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НОВЫЙ ДЕНЬ В МЕДИЦИНЕ
NEW DAY IN MEDICINE**

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www.bsmi.uz
<https://newdaymedicine.com> E:
ndmuz@mail.ru
Тел: +99890 8061882

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ECTOPIC PREGNANCY – A NEW LOOK AT THE PROBLEM

*Khamdamova M.T. <https://orcid.org/0000-0003-3128-6120>
Khakimboeva K.A. <https://orcid.org/0000-0002-2267-3922>*

Bukhara State Medical Institute named after Abu Ali ibn Sina, Uzbekistan, Bukhara, st. A. Navoi.
1 Tel: +998 (65) 223-00-50 e-mail: info@bsmi.uz

✓ **Resume**

Quality of life indicators in patients with acute gynecological diseases significantly differed from baseline data as early as 6 months after surgery, and by 12 months, they had even more closely approximated normal values. Moreover, in the group of patients undergoing fast-track surgery, the differences were more pronounced.

Keywords: ectopic pregnancy, rare forms of ectopic pregnancy, fertility restoration.

ВНЕМАТОЧНАЯ БЕРЕМЕННОСТЬ – НОВЫЙ ВЗГЛЯД НА ПРОБЛЕМУ

*Хамдамова Мухайё Тухтасиновна <https://orcid.org/0000-0003-3128-6120>
Хакимбоева К.А. <https://orcid.org/0000-0002-2267-3922>*

Бухарский государственный медицинский институт имени Абу Али ибн Сины, Узбекистан,
г. Бухара, ул. А. Навои. 1 Тел: +998 (65) 223-00-50 e-mail: info@bsmi.uz

✓ **Резюме**

Показатели качества жизни пациенток с острыми гинекологическими заболеваниями достоверно отличались от исходных данных уже через 6 месяцев после оперативного лечения, через 12 месяцев они еще больше приближались к нормативным значениям, причем в группе пациенток, оперированных с применением элементов «fast track surgery», отличия носили более выраженный характер.

Ключевые слова: внематочная беременность, редкие формы внематочной беременности, восстановление fertильности.

EKTOPIK HOMILALIK - MUAMMOGA YANGI QARISH

*Khamdamova M.T. <https://orcid.org/0000-0003-3128-6120>
Khakimboeva K.A. <https://orcid.org/0000-0002-2267-3922>*

Abu Ali ibn Sino nomidagi Buxoro davlat tibbiyot instituti, O‘zbekiston, Buxoro sh. A. Navoiy
kochasi 1 Tel: +998 (65) 223-00-50 e-mail: info@bsmi.uz

✓ **Rezyume**

O’tkir ginekologik kasalliklar bilan og’rigan bemorlarning hayot sifati ko’rsatkichlari operatsiyadan keyingi 6 oy ichida dastlabki ma’lumotlardan sezilarli darajada farq qildi va 12 oydan keyin ular odatdagagi qiymatlarga yaqinroq bo’ldi, farqlar “tezkor jarrohlik” elementlaridan foydalangan holda operatsiya qilingan bemorlar guruhibda aniqroq bo’ldi.

Kalit so’zlar: ektopik homiladorlik, ektopik homiladorlikning noyob shakllari, tug’ilishni tiklash.

Relevance

Ectopic pregnancy consistently ranks third to fourth among the leading causes of maternal mortality in industrialized countries, and fifth in the Russian Federation [1,2,14]. Discussion of this issue at the recent XIX World Congress of Obstetricians and Gynecologists (FIGO, 2009) showed that diagnosis, treatment selection, and surgical intervention require further improvement.

Ectopic pregnancy (EP) currently ranks second among acute gynecological diseases and first among nosological entities associated with intra-abdominal bleeding [1,3,10,11,12,13]. In recent years, due to the increasing incidence of inflammatory diseases and external genital endometriosis, there has been a clear trend toward an increase in ectopic pregnancy rates—more than doubling compared to research data from the 1970s, often with an atypical clinical course [1,4,5,8,9].

Among urgent gynecological surgeries, ectopic pregnancy (EP) ranks high, accounting for approximately 50% (9). In modern global healthcare, there is a "gold standard" for diagnosing fallopian tube ruptures (FB): priority is given to testing serum for the presence of beta-hCG in combination with transvaginal ultrasound to localize the trophoblast—either within or outside the uterus. However, despite advances in recent years in diagnosing FB, a high incidence of fallopian tube ruptures and intra-abdominal bleeding remains. These conditions necessitate radical surgery (removal of the fallopian tube), requiring lengthy and expensive rehabilitation. Subsequent complications of FB negatively impact women's reproductive function and quality of life.

The informative value of laparoscopy is currently both undeniable and debatable. A laparoscopic approach reduces the time required for differential diagnosis, allows for a visual assessment of the extent of the "catastrophe" in the abdominal cavity, and the selection of an appropriate treatment method [1,6,7]. However, this becomes possible only after a certain period of time, especially in tubal pregnancy: up to 2.5-3 weeks, a progressive tubal pregnancy does not deform the fallopian tube, which dramatically increases the rate of false-negative results. Endovideosurgery, a surgical method for treating tubal pregnancy, is a different matter, offering optimal benefits: fewer adhesions and greater opportunities for organ-preserving surgery [1,2,15].

Despite this, laparoscopic surgery has not yet become a priority in emergency medical care for patients with ectopic pregnancy; only 10% of surgical interventions in the country for this condition are performed endoscopically.

To date, the following issues remain poorly understood:

- Medical and organizational measures for early treatment; time parameters and diagnostic criteria for laparoscopy in progressive ectopic pregnancy.
- Reproductive function and quality of life in women who have had ectopic pregnancy.

Thus, despite belonging to the same nosological entity, different types of acute gynecological diseases have different etiologies. As a result, the pathogenesis of decreased reproductive function after surgery also varies, but some physiological aspects are quite similar. This allows, while remaining within the standards adopted by the Ministry of Health, to develop a unified strategy for more effective restoration of reproductive function in patients with acute gynecological diseases, which is in great demand in modern clinical practice.

The aim of the study was to optimize the tactics, diagnosis, treatment, and rehabilitation of patients with ectopic pregnancy using modern therapeutic, diagnostic, and organizational medical technologies.

Material and method

In accordance with the stated goal and objectives of the study, we examined and treated 69 patients with acute gynecological diseases of the uterine appendages.

All patients were subsequently divided into subgroups according to management tactics. Treatment and diagnostic measures for hospitalized patients were carried out according to a previously proposed model [4], which incorporated elements of "fast-track surgery" to reduce the stress response and organ dysfunction. Certain principles of the multimodal "fast-track surgery" strategy, such as minimally invasive surgical techniques, optimal postoperative pain relief, and "aggressive" postoperative rehabilitation, were incorporated into the proposed management algorithm to reduce the incidence of complications, accelerate rehabilitation, and improve the effectiveness of reproductive function restoration.



The first group consisted of 53 patients with tubal pregnancies who underwent standard rehabilitation in the postoperative period. The second group consisted of 16 patients with tubal pregnancies who underwent fast-track surgery and subsequent rehabilitation according to our proposed algorithm.

All studies were conducted in accordance with the principles of biomedical ethics set forth in the 1964 Declaration of Helsinki and its subsequent updates.

The study excluded patients with decompensated mental or extragenital diseases, malignant or autoimmune diseases, acute infectious or inflammatory diseases, or polyvalent allergies. Each patient participating in the study provided voluntary written informed consent, which she signed after explaining the potential risks and benefits, as well as the nature of the upcoming study. During laparoscopy, examination of the pelvic organs and abdominal cavity and description of the findings were performed according to the protocol of the American Association of Gynecological Laparoscopists (1985). The severity of the adhesion process in the pelvis was assessed according to the Hulka classification (1998), with the degree of involvement of the uterine appendages. After visual assessment of the pelvic organs, chromosalpingoscopy was performed by introducing a 0.5% indigo carmine solution into the uterine cavity and assessing the patency of the fallopian tubes.

Results and discussion

The results of the clinical and anamnestic analysis indicate that patients with acute gynecological diseases have a number of pathogenetically significant factors for reproductive health disorders: patients with intra-abdominal bleeding - younger age (69.6%), a high incidence of dysmenorrhea (27.6%), inflammatory diseases of the uterine appendages (41.6%) and benign diseases of the cervix (30.4%); In patients with impaired blood supply to the uterine appendages, there is a predominance of schoolchildren (19.0%), neglect of contraceptive methods (40.5%), a high frequency of menstrual cycle disorders such as menorrhagia (24.6%), a history of benign ovarian tumors (68.3%) and benign cervical diseases (23.0%), as well as a high incidence of acute respiratory viral infections (41.3%); in patients with GERD, the majority of patients (45.3%) belong to the older age group (35-43 years), preference for IUD as contraception (50.7%), a high frequency of PID (44.7%), intrauterine manipulations (27.3%) and appendectomies (48.7%) in the anamnesis.

One of the leading factors in the functional failure of pelvic organ tissues during organ-preserving surgeries is ischemia caused by thermal damage during surgery and subsequent edema, which leads to impaired trophism. This can have a decisive impact on follicle maturation and oogenesis, leading to irreversible loss of reproductive function [1]. For example, decreased and complete loss of fertility with age correlates with decreased ovarian blood flow [2004].

On the other hand, an increase in the vascularization index suggested more effective restoration of ovarian trophism and, consequently, preservation of a larger volume of functionally active tissue.

Therefore, we hypothesized that in the patient groups with rehabilitation, the number of antral follicles, as one of the biomarkers of ovarian reserve, would be higher than in the groups without rehabilitation. However, according to ultrasound data, there were no significant differences in ovarian volume or the number of antral follicles between the groups, regardless of the approach used.

Nevertheless, it should be noted that the number of antral follicles does not always reflect their maturity and, therefore, their ability to ovulate and subsequently fertilize. Hormonal dysfunction is expected in the early postoperative period, due to a decrease in the volume of receptive tissue for hormones from the anterior pituitary gland. After surgical treatment of patients with tubal pregnancy, ovarian apoplexy, uterine adnexal torsion, and purulent adnexal diseases, estradiol levels were higher (by 1.23, 1.45, 1.66, and 1.83 times, respectively), while follicle-stimulating hormone levels were lower (by 1.13, 1.42, 1.34, and 1.42 times, respectively) when using an optimized management strategy.

The growing oocyte in the follicle produces the paracrine growth factor

GDF9 (a member of the TGF β family of growth factors), which stimulates granulosa cell proliferation [3]. These follicular cells, in turn, secrete growth and differentiation factors, which, through a feedback mechanism, stimulate oocyte growth and promote the formation of blood vessels in the follicle area [4]. Among these factors produced by granulosa cells, anti-Müllerian hormone (AMH) stands out. It has recently been used much more frequently than inhibin B as a marker of ovarian reserve due to the latter's dependence on follicle-stimulating hormone (FSH) secreted by the anterior pituitary

gland. Furthermore, AMH as a marker has not only ascertaining value but also predictive [2], which is relevant for patients after tubectomy to assess the risk of ovarian hyperstimulation syndrome.

Therefore, anti-Müllerian hormone levels were measured on day 3 of the menstrual cycle in patients 3 months after surgery. As expected, in the tubal pregnancy group, regardless of the management and rehabilitation strategy used, AMH levels were within the age-appropriate norm (1-10.6 ng/ml), indicating a moderate level of ovarian reserve. However, in other groups, the use of optimized management and rehabilitation standards resulted in AMH levels remaining higher.

A statistical analysis of reproductive outcomes in patients managed using optimized standards and receiving rehabilitation therapy compared to the retrospective sample groups indicates an increase in the number of successful reproductive outcomes. The rate of successful pregnancies was highest in the comprehensive rehabilitation groups after tubal pregnancy and ovarian apoplexy procedures, accounting for almost half of all reproductive needs. It was almost twice as high compared to similar standard rehabilitation groups: 47.2% versus 17.8% for tubal pregnancy and 50.0% versus 28.4% for ovarian apoplexy, respectively ($p < 0.05$). Moreover, in the tubal pregnancy and comprehensive rehabilitation group, the rate of reproductive losses (negative outcomes) was almost two times lower ($p < 0.05$) than in the similar standard rehabilitation group: 13.9% versus 26.7%.

The results indicate that the combined use of early activation through fast-track surgery and physiotherapy procedures leads to a significantly more pronounced restoration of intraovarian blood flow, especially in cases of impaired blood flow, such as ovarian apoplexy. Furthermore, this recovery is sustainable, as evidenced by data obtained three months after surgery: patients managed according to the proposed approach had higher blood flow indices than those without it.

In virtually all study groups, we observed an increase in the vascularization-flow index, primarily due to an increase in the vascularization index. Furthermore, the proposed approach not only increased the number of positive reproductive outcomes but also significantly impacted the quality of life of patients after acute gynecological diseases. Regardless of the management strategy, patients' quality of life improved after just six months, with the differences being more pronounced in the groups of patients operated on using elements of "fast track surgery," approaching normal levels 12 months after surgery.

Thus, the approach used was quite successful due to its comprehensiveness: on the one hand, a key element of fast-track surgery, such as early activation and rehabilitation therapy, aimed to stimulate blood flow in the operated ovary and, consequently, improve its nutrition and conditions for follicle maturation, which is one of the key factors for the successful implementation of reproductive function. The obtained results demonstrate the possibility of using unified, physiologically sound rehabilitation methods for the etiology of various acute gynecological diseases. However, further improvement in the effectiveness of successful pregnancy can likely be based on personalized medicine approaches.

Conclusion

1. Patients with acute gynecological diseases have a number of pathogenetically significant factors for reproductive health impairment: younger age in patients with intra-abdominal bleeding; In patients with impaired uterine adnexal blood supply, this is due to neglect of contraceptive methods and a high incidence of benign ovarian tumors; in patients with pelvic inflammatory disease, this is due to the majority of patients belonging to an older age group and a preference for intrauterine contraception.

2. A comparative analysis of the vascularization index, blood flow index, and vascularization-flow index in the dynamics of intraovarian blood flow assessment in women after urgent surgery for acute gynecological diseases revealed a significantly less pronounced ($p < 0.05$) decrease in the groups with optimized standards of care and rehabilitation, especially in persistent chronic inflammatory diseases of the pelvic organs.

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