Abstract. Goal. To evaluate the effectiveness of Dostinex in the treatment of infertile women with hyperprolactinemia.

Methods. We examined 50 women of reproductive age with functional hyperprolactinemia, suffering from endocrine infertility and with completely excluded male factor of infertility. Inclusion criteria: female age ≥19 years and <42 years; history of infertility over one year. The control group consisted of 30 women with a history of spontaneous pregnancies, who did not have infertility, reproductive losses, or increased prolactin levels. All patients were assessed for total prolactin by Macro ELISA using the Access 2 laboratory system. Hyperprolactinemia was diagnosed with prolactin levels above 25 ng/ml. When diagnosed with hyperprolactinemia, Dostinex was prescribed. The dose and duration of the drug were determined individually, taking into account the initial level of prolactin. The criteria for discontinuation of the drug were reduction/normalization of prolactin levels in the blood, cessation of galactorrhea, normalization of the menstrual cycle, and restoration of ovulation.

Results. In hyperprolactinemia, regardless of the cause, the key link is an increase in prolactin levels. The basal level of prolactin in the blood plasma of patients with functional hyperprolactinemia varied widely – from 37.6 ng/ml to 100.5 ng/ml. The average value was 63.6±3.49 ng/ml. The average prolactin level in women in the control group was 20.8±1.29 ng/ml (p<0.001).

In order to reduce the level of prolactin, all patients were prescribed the drug Dostinex. Taking into account the individual initial level of prolactin, the average therapeutic dose of the drug was determined, which was 0.35±0.1 mg per week. To obtain a clinical effect, 26 (52.0%) patients had enough 0.25 mg, and 24 (48.0%) - 0.5 mg of the drug per week. In patients treated with Dostinex, changes in the dynamics of treatment related to the following laboratory parameters. The PRL level decreased 2.3 times (28.2±0.76 ng/ml vs 63.6±3.49 ng/ml before treatment; p<0.001). The study of the effectiveness of therapy with Dostinex after 1 month of therapy showed that the level of prolactin in the observed patients was within the laboratory norms in 43 (86.0%) patients. In 7 (14.0%) patients whose prolactin values did not reach laboratory standards after one month, it returned to normal after 3 months.

Conclusion. Drug therapy of hyperprolactinemia with Dostinex allows to achieve a normal level of prolactin, normalize menstrual function, and eliminate galactorrhea in all observed patients.

Key words: infertility, prolactin, hyperprolactinemia, treatment, Dostinex.

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CLINICAL AND DIAGNOSTIC ASPECTS OF GENITAL ENDOMETRIOSIS IN WOMEN OF REPRODUCTIVE AGE

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The connection of the publication with planned research works. This work is a fragment of the dissertation for the degree of Doctor of Philosophy in medicine "Clinical and diagnostic aspects of optimal diagnosis of genital endometriosis in women of reproductive age»

Introduction. In recent years, special attention has been paid to the problem of women's reproductive health. The issues related to the study of genital endometriosis (GE) in women of reproductive age are of particular relevance and practical significance from the point of view of the modern view of this problem [1, 2, 3]. It is known that the frequency of genital endometriosis varies from 12 to 60% according to various literature sources. Endometriosis occupies the third place in the structure of gynecological diseases [4]. The relevance of the study of pathology is associated not only with the high frequency of occurrence [5].

Despite numerous studies devoted to various aspects of endometriosis, many questions related to both the features of the clinical picture, depending on the localization of the process, and the issues of modern and informative diagnosis and treatment, which is of fundamental practical importance, remain open. These issues are caused by a number of factors: 1) long-term, chronic and recurrent course of GE, leading to the suppression of the reproductive function of women; 2) the tendency to a steady and progressive growth of endometrioid heteropathies with a subsequent rapid spread in the body, the development of serious complications from other organs and systems, eventually leading to organ loss in the reproductive system; 3) a decrease in working capacity, a change in the psychoemotional sphere and a deterioration in the quality of life of a woman [6, 7].

Currently, laparoscopy is recognized as the most informative and indispensable method of diagnosing GE [8]. The effectiveness of this method is not only in the diagnosis of genital endometriosis, but also infertility of uncertain origin, etc. At the same time, the use of laparoscopy for therapeutic purposes in infertility is also relevant. Undoubtedly, the significance of the use of laparoscopy is not in doubt, since diagnostic findings of pathology on the part of the pelvic organs in the form of external GE or adhesive process in the pelvis, obstruction of the fallopian tubes, etc., allows it to be used as a method for expert analysis in the most difficult diagnostic situations.

Thus, genital endometriosis is the leading medical and social problem of modern gynecology and indicates the feasibility of conducting a comprehensive clinical and instrumental study of women of reproductive age with this pathology.

The purpose of the study. To evaluate the effectiveness of modern, informative methods for optimal diagnosis of genital endometriosis.

Object and methods of the research. The study involved 120 women of reproductive age with genital endometriosis. To achieve this goal, the following methods were used: clinical, laboratory (blood and urine tests, biochemical studies, coagulogram, bacteriological and microscopic studies of the separated cervical canal and vagina, cytological studies); instrumental and special research methods. Clinical studies included: collection and study of the features of the obstetric and gynecological history of patients, standard gynecological examination and retrovaginal examination; assessment of the state of health by functional systems. The following scales were used: the visual-analog scale (VAS) according to the recommendation of IMMPACT (1998) for the quantitative assessment of pain symptoms; scale of the MacLaverty S. M., Shaw R. W. (1995), for determining the cause of pelvic pain (nature, frequency of occurrence); the McGill pain questionnaire (MPQ) (1986) modified by Kuzmenko V. V.; the classification of Hulka J. F., Reicli H. (1998) was applied to determine the severity of the adhesive process of the pelvic organs. The stages of the spread of endometriosis were evaluated according to the following classifications: American Association of Gynecological Laparoscopists (AAGL), combining the r-AFS classification (1996) and the severity of clinical symptoms; ENZIAN (2012, revised in 2019), reflecting the localization, stages of development and depth of the spread of genital endometriosis (According to the Endometriosis Research Foundation, SEF). Individual maps were developed.

Instrumental methods of investigation included: colposcopy (according to indications); transvaginal and transabdominal ultrasound of the pelvic organs (the device "LOGIK 500GE" and "MEDISONSA-8000" Korea with the use of electronic sensors with a frequency of – 5; 7 MHz on the 6-7 day of the menstrual cycle); urography (according to indications); X-ray examination (RH) of the pelvic organs; hysterosalpingography (according to indications); hysteroscopy (assessment of the state of the uterus and fallopian tubes). A consultation of narrow specialists was held: an endocrinologist, a therapist, a gastroenterologist according to the indications. We also used laparoscopy to diagnose the genital form of endometrioid disease. For statistical analysis, a biometric method was used (the software package "STATISTICA-10", the graphs were built using "ORIGN-6.1").

The results of the study and their discussion. The study included 120 patients with genital endometriosis, the average age of women was 35±15 years. The examined patients were divided into the following groups: group I (retrospective studies) consisted of n=70 patients with genital endometriosis; group II (prospective studies) consisted of n=50 patients with this disease; group III (CG) consisted of n=30 conditionally healthy fertile women without this pathology. Clinical, laboratory and diagnostic examinations of patients revealed the following forms of genital endometriosis: peritoneal endometriosis was detected in 51 (42.5%) cases; extraperitoneal endometriosis – in 38 (31.7%) cases; endometriosis of the uterine body – in 19 (15.8%) cases; retrocervical endometriosis was noted in 12(10%) cases, respectively.

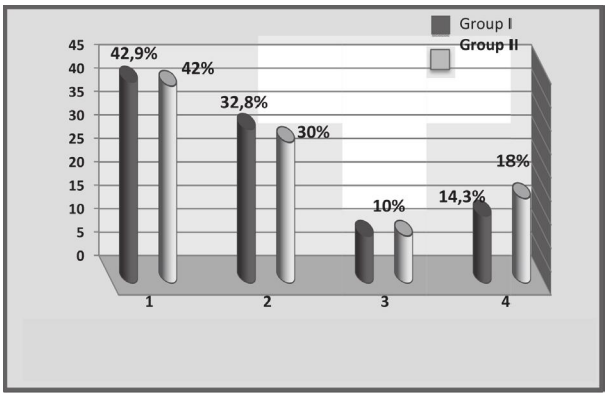

Figure 1 – Endometriosis distribution diagram depending on the form of localization

Statistical analysis of the frequency of detection of endometriosis in the compared groups, depending on the form of localization, in the examined patients did not reveal significant differences. Thus, in both main groups, peritoneal endometriosis was observed with almost the same frequency in 30 (42.9%) and 21 (42%) cases, respectively **(Figure 1)**. Ovarian endometriosis was also detected with the same frequency in 12 (17.2%) and 9 (18%) cases in groups I and II, respectively. Endometrioid ovarian cysts were observed in 15 (21.4%) cases in group I and 10 (20%) cases in group II. Endometriosis of the fallopian tubes was detected in 3 (4.28%) and 2 (4%) cases in both groups.

Endometriosis of the uterine ligaments was diagnosed in 4 (5.7%) cases in group I and 2 (4%) cases in group II. Retrocervical endometriosis was detected with the same frequency in both groups I and II, respectively. Endometriosis of the uterine body (adenomyosis) was diagnosed in 9 (18%) cases in group II and 10 (14.3%) cases in group I. It should be noted that the forms of endometriosis were diagnosed with almost the same frequency, taking into account the localization in the examined patients in accordance with the main groups.

Using the ENZIAN classification was estimated parameters of the area and depth of endometrial heteropathy, which were expressed in points **(Fig. 2)**: stage I indicates minimal endometriosis in 1-5 points was observed in 42 (35%) patients, stage II, representing light endometriosis was evaluated in the range of 6-15 points in 47 (39,2%), stage III showed moderate endometriosis and evaluated on a scale 16-40 points respectively in 29 (24.2%) of patients with stage IV presented severe endometriosis, which was assessed on a scale of more than 40 points were noted in 2 (1,6%) cases **(Fig. 2)**. Comparative analysis of anamnestic data on menstrual

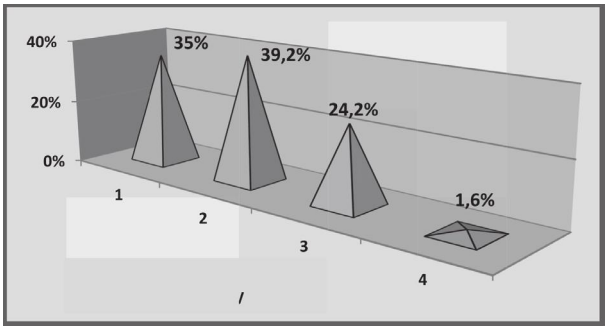

Figure 2 – Diagram of the distribution of endometriosis depending on the stage of spread

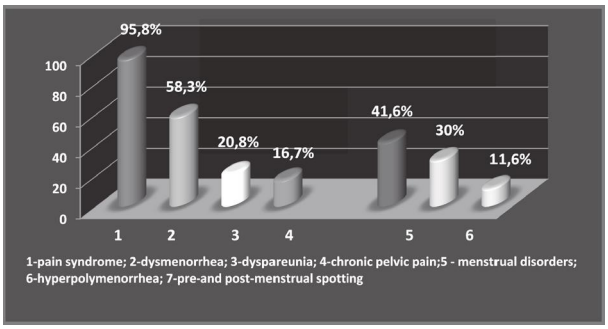

Figure 3 – Diagram of the frequency of clinical manifestations in the observed patients with genital endometriosis

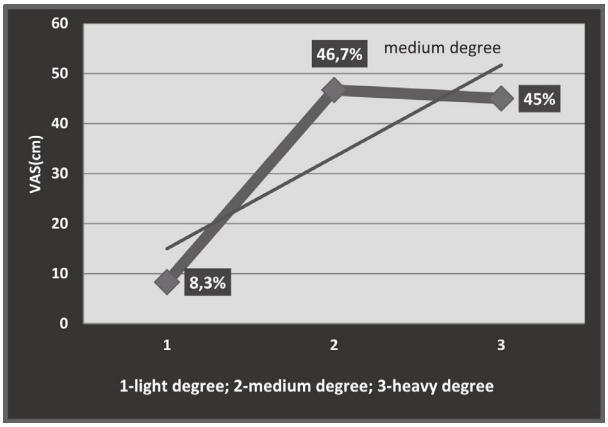

Figure 4 – Diagram of pain syndrome as a function of intensity in patients with genital endometriosis on the scale of VAS and MacLaverty S. M., Shaw R. W.

function showed that the time of onset of menstruation (menarche) ranged from 11 to 14 years. The mean age of the menarche in connection was almost the same in the study groups: 12.5±1.5 years; 12.6±1.6 years, respectively.

The duration of menstrual bleeding was normal for 4-6 days in 52 (43.3%) cases, in 49 patients, which was 40.8% of cases, there were abundant, prolonged menstruation, in 19 (15.8%) cases, the cycle duration was unstable and ranged from 11 to 32 days. It should be noted that in most patients, menarche was accompanied by pain of varying intensity and stability, which contributed to the use of analgesic drugs.

A comparative analysis of the anamnesis of all patients showed that among the extragenital diseases, the first place was occupied by endocrine diseases in 31 (25.8%) cases, among which diabetes mellitus 13 (10.8%) and thyroid diseases (hypothyroidism, goiter) 18 (15%) cases were registered, respectively. In the second place, diseases of the urinary system were noted, which accounted for 21 (17.5%) cases, the prevailing pathology among them was pyelonephritis 11 (9.2%) and cystitis – 10 (8.3%) cases. Diseases of the gastrointestinal tract were also observed in 18 (15%) cases; hyperacid gastritis was mainly observed in 12 (10%) and cholecystitis in 6 (5%) cases.

All the variety of clinical manifestations were grouped into 3 groups: pain syndrome -115 (95.8%) cases; menstrual disorders – 50 (41.6%) and infertility (St I; St II) -37(30.8%) cases. It should be noted that in the majority of patients, 72 (60%), the symptoms of the disease were combined in various combinations. In the isolated form, the symptoms occurred in 48 patients, which accounted for 40% of cases. The frequency of clinical manifestations of the disease in the studied groups is shown in the diagram **(Fig. 3).** The study groups did not differ significantly in the frequency of the leading symptoms. According to the conducted studies, pain syndrome was observed in all forms of endometriosis – 67 (95.7%) cases in group I and 48 (96%) in group II, which was presented as dysmenorrhea in 42 (60%) cases and 28 (56%) cases in group I and II, respectively. Dyspareunia and chronic pelvic pain occurred in almost every 5th patient, while 14 (20%) cases were observed in group I patients and 11 (22%) cases in group II, respectively. The frequency of chronic pelvic pain not associated with menstruation was noted in 11 (15.7%) cases in groups I and 9 (18%) in groups II, respectively. The intensity of the pain syndrome was estimated by us on a visual-analog scale (VAS, 1998), which allowed us to quantify the pain symptoms in this cohort of patients: mild (1-3 points) of the pain experienced was observed in 54 (45%) patients, moderate (4-7 points) – in 56 (46.7%), severe (unbearable pain – 8-10 points) – in 10 (8.3%) patients. **Figure 4** shows the results of assessing the intensity of pain syndrome according to VAS and on the MacLaverty S. M., Shaw R. W. scale. A systematic assessment of the cause of pain and their intensity (before the start of therapy) was carried out. It should be noted that the pain intensity averaged 7 cm in the study groups.

Unbearable pain was observed in patients requiring mandatory administration of analgesics in 10 (8.3%), which were more often observed in patients of both groups: 7 (10%) in group I, while in group II it was noted only in 3 cases, which was 6%, respectively. Moderate pain, in patients who periodically use analgesics, was observed with almost the same frequency in both groups: in group I – 29 (41.4%) cases, in group II – 27 (54%), respectively. Mild pain that did not require analgesics was observed in 34 (48.6%) patients in group I, while in group II it was observed in 20 (40%) patients. It should be noted that infertility was detected in 30% of cases and was found among women with a combined form of endometriosis and retrocervical endometriosis, who suffered from primary infertility. Infertility was found in endometriosis of the ovaries, fallopian tubes, and pelvic peritoneum. In infertility, endometriosis is diagnosed on average within 3-4 years from the diagnosis of infertility. Primary and secondary infertility was most often observed in women with a combined form of endometriosis. It should also be noted that many patients, 32%, did not seek medical help for 2 years, due to the fact that they did not associate painful menstruation with endometriosis and continued to take painkillers. The study of pain intensity depending on the location showed that in ovarian endometriosis, it was higher on average by 1.5-1.7 cm compared to other forms of external endometriosis. In a two-handed gynecological study, changes in the internal genitalia were detected in 100% of cases.

As our studies have shown, in the majority of patients in 82 (68.3%) cases with external GE, the uterus was of normal size. Peritoneal endometriosis was most characterized by tumor-like formations in the appendages of 34 (66.6%) of a tight-elastic consistency, with a smooth surface, limited mobility and painful on palpation. Endometrioid cysts were unilateral in 21 (41.2%) cases, and bilateral in 13 (25.4%)

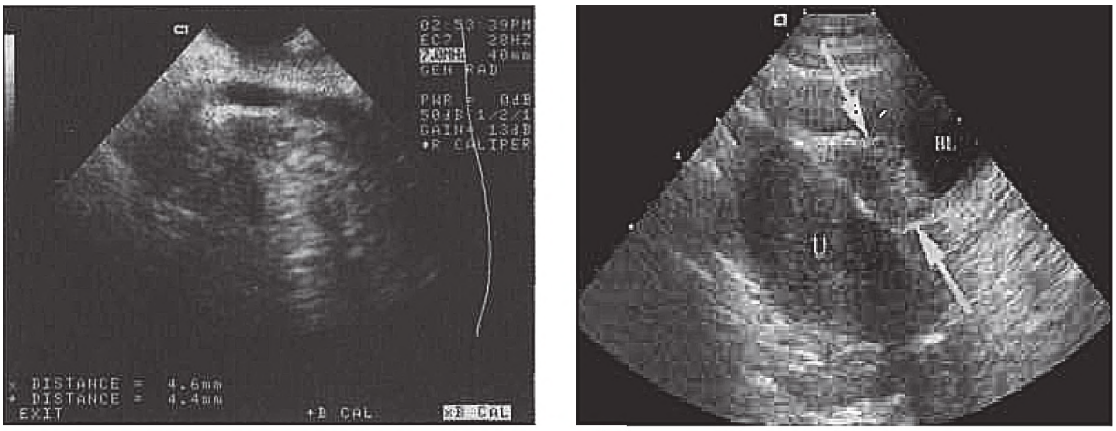

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Figure 5 (a; b) – Ultrasound. Structural changes of the endometrium and myometrium in patients with endometriosis on ultrasound (own observation)

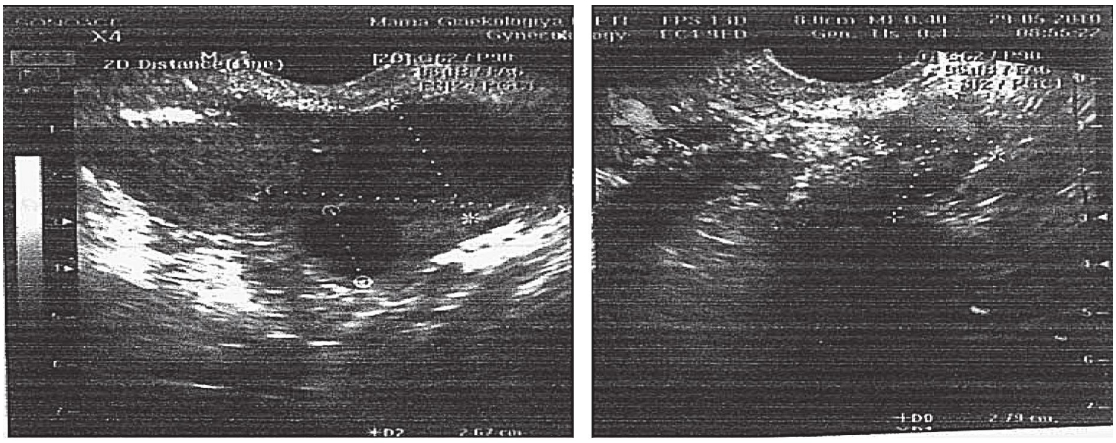

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Figure 6 (a; b) – Ultrasound. Dense tumor in a patient with endometriosis (own observation)

cases. Retrocervical endometriosis was characterized by tension of the sacro-uterine ligaments in 7 (58.3%) cases and pain in the posterior arch 7 (58.3%). The extraperitoneal form of endometriosis was most characterized by tension and compaction of the sacro-uterine ligaments 21 (55.3%).

With combined endometriosis, retroflexia of the uterus was most often determined 12 (10%), in contrast to other localizations. Round or oval formations of 1-2 cm were detected in 6 (5%) cases; 2-4 cm in 16 (13.3%) cases; 4-6 cm in 19 (15.8%); 6-8 cm in 5 (4.2%) cases. **Figure 5 (a, b)** shows structural changes in the endometrium and myometrium in patients with endometriosis during ultrasound examination. **Figure 6 (a, b)** shows an ultrasound picture of a patient with genital endometriosis, where a dense tumor is visualized. According to the ultrasound picture, inhomogeneous echostructural changes in the retrocervical fiber, as well as formations with uneven edges, were visualized.

Conclusions. Genital endometriosis is a recurrent disease characterized by a chronic course with a tendency to rapid progression, which leads to a violation of the reproductive ability of women and a decrease in their quality of life.

Prospects for further research. It is planned to further improve the diagnosis and treatment of genital endometriosis.

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КЛІНІЧНІ ТА ДІАГНОСТИЧНІ АСПЕКТИ ГЕНІТАЛЬНОГО ЕНДОМЕТРІОЗУ У ЖІНОК РЕПРОДУКТИВНОГО ВІКУ

Бадалова А. А.

Резюме. *Мета*. Оцінити ефективність сучасних інформативних методів для оптимальної діагностики генітального ендометріозу.

Об'єкт і методи дослідження. У дослідженні приймали участь 120 жінок репродуктивного віку з генітальним ендометріозом. Були застосовані наступні методи: клінічні, лабораторні, інструментальні. Було розроблено індивідуальні карти.

Інструментальні методи дослідження включали: кольпоскопію; трансвагінальне та трансабдомінальне ультразвукове дослідження органів малого тазу (апарат «LOGIK 500GE» та «MEDISONSA-8000», Корея); урографія; рентгенологічне дослідження (RH) органів малого тазу; гістеросальпінгографія; гістероскопія (оцінка стану матки та маткових труб).

Результати дослідження та їх обговорення. Обстежувані пацієнтки були розподілені на відповідні три групи: I групу (ретроспективне дослідження) склали n=70 пацієнток з генітальним ендометріозом; II групу (проспективне дослідження) складали n=50 пацієнток з даним захворюванням; III контрольну групу (КГ) склали n=30 умовно-здорових фертильних жінок без даної патології. При проведенні клінічно-лабораторних та діагностичних досліджень хворих виявили наступні форми генітального ендометріозу: перитонеальний ендометріоз було виявлено в 51 (42,5%) випадках; екстраперитонеальний ендометріоз – в 38 (31,7%) випадках; ендометріоз тіла матки – в 19 (15,8%) випадках; ретроцервікальний ендометріоз – в 12 (10%) випадках відповідно.

Отримані результати підкреслюють, що генітальний ендометріоз є рецидивуючим захворюванням, що характеризується хронічним перебігом зі схильністю до швидкого прогресування, що призводить до порушення репродуктивної здатності жінок та зниження якості їхнього життя.

Висновки. Генітальний ендометріоз будь-якої локалізації має схильність до швидкого прогресування, що досить часто є причиною зниження якості життя жінки, а також може негативні наслідки для репродуктивної функції.

Ключові слова: генітальний ендометріоз, ультразвукове дослідження органів малого тазу, лапароскопічна діагностика.

CLINICAL AND DIAGNOSTIC ASPECTS OF GENITAL ENDOMETRIOSIS IN WOMEN OF REPRODUCTIVE AGE

Badalova A. A.

Abstract. The purpose of the study. To evaluate the effectiveness of modern informative methods for optimal diagnosis of genital endometriosis.

Object and methods of the research. The study involved 120 women of reproductive age with genital endometriosis. The following methods were used: clinical, laboratory, and instrumental. Individual maps were developed. Instrumental methods of examination included: colposcopy; transvaginal and transabdominal ultrasound of the pelvic organs (the device "LOGIK 500GE" and "MEDISONSA-8000", Korea); urography; X-ray examination (RH) of the pelvic organs; hysterosalpingography; and also hysteroscopy (assessment of the state of the uterus and fallopian tubes).

The results of the study and their discussion. The examined patients were divided into the corresponding groups: group I (retrospective studies) consisted of n=70 patients with genital endometriosis; group II (prospective studies) consisted of n=50 patients with this disease; group III (CG) consisted of n=30 conditionally healthy fertile women without this pathology. Clinical, laboratory and diagnostic examinations of patients revealed the following forms of genital endometriosis, such as: peritoneal endometriosis that was detected in 51 (42.5%) cases; extraperitoneal endometriosis was in 38 (31.7%) cases; endometriosis of the uterine body - in 19(15.8%) cases; retrocervical endometriosis was noted in 12 (10%) cases, respectively.

The obtained results emphasize and show us that genital endometriosis is a recurrent disease, characterized by a chronic course with a tendency to rapid progression, leading to a violation of the reproductive ability of women and a decrease in their quality of life.

Conclusions. Genital endometriosis of any localization has a tendency to rapid progression, which is often the cause of reduced quality of life in women, and can also cause impaired reproductive function.

Key words: genital endometriosis, pelvic ultrasound, laparoscopic diagnosis.

Рецензент – проф. Тарасенко К. В.

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