005 mIU/ml), Prl (316.5±85.5 ng/ml), DHEA-S (180.0±29.5 ng/ml), and E_1 (117.36±3.61 pg/ml) were increased, but FSH (429.8±1.93 mIU/ml), E_2 (14 ,8±1.43 pg/ml), P (0,22±0,03 mg/ml), T (0,21±0,01 ng/dl) were decreased (P<0, 05).

During the neoplastic process in women with ovarian cancer, the increase of hyperprolactinemia Prl (1211.65±81.35 ng/ml), adrenal DHEA-S (89.71±17.66 ng/ml) E_1 pg/ml (116.31±2.39 pg/ml) in the context of hyperandrogenism was observed. A statistically significant decrease in Estradiol (14.15±5.67 pg/ml) and Testosterone (0.23±0.12 ng/ml) was determined in those women.

In women with cervical cancer, an increase in hyperprolactinemia Prl (2239.5±114.5 ng/ml) and adrenal hyperandrogenism DHEA-S (134.74±19.61 ng/ml), E_1 (76.1±2.11 pg/ml), as well as a decrease in E_2 (8.68±1.28 pg/ml) and T (0.16±0.03 ng/ml) were noted (P>0.05).

As a result of the study, it was determined that hyperplactinemia and hyperandrogenism of adrenal origin were observed in postmenopausal women with benign preinvasive and invasive derivatives of the reproductive organs, regardless of the derivatives.

Results of the detection of CA125 (Cancer antigen), E_3 (estriol) and Cytomegalovirus in the blood of postmenopausal women with reproductive organs. The informative content of CA-125 (cancer antigen), E_3 (estriol) and SMV Ig (cytomegalovirus immunoglobulin G) in the blood serum of postmenopausal women with various derivatives of reproductive organs was investigated in this study. The obtained results are described in Table 2.

As can be seen from the Table, CA-125, E_3, and SMV ImG are considerably higher in postmenopausal women with derivatives of reproductive organs.

It should be noted that the indicator of CA-125 oncomarker in women with myoma was consistent with physiological indicators as per laboratory results. The same result is noticed in women with endometrial hyperplasia.

Table 2.

Indicators of oncomarkers and cytomegalovirus in women with derivatives of reproductive organs in the postmenopausal period

Indicators	CA-125, U/ml	E_3, nq/ml	SMV IgG
Myomas (n=39)	18,4±4,28 (1-48,65)	1,1±0,99 (0,07-20,79)	625,6±50,2 (9,8-4093)
Endometrial hiperplasia (n=23)	21,95±9,72 (7,6-50)	1,31±0,2 (0,07-17,07)	693,5±59,15 (71,67-1704)
Tumor-like lesions of the ovaries (n=17)	40,84±12,18 (9,7-129,8)	0,09±0,01 (0,07-0,2)	732,4±29,73 (176,4-1818,0)
Uterine sarcoma (n=16)	96,86±29,27 (1,7-204,6)	0,08±0,0009 (0,03-1,44)	443,11±53,38 (71,67-813,9)
Endometrial cancer (n=20)	29,86±15,05 (2-90,9)	0,08±0,006 (0,07-0,09)	419,95±42,95 (177-262,9)
Ovarian cancer (n=16)	58,0±15,1 (12,6-129,8)	0,09±0,02 (0,07-0,144)	472,0±33,2 (138,8-205,2)
Cervical cancer (n=7)	55,45±11,1 (11,5-157,5)	0,06±0,01 (0,007-0,07)	536,2±77,2 (258,5-813,9)
P	P<0,05	P<0,05*	P>0,05**

As can be seen from the Table, CA-125 oncomarker is statistically substantially higher in postmenopausal women with uterine sarcoma, ovarian cancer, and cervical cancer than the women with myoma.

There is noted a rise in CA-125 in malignant tumors of the uterus and ovaries.

When studying the amount of E_3 in postmenopausal women, it was found that the amount of E_3 was higher than the standard values for myoma and endometrial hyperplasia, and the amount of E_3-estriol was noted at a low level in the cancers of the uterus, endometrium, ovaries and cervix. And this has no diagnostic value in the women examined.

It was mentioned in the study conducted, that there occurred a statistically substantial increase of SMV IgG in women with benign, preinvasive and invasive diseases of the uterus and ovaries in the postmenopausal period.

It is worthy to note that the indicators of SMV IgG were significantly higher ($P<0.05$) in women with myoma, endometrial hyperplasia, cervical cancer, and ovarian tumor-like derivatives. In the event of endometrial and ovarian cancer, this figure was somewhat lower.

Thus, it is expedient to detect CA-125, E_3, SMV ImG in postmenopausal women with various derivatives of the reproductive organs.

Ultrasound results of the uterus and ovaries in postmenopausal women with derivatives of reproductive organs. In this study, postmenopausal women with derivatives of reproductive organs underwent transvaginal ultrasound.

The length, width, anterior and posterior sizes of the uterus, the thickness of the endometrium, and the echographic dimensions of the detected derivatives were identified during the study. Meantime, there were defined the length, width, thickness of the ovaries and echographic dimensions of the derivatives in the ovaries. The results obtained were compared with echographic indicators of the thickness of the uterus, ovaries, and endometrium of women who experienced the postmenopausal period without complications.

There was observed a statistically significant increase in the length, width, anterior and posterior sizes of the uterus ($P<0.05$) in postmenopausal women with myoma.

It is worthy to note that the thickness of the endometrium in those women is substantially increased ($P<0.05$). And based on this, postmenopausal women with myoma were also diagnosed with endometrial hyperplasia. As a result of the echographic examination, there were determined multiple nodules in the uterus. The average diameter of the biggest of those nodules was 45.1±4.83 (12.7-110) and the smallest was 24.66±3.31 (1.5-66) mm.

There was also observed a statistically significant increase in the length, width, and thickness of both ovaries in those women ($P<0.05$). Meanwhile, 4 (10.3%) of 39 women with myoma in the postmenopausal period had tumor-like derivatives (cysts) in the ovaries.

Thus, a statistically substantial increase was noted in echographic indicators of the uterus and both ovaries of postmenopausal women with myoma ($P<0.05$).

Simultaneously, there was detected an increase in the thickness of the endometrium of those women, which did not correspond to the postmenopausal period. And this indicates the presence of endometrial hyperplasia in women with myoma.

There was determined an increase in the width, anterior and posterior sizes of the uterus ($P<0.05$) in postmenopausal women with hyperplasia of the endometrium. The thickness of the endometrium was noticeably higher compared to postmenopausal women without complications ($P<0.05$).

The likelihood of neoplasia of the reproductive organs is highly increased in postmenopausal women with hyperplasia of the endometrium.

The study revealed that 17 (13.1%) of 130 postmenopausal women with various derivatives had ovarian tumor-like derivatives. There was observed a statistically substantial increase in the thickness of the endometrium in women with ovarian tumors ($P<0.05$). It should be noted that echographic indicators of the uterus in the women examined practically do not differ from

echographic indicators of the uterus in women experienced the postmenopausal period without complications (P>0.05).

In the study conducted, there was determined a statistically significant increase in the length, width, and thickness of both ovaries in women with ovarian tumor-like derivatives (P<0.05).

Based on the study, 16 (12.3%) of 130 postmenopausal women were diagnosed with uterine sarcoma. Echographic indicators of the reproductive organs in those women are described in Table 3.

The table indicates a statistically substabtial increase in the thickness of the uterus and endometrium, including the echographic indicators of both ovaries in postmenopausal women with uterine sarcoma (P<0.05).

It is important to note that in women with uterine sarcoma, there were found tumors of various sizes spreading into the uterine cavity and causing its deformation. In the majority of cases, derivatives had an uneven, heterogeneous, hypoechoic structural appearance. The large diameter of the derivatives was 44.39±7.9 (9.7-100) mm and the small diameter was 27.16±3.38 (9.1-51) mm.

Based on clinical-functional, hormonal, biochemical-morphological examinations, 20 of 130 patients (15.4%) were diagnosed with endometrial cancer.

Echographic features of the reproductive organs in patients with uterine and endometrial cancers are described in Chart 1.

As it can be seen from the Chart, there were determined a significant decrease in the length and width of the uterus, and a statistically substantial increase in the thickness of the endometrium (P<0.05) in women with endometrial cancer.

Table 3.

Echographic Indicators of Women with uterine sarcoma in the postmenopausal period. (M±Se)

Echographic indicators	Women with uterine sarcoma in the postmenopausal period	Women without complications in the postmenopausal period	P
Uterus:			
– lenght, mm	73,66±4,31 (39,6-126)	44,44±0,92 (25-58)	<0,05
– width, mm	49,47±2,93 (34,3-65)	40,66±0,08 (35-45)	<0,05
– front-back sizes, mm	54,93±1,55 (40,6-78)	27,76±0,025 (18-32)	<0,05
– width of the endometrium, mm	22,47±1,75 (11-24)	2,22±0,05 (0.6-1.4)	<0,05
Right ovary:			
– length, mm	24,69±1,53 (19-30)	18,82±0,09 (10-20)	<0,05
– width, mm	15,0±1,20 (11,20)	11,1±0,04 (8-14)	<0,05
– thickness, mm	14,36±0,31 (12-21)	15,49±0,07 (12-25)	<0.05
Left ovary:			
– length, mm	20,0±1,53 (16-27)	19,74±0,07 (10-25)	<0,05
– width, mm	14,67±0,88 (12,18)	10,74±0,05 (8-14)	<0,05
– thickness, mm	12,26±0,11 (13-19)	14,99±0,08 (12-18)	<0.05

As a result of the study, it was determined that the echographic indicators of the length, width and thickness of both ovaries of postmenopausal women with endometrial cancer were not distinguished from those of postmenopausal women without complications.

Ovarian cancer was detected in 7 (5.4%) of 130 postmenopausal patients involved in the study. There was a statistically significant increase in the echographic indicators of the uterus, endometrium and both ovaries ($P<0.05$) in women with ovarian cancer.

The ultrasound parameters of the uterus and both ovaries were not modified in postmenopausal women with cervical cancer compared to postmenopausal women without complications. Meantime, there was noted a statistically substantial increase in the thickness of the endometrium and detected a derivative of an uneven, non-homogeneous structure from the cervix to the uterus in those women.

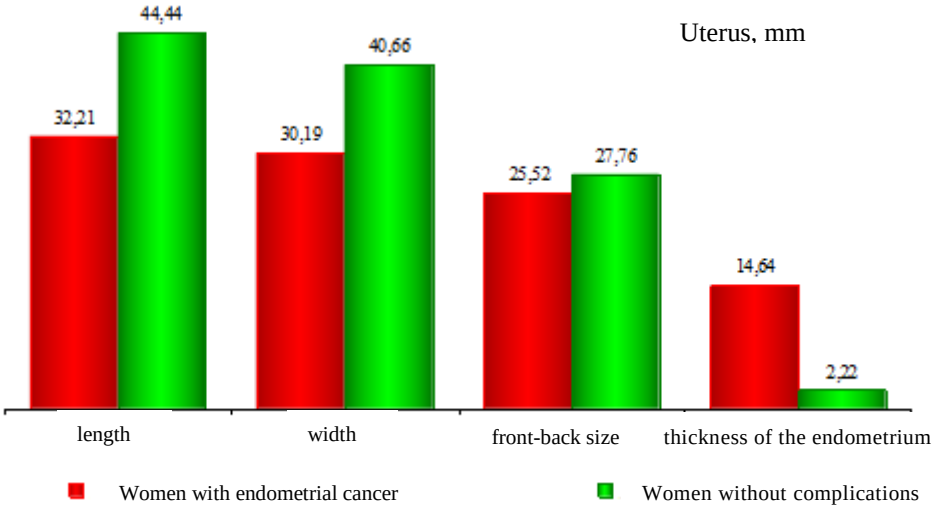

Chart 1. Echographic indicators of the uterus in postmenopausal women with endometrial cancer

Characteristics of changes in the thickness of the endometrium in postmenopausal women with various derivatives as per the results of the ultrasound scan. The purpose of the study was to investigate the clinical, laboratory hormonal, and morphological characteristics of the endometrial hyperplasia in postmenopausal women with various derivatives of the genitals. It was found out that there was endometrial hyperplasia in all the women examined, regardless of the derivatives of the reproductive organs.

It is worth of noting that 17.7% was assessed as an independent nosological unit of endometrial hyperplasia in the postmenopausal period.

The present study identified a statistically substantial increase in the echographic indicator of the thickness of the endometrium, regardless of the derivatives in the postmenopausal period.

As per the ultrasound scan, the indicator of the thickness of

the endometrium in different derivatives in the postmenopausal period is mentioned in Figure 2.

As can be seen from the chart in the Figure, there was determined a statistically substantial increase in the thickness of the endometrium in postmenopausal women with different derivatives regardless of their origin.

As it is described in the Figure, it was determined that the thickness of the endometrium in uterine sarcoma is 22.74±1.75 mm, in endometrial cancer 14.64±1.31 mm, in uterine fibroids/myoma 13.63±0.56 mm, in ovarian tumor-like derivatives 11.1±1.64 mm, in ovarian cancer 7.98±2.48 mm. Based on the results obtained, endometrial hyperplasia detected by the transvaginal transmission of ultrasound scan in the postmenopausal period in most cases reflects the presence of benign and malignant derivatives of the uterus and ovaries.

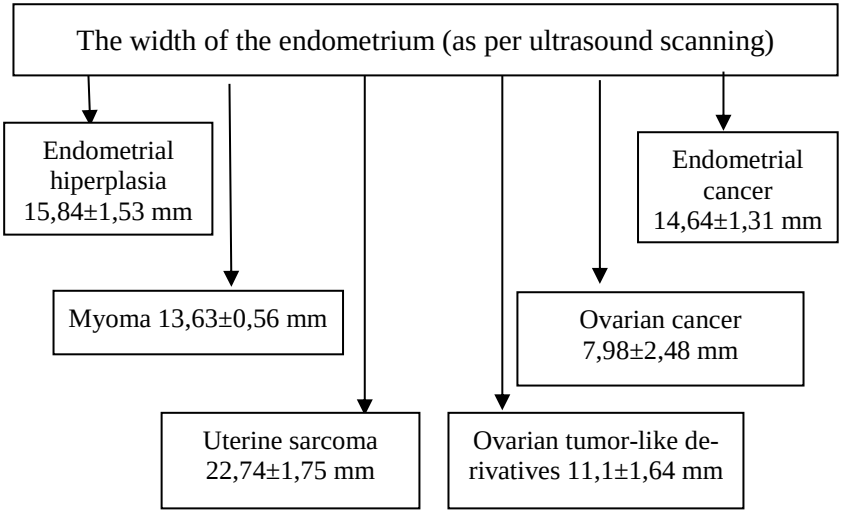

Figure 2. Characteristics of changes in the endometrium in women with different derivatives in the postmenopausal period

Consequently, an increase in the echographic indicator of the thickness of the endometrium in the postmenopausal period reflects the pathological course of this period. There is noted a difference between benign, preinvasive, and invasive processes of the reproductive organs of women with pathological thickness of the endometrium.

It is expedient to conduct other radiological examinations to determine the genesis of the detected derivatives.

Results of Magnetic Resonance Imaging (Magnetic Tomography) in postmenopausal women with neoplastic processes of the reproductive organs. In the current study, 51 (39.2%) of 130 postmenopausal women with various derivatives were diagnosed with uterine and ovarian cancer as a result of clinical-functional-hormonal-morphological research. Magnetic resonance imaging was performed on those women to determine the characteristics of changes in the tissues of the pelvic organs.

Based on the results of MRI-examinations, filling derivatives of the endometrial cavity (n=16) were found in women with uterine sarcoma. The length of the stems of the derivatoves was 48.2±3.14 (30-100), and the width was 27.6±6.7 (16-51) mm. There were detected lymph nodes in both iliac glands. The size of the lymph nodes was 15.25±4.0 (7-40) mm. Myomatous nodes were found in 4 out of 16 patients (25%) with uterine cancer. The length of the nodes was 25.5±4.2 (13-44) mm and the width was 20.38±1.31 (8-35) mm. In women with uterine sarcoma the thickness of the endometrium was 19.64±2.1 (8-23) mm. The sizes of the ovaries were larger than the ones of the postmenopausal women without complications.

The size of endometrium-related derivatives was 31.6±3.39 (24-58) mm, and the size of lymph nodes in both iliac glands was 10.25±0.85 (8-12) mm in women with endometrial cancer (n=20). The thickness of the endometrium was 15.81±1.68 (11-19) mm.

According to echographic indicators of ultrasound scan, the sizes of derivatives in the right and left ovaries practically do not differ in women with ovarian cancer (n=7). Simultaneously, in the omentum and peritoneum of 3 out of 7 patients there were detected

nodes of 12.0±1.2 mm diameter and metastases.

The endometrial thickness dimensions of the uterus and both ovaries of women with cervical cancer (n=8) did not differ practically with the echographic indicators of the ultrasound scan. Meantime, enlarged lymph nodes (average size 11.98±0.96 mm) were detected in the iliac glands of 5 patients.

Hence, magnetic resonance imaging should be performed in postmenopausal women with neoplastic derivatives of reproductive organs. The exact dimensions of the thickness of the endometrium of the uterus, ovaries, and regional lymph nodes determine the extent of the neoplastic process by this examination method. And this helps define the extent of the surgical operation.

Features of light microscopic and electron microscopic images of the endometrium in the derivatives of the reproductive organs in the postmenopausal period. In the course of the study, there were determined images of the endometrium of women with 10 different localized genital warts by light microscopic and electron microscopic methods.

It was found that, 1 (10%) of 10 women with various derivatives in the postmenopausal period had ovarian carcinoma, 6 (60%) myoma, 1 (10%) uterine sarcoma, and 1 (10%) endometrial hyperplasia. Endometrial sections of 1-mm - 10-mm thick were prepared for conducting electron microscopic examination in all patients. A section of the endometrium was taken regardless of the type of tumor.

As per the light and electronic images, 5 women with myoma were found to have complex endometrial hyperplasia, and 1 a polyp associated with simple endometrial hyperplasia.

Women with ovarian carcinoma and endometrial hyperplasia were found to have degenerative endometrial hyperplasia. Complex endometrial hyperplasia was determined by light microscopic images. The light microscopic structure of the endometrial lining, glandular epithelium and stromal cells, including the part where connective tissue components were found is described in Figure 3. The latter can be evaluated as an ultrastructural sign of the acceleration of the proliferative process in the epithelial cells of the

mucous membrane of the uterus.

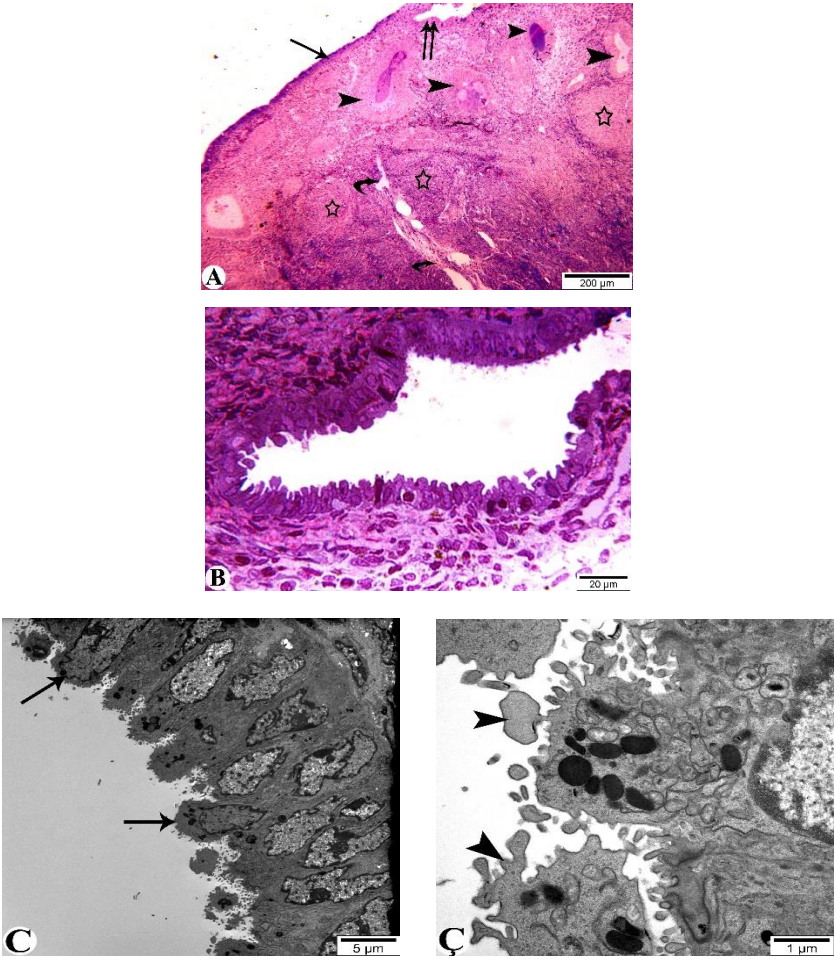

Figure 3. Light microscopic images of the lining epithelium of the uterus, glandular epithelial arrangements of different shapes and content (A), and the fold (B) formed by the lining epithelium, as well as electron microscopic images of elevations (pinopods – C, Ch), micropiles and cilia (D, E) located on the luminal surfaces of the lining epithelium.

Thus, based on the electron microscopic images, the complex endometrial hyperplasia in the postmenopausal period suggests that it is a complex endometrial hyperplasia without signs of atypia observed by the location of epithelial components in a morula-like form and the proliferation of stromal elements.

There was determined a polyp in one woman by light and electron microscopic images in the context of simple hyperplasia. As per these images, along with glandular elements of different shapes and progress, the existence of cyst cavity-like enlargement in the lower right part of the photomicrograph and the predominance of stromal elements are generally accepted as symptoms characteristic of endometrial polyps. When examining the gland structures, it was found out that along with the areas where the integrity of the epithelial cover was maintained, there were also surfaces that had undergone desquamation. The fact that the main mass of the polyp is composed of bundles of collagen fibers located in different regions and connective tissue components dominated by spindle-shaped stromal cells allows to diagnose a polyp for being clearly visible during light or electron microscopic examination.

In complex endometrial hyperplasia, which is not observed with atypia, changes in the structures of the uterine glands can be detected using light and electron microscopy. Based on the light and electron microscopic images, the first noticeable thing in the material taken from the endometrium is that epithelial elements involved in the formation of glandular structures cover a wider area compared to the stromal elements located within the special surface of the mucous layer of the uterus. As it can be seen from Figure 3.8.7A, although stromal elements are identified in the form of a thin strip, there are not detected any stromal elements between some glands by light microscopy.

Only few of the epithelial cells surrounding the deformations of the endometrial glands preserve their prismatic shape. In the latter, most of such nuclei have a vague shape.

As a result of electron microscopic examination, it was determined that inflammatory changes in degenerative and chronic deseases were noticed in the context of simple and complex

endometrial hyperplasia. And this is proved by the determination of plasmatic cells located in groups inside the stromal elements.

RESULTS

1. It was determined that in the postmenopausal period, 30% of women with various derivatives had myoma, 17.7% endometrial hyperplasia, 13.1% ovarian tumor-like derivatives, 15.4% endometrial cancer, 12.3% uterine sarcoma, 6.2% cervical cancer, and 5.4% ovarian cancer [1,5,6,7].

There were observed benign (36.8%) and invasive (34%) neoplasias with a high frequency and preinvasive (21.7%) neoplasias with a relatively less frequency in the uterus in the postmenopausal period.

In the postmenopausal period, 26.2% of women with various derivatives had no complaints, and 73.8% had multiple complaints with different frequencies.

2. In postmenopausal women with various derivatives of the reproductive organs, Prolactin (756.1±83.37 ng/ml), Dehydroepiandesterone sulfate (125.83±10.89 ng/dl), and Estrone (97.0±2.89 pg/ml) were increased and Estradiol (13.91±1.41 pg/ml), Progesterone (0.29±0.04 ng/m), and Testosterone (0.17±0.01 ng/ml) wered decreased [2,4,9,10].

3. An increase is observed in CA-125 oncomarker (50.01±12.32 U/ml), Estriol (0.89±0.4 ng/ml), and Cytomegalovirus IgG (723, 39±150.0) in the diagnoses of various derivatives of the uterine, endometrium, and ovaries in the postmenapausal period. In this period, it is reasonable to note the high level of CA-125, Cytomegalovirus IgG as a diagnostic criterion in invasive diseases of reproductive organs [2,3,9,10].

4. Endometrial hyperplasia is observed in the postmenopausal period regardless of benign, preinvasive, and invasive derivatives of the reproductive organs. Endometrial hyperplasia occurred with a frequency of 17.7% as an independent nosological unit and as per the ultrasound scan, the thickness of the endometrium was 15.58±1.53 mm. This indicator was 22.74±1.75 mm in uterine sarcoma, 14.64±1.31 mm in endometrial cancer, 13.63±0.56 in myoma,

11.1±1.64 mm in ovarian tumor-like derivatives, 7,98±2.48 mm in ovarian cancer [1,7,11,12].

5. Magnetic Resonance Imaging in postmenopausal women determines the exact dimensions of the uterus, ovaries, and derivatives, as well as the thickness of the endometrium, the size of the regional lymph nodes, and the extent of metastasis of neoplastic processes, which allows planning the scope of the surgical intervention [3,4,5,8].

6. Electron microscopic examination revealed simple endometrial hyperplasia accompanied by the presence of desquamated areas in the epithelial structure with predominant stromal components. There is observed the location of epithelial components in a morula-like form, the proliferation of stromal components and the absence of atypia symptoms in complex hyperplasia. As per electron microscopy, the polyp obviously shows itself with the predominant collagen fibers and spindle-shaped stromal cells located in different regions. Inflammatory changes in degenerative and chronic deseases are visible in both simple and complex endometrial hyperplasia [5,6,7,8].

PRACTICAL RECOMMENDATIONS

1. Taking into consideration the neurohormonal changes in all postmenopausal women, it is necessary to conduct ultrasound scan in dynamic range as a screening method.

2. Based on the ultrasound scan, the pathological increase in the thickness of the endometrium proves the presence of benign, preinvasive, and invasive derivatives of the endometrium and reproductive organs.

3. It is reasonable to determine prolactin, androgen, estrone and blood sugar levels in women with endometrial hyperplasia, regardless of their origin.

4. In postmenopausal women with endometrial hyperplasia, regardless of their origin, it is imperative to conduct magnetic resonance imaging. As a result of the radiological examination, the extent of metastasis of neoplastic process allows to define the exact size of the derivatives and determine the scope of the surgical intervention.

The list of published scientific works related to the content of the dissertation:

1. Əliyeva E.M., Qaraşova M.A., Sultanova S.H., Məmmədova S.M. Postmenopauzal dövrdə müxtəlif törəmələri olan qadınlarda ultrasəs müayinəsinə görə endometriumun qalınlığının dəyişmə xüsusiyyətləri // Az.Resp.SN, ATU ə.e.x., prof. A.Ə.Axundbəylinin anadan olmasının 80 illik yubileyinə həsr olunmuş elmi konfransın materialları, – Bakı: 2018. – s. 148-149.
2. Əliyeva E.M., Qaraşova M.A., Sultanova S.H., Məmmədova S.M. Postmenopauzal dövrdə uşaqlığın neoplastik proseslərində hormonların dəyişmə xüsusiyyətləri // Təbabətin aktual preblemləri, – Bakı: 2018. №3, – s. 93-95.
3. Əliyeva E.M., Qaraşova M.A., Sultanova S.H., Məmmədova S.M. Postmenopauzal dövrdə reproduktiv orqanların xoşxassəli preinvaziv şişləri və şişəbənzər törəmələrinin exoqrafik göstəricilərinin xüsusiyyətləri // Sağlamlıq, – 2018. №6, – s. 72-76.
4. Гарашова М.А., Алиева Э.М., Султанова С.Г., Мамедова С.М. Состояние гипоталамо-гипофизарно-надпочечниково-яичниковой системы у женщин с опухолями и опухолевидными образованиями органов репродуктивной системы в постменопаузальный период // Здоровье женщины, – Киев: – 2018. №7, вып.133, – с. 96-99.
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7. Əliyeva E.M., Qaraşova M.A., Məmmədova S.M. Postmenopauzal qanaxmalara səbəb olan endometriumun hiperplastik prosessləri // Ümummilli lider H.Ə.Əliyevin ad gününə həsr olunmuş elmi-praktik konfransın materialları, – Bakı: – 2018. – s. 114-115.
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10. Əliyeva E.M., Qaraşova M.A., Sultanova S.H., Məmmədova S.M. Postmenopauzal dövrdə reproduktiv orqanların müxtəlif törəmələrinin diaqnostikasında onkomarkerlərin və sitomeqalovrusun göstəricilərin informativliyinin xüsusiyyətləri // Müasir ginekologiya və perinatologiyanın aktual məsələləri, – 2019, №1, – s. 34-35.
11. Məmmədova S.M. Postmenopauzal dövrdə endometriumun, yumurtalıqların, uşaqlıq boynunun xərçəngində reproduktiv orqanların exoqrafik göstəricilərinin xüsusiyyətləri // Müasir ginekologiya və perinatologiyanın aktual məsələləri, – 2019. №1, – s. 34-35.
12. Garashova M.A., Aliyeva E.M., Abbasova F.Y. Mammadova S.M. Obesity as a risk factor of endometrial cancer in postmenopausal women // XVIII İnternational Europain Congress of Surgery and Hepatogastroenterology, – 2019. – 11-14 september, – p. 353.

List of Acronyms

ALT – Alanine Aminotransferase
AST – Aspartate Aminotransferase
DHEA-S – Dehydroepiandrosterone-sulfate
CT – Computer Tomography
LH – Luteinizing Hormone
MRI – Magnetic Resonance Imaging
P – progesterone
Prl – prolactin
UC – uterine cancer
T – testosterone
USS – ultrasound scan
FSH – Follicle-stimulating Hormone
E1 – estrone
E2 – estradiol
CA-125 – Cancer Antigen 125
SMV IgG - Cytomegalovirus

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Address: A.Gasimzade st. 14, AZ 1022, Baku, (conference hall).

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