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Features of management of ovarian cystic lesions in puberty: literature review

M. Yu. Sergienko[1], V. H. Siusiuka[1], O. D. Kyryliuk[1, 2], N. Yu. Boguslavska[1, 2], O. A. Roslik[1], Yu. V. Rublyova[3]

[1]Zaporizhzhia State Medical and Pharmaceutical University
[2]MNPE "Territorial Medical Association "Healthy Family" of Zaporizhzhia Regional Council, Zaporizhzhia
[3]MNPE "City Children's Hospital No. 5" of Zaporizhzhia City Council, Zaporizhzhia

In gynecological practice, ovarian cysts are a pressing problem. According to the literature, their frequency is increasing, and the majority is represented by follicular cysts and *corpus luteum* cysts. Most abdominal neoplasms in girls and adolescent girls originate from the ovaries. Functional ovarian cysts in girls account for 60% of all ovarian lesions, while true neoplasms are rare. Frequency, clinical presentation and histological distribution of these lesions differ from those in adults and require a specific therapeutic approach. It is essential to determine the likelihood of malignancy when evaluating ovarian cystic masses in children, as treatment approaches for benign and malignant lesions differ significantly. The main tool for their visualization is ultrasound examination, which can assess the size, location, and characteristics of masses. Magnetic resonance imaging or computed tomography are used for further evaluation if ultrasound findings are inconclusive or if malignancy is suspected. Serum markers may be considered to help assess the risk of tumor malignancy. Surgery is indicated in cases of failure to reduce cysts, large masses that cause symptoms, or if malignancy is suspected. Ovarian-sparing laparoscopy is preferred. Torsion, rupture, or hemorrhage may require urgent surgical intervention. Treatment should be performed in specialized centers to avoid unnecessary oophorectomies and to ensure the best outcome for preserving ovarian function, maintaining hormonal balance, sexual development, fertility, and overall health.

Keywords: *functional ovarian cysts, ovarian formation, oophorectomy, girls, adolescent girls, diagnostics, treatment.*

Особливості менеджменту кістозних утворень яєчників у пубертатному періоді: огляд літератури

М. Ю. Сергієнко, В. Г. Сюсюка, О. Д. Кирилюк, Н. Ю. Богуславська, О. А. Рослік, Ю. В. Рубльова

У гінекологічній практиці кістозні утворення яєчників є актуальною проблемою. За даними літератури, їх частота зростає, а основна маса представлена фолікулярними кістами та кістами жовтого тіла. Більшість новоутворень черевної порожнини у дівчаток і дівчат-підлітків походять з яєчників. Функціональні кісти яєчників у дівчат становлять 60% усіх уражень яєчників, тоді як справжні новоутворення зустрічаються рідко. Частота, клінічна картина та гістологічний розподіл таких уражень відрізняються від таких у дорослих і вимагають спеціального терапевтичного підходу. Під час оцінювання кістозних утворень яєчників у дітей принциповим є визначення ймовірності злоякісності, оскільки підходи до лікування доброякісних і злоякісних уражень суттєво відрізняються. Основним інструментом їх візуалізації є ультразвукове дослідження, за допомогою якого можна оцінити розмір, розташування та характеристики утворень. Магнітно-резонансну томографію або комп'ютерну томографію використовують для подальшого оцінювання, якщо результати ультразвукового дослідження є неоднозначними, або існує підозра на злоякісність новоутворень. Сироваткові маркери можуть бути розглянуті, щоб допомогти оцінити ризик злоякісності пухлини. Хірургічне втручання показано у випадках відсутності редукції кіст, великих утворень, які зумовлюють симптоми, або якщо є побоювання щодо злоякісності. Перевагу віддають лапароскопії зі збереженням яєчників. Перекрут, розрив або крововилив можуть вимагати термінового хірургічного втручання. Лікування слід проводити у спеціалізованих центрах, щоб уникнути непотрібних оваріоектомій та забезпечити найкращий результат для збереження функції яєчників, підтримки гормонального балансу, статевого розвитку, фертильності й загального здоров'я.

Ключові слова: *функціональні кісти яєчника, утворення яєчника, оваріоектомія, дівчатка, дівчата-підлітки, діагностика, лікування.*

Puberty is an extremely important phase of human development, when the body undergoes changes that contribute to the onset of reproductive maturity and determine its quality. Data on the increase in gynecological pathology among adolescent girls are alarming [1]. Ovarian cysts are a pressing issue in gynecological practice. Their frequency is increasing, and the majority are follicular cysts and *corpus luteum* cysts according to the literature [2]. They account for up to 80% of benign ovarian neoplasms. Statistics show that 20% of women have had at least one ovarian cyst detected during their lifetime [3].

Functional ovarian cysts (FOC) are benign growths associated with the cyclical functioning of the female body. They can occur at any age, especially in girls with

menstrual disorders after menarche or during perimenopause, and are considered variations of the ovulatory process. Follicular cysts are the major findings (66.4%) during prophylactic check-ups among women without clinical manifestations. For those patients who have clinical symptoms – menstrual cycle disorders predominate in 34.5%. Ovarian retention formations can be observed in clinically healthy patients (7.8%) and slightly more than half of women (52.3%) suffering from lower abdominal pain and/ or menstrual cycle disorders [4, 5].

Functional cysts are increasingly being detected thanks to the use of ultrasound (US) in everyday clinical practice [6]. It is well known that such factors as endocrine diseases, cholecalciferol deficiency, obesity, all types of stress, ecology and harmful habits are the provoking factors for their frequency, an increase in gynecological morbidity among women of all ages [7, 8].

The goal of ovarian neoplasm management is to actively identify groups with high, moderate, and low risk of developing malignant tumors [9].

Ovarian non-neoplastic and neoplastic tumors can be found in all age groups of adolescents and younger girls. They require a specific therapeutic approach because of the difference in clinics and histological results compared to adult women [10, 11]. Ovarian cysts in girls account for 60% of all ovarian lesions, while true neoplasms are rare. According to the literature, the latter are observed in 3–8% of girls with appendages and account for 1–2% of all cases of cancer in children [12–15].

Such types of tumors like endometriomas, lymphangiomas, FOC and abscesses in them are not composed of neoplastic cells. Various hormonal abnormalities in girls are the main cause of FOC appearance. The release of gonadotropins by the developing pituitary gland during prepuberty, and ovulatory dysfunction during adolescence are usual ways of their appearance and growth [16].

During management of patients with FOC, it is important to differentiate functional formations from those requiring surgical removal, since unjustified surgical activity may lead to a further decrease in fertility. According to world statistics 10–15% of women of reproductive age have had surgical interventions on pelvic organs, among which operations for tumors and tumor-like formations of the ovaries take second place [5, 17–19].

The main goal in differential diagnosing of ovarian masses is to determine the nature of tumor, if it is malignant or not, as the protocol of treatment differs significantly [12]. The main role in differential diagnosis is played by pelvic US, which can diagnose FOC in 97.8% of cases before surgery. Subjective assessment of sonographic images by an expert sonographer enables differentiation between benign and malignant adnexal masses. The standardized terminology developed by the International Ovarian Tumor Analysis group allows specialists with varying levels of experience to accurately classify these lesions [19]. In 2019, the results of a large multicenter study conducted in 14 countries and including 8,519 women were published, which showed that dynamic monitoring of patients with FOC based on US data is possible, since the risk of malignancy and acute complications is low [20]. FOC is defined as an ovarian cyst with an anechoic pattern, a mean diameter greater than 15 mm, visualized in the early follicular phase and absent on US scanning performed in the previous natural cycle. FOC presents as simple, single-color, anechoic cysts with a thin, smooth wall, without the presence of enhancing nodules or other solid components and septation on US [5]. The clear criteria for simple cysts include: single-color, thin, smooth wall, anechoic, with the absence of internal flow. If any cyst is not in the frame of these criteria, then dynamical observation in 2–6 months is recommended. Another one criterion is the speed of growth in 6–12 months. If after this period there is no increasing of a cyst in size and no clinical manifestation, there is no need in further follow-ups [21].

Follicular cysts are described as thin-walled anechoic lesions up to 10 cm in diameter. *Corpus luteum* cysts have thick walls and hyperechoic contents, which are also referred to as cobweb-like. Occasionally, they may contain solid elements due to blood clots [22].

US is the most common method for diagnosing FOC in adolescents. The method is simple, easily accessible, safe, and does not require sedation. The transabdominal approach is more commonly used, while transvaginal US is reserved exclusively for sexually active patients [13, 23].

In some cases, differential diagnosis of ovarian lesions using US alone can be difficult and requires additional examination methods. Magnetic resonance imaging (MRI) does not involve the use of ionizing radiation, provides excellent soft tissue contrast and allows for a comprehensive assessment of the pelvic cavity [12, 13, 24]. Therefore, it is ideal for accurate characterization, localization, and differential diagnosis. However, the examination is time-consuming, expensive, has limited availability in the acute phase, and may require sedation in younger children [13, 24, 25]. Computed tomography (CT), despite the use of radiation, can be easily performed in emergency situations and remains a useful diagnostic method for differentiating neoplasms and planning surgical intervention due to the above-mentioned disadvantages of MRI [13, 14, 24].

Imaging using US, MRI, CT, and serum tumor markers helps differentiate between benign and malignant lesions and thus determine the optimal treatment approach [11, 26]. Benign tumors are smaller (< 8–10 cm) and have a cystic, homogeneous structure without papillary growths. Malignant tumors are primarily characterized by their large size (≥ 8–10 cm), heterogeneous consistency, presence of hard components and papillary growths [11].

Cancer antigen 125, α-fetoprotein, lactate dehydrogenase, and the β-subunit of human chorionic gonadotropin are the most commonly used markers for the differential diagnosis of ovarian cysts in children and adolescents [13, 26–33]. Functional cysts are usually asymptomatic and typically resolve without intervention within 8–12 weeks [19, 34, 35]. Today, as there is evidence that a wait-and-see approach is as effective as hormone therapy, the use of any therapy in the presence of functional cysts is not indicated. According to Cochrane review, combined oral contraceptives do not accelerate the regression of ovarian cysts [36]. Cystic formations

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that do not reduce within a few months can at the same time be hardly considered functional [37, 38]. Oral contraceptives may be prescribed to prevent the formation of new cysts, i.e., oral contraceptives can prevent the formation of functional cysts, but they do not affect existing ones [5, 39].

There is no consensus on this issue in pediatric gynecology. It has been proven that the presence of an ovarian cyst and its type have a negative impact on the quality of life related to the physical and mental health of adolescent girls [40].

The difficulty in choosing a treatment strategy is associated with the high frequency of inflammatory diseases of the pelvic organs, menstrual cycle disorders, and the possibility of apoplexy and ovarian torsion. More often, the latter affects the ovary along with part of the fallopian tube; isolated cases are rare [12, 25, 41–43]. Although it can be observed in children of any age, 16% of cases occur in infants and 52% in the perinatal period [16]. Most patients with torsion are between 7 and 15 years old [6]. Pathological conditions are diagnosed in the affected appendages in 51–84% of children with ovarian torsion, which are usually benign. These are follicular cysts and mature teratomas. Torsion of malignant tumors is rare, possibly due to the presence of a fibrous band [24, 25].

Torsion of the normal uterine appendages is a fairly common occurrence in childhood due to their greater length and the weakness of the ligaments in some girls [24, 25]. It is rarely seen in the context of pelvic inflammatory disease and endometriosis, possibly due to the presence of adhesions with surrounding organs [42].

The classic clinical manifestations of adnexal torsion include severe, acute, one-sided lower abdominal pain, nausea, vomiting, and possibly fever and dysuria. These symptoms may not be very specific and can mimic other pathologic conditions of the gastrointestinal and genitourinary systems [24, 42, 44]. The primary tool in differential diagnosis is pelvic US, which can detect unilateral ovarian enlargement caused by stromal edema and hemorrhage [11, 24, 44].

According to Sintim-Damoa et al., a sign of torsion is an increase in ovarian volume of at least three times the normal size [24]. Other sonographic criteria for the condition include comparing the size of the affected ovary with that of the contralateral ovary, the absence of blood flow on Doppler imaging, uterine displacement toward the twisted ovary, presence of free fluid, the “twisted vessel sign”, and medialization of the ovary [24, 25].

The presence or absence of Doppler blood flow cannot establish a definitive diagnosis due to the unique characteristics of ovarian blood supply in children, as the ovaries receive blood from both the ovarian and uterine arteries [24, 25, 44]. CT and MRI are used as additional methods of diagnosing in complicated clinical situations [12, 24, 25].

Delays in diagnosis and surgical treatment can lead to impaired function or complete loss of the ovary due to persistent ischemia. Therefore, emergency laparoscopy, visual inspection, and detorsion help to preserve the ovarian tissue [24].

Preserving gonadal function in girls and adolescents is important not only for future reproduction but also for proper sexual maturation. Cosmetic defects on the abdomen following laparotomy can have significant psychological consequences [10]. Therefore, treatment of FOC in children and adolescents should be conservative; in cases of torsion, it should be organ-preserving and minimally invasive whenever possible. Laparoscopic surgery offers these options [10, 13, 27].

The peculiarities of the reproductive system in adolescence and the importance of preserving gonadal function in girls with ovarian cysts require the development of clear algorithms for primary care physicians treating young patients. An example of such an algorithm is the clinical pathway for primary care for children and adolescents (≤ 18 years) with ovarian cysts in the province of Alberta (Canada) [45]. This pathway was developed by primary care physicians, specialists (pediatric and adolescent gynecologists, surgeons), and the regional health care department. The availability and use of US examinations in childhood have led to an increase in the detection of ovarian cysts, most of which are FOC and do not require treatment. The purpose of this document is to identify patients at risk of complications, recommend necessary examinations, and refer them to specific specialists. Options for their clinical pathway are compiled taking into account the presence of complaints, gynecological, somatic, and endocrine history, the results of dynamic US, and the assessment of tumor markers. At the first stage, the clinical pathway depends on only two aspects: the presence of clinical symptoms in a girl or the accidental discovery of a cyst during US or examination. Red flags include signs of ovarian torsion (sudden onset of abdominal pain, nausea, vomiting, symptoms of peritoneal irritation) or large abdominal masses palpable during examination and confirmed by US. These cases are considered indications for immediate referral of the patient to the appropriate specialist/department for further examination or emergency care. The management of formations that are not palpable and have no clinical manifestations depends on their size, structure, the results of tumor marker screening, and dynamic US monitoring. It involves the participation of other specialists, including a pediatric gynecologist.

CONCLUSIONS

Ovarian tumors in children and adolescents range from simple functional cysts to malignant neoplasms, but FOC is the most common diagnosis. In more than 90% of cases, dynamic US helps with differential diagnosis.

The peculiarities of the reproductive system development in adolescence and the importance of preserving gonadal function in girls with ovarian formations require the development of clear algorithms for primary care physicians treating young patients.

Girls and adolescent girls with ovarian cysts should be monitored and treated in specialized healthcare facilities that can provide optimal diagnosis, examination, and recommendations, avoiding unnecessary oophorectomies, which will help preserve ovarian function to maintain hormonal balance, fertility, and overall health.

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Information about the authors

Sergienko Marina Yu. – Zaporizhzhia State Medical and Pharmaceutical University. *E-mail: smugynec@gmail.com*
ORCID: 0000-0001-6795-769X

Siusiuka Volodymyr H. – Zaporizhzhia State Medical and Pharmaceutical University. *E-mail: svg.zp.ua@gmail.com*
ORCID: 0000-0002-3183-4556

Kyryliuk Oleksandr D. – Zaporizhzhia State Medical and Pharmaceutical University. *E-mail: rdom5@i.ua*
ORCID: 0000-0002-0173-5661

Boguslavska Nataliia Yu. – Zaporizhzhia State Medical and Pharmaceutical University. *E-mail: rdom5@i.ua*
ORCID: 0000-0001-5401-3999

Roslik Olha A. – Zaporizhzhia State Medical and Pharmaceutical University. *E-mail: kosch.olga@ukr.net*
ORCID: 0000-0002-4729-5155

Rublyova Yulia V. – MNPE "City Children's Hospital No. 5" of Zaporizhzhia City Council, Zaporizhzhia. *E-mail: nancyspagen@gmail.com*
ORCID: 0009-0005-5529-8144

Відомості про авторів

Сергієнко Марина Юріївна – Запорізький державний медико-фармацевтичний університет. *E-mail: smugynec@gmail.com*
ORCID: 0000-0001-6795-769X

Сюсюка Володимир Григорович – Запорізький державний медико-фармацевтичний університет. *E-mail: svg.zp.ua@gmail.com*
ORCID: 0000-0002-3183-4556

Кирилюк Олександр Дмитрович – Запорізький державний медико-фармацевтичний університет. *E-mail: rdom5@i.ua*
ORCID: 0000-0002-0173-5661

Богуславська Наталія Юріївна – Запорізький державний медико-фармацевтичний університет. *E-mail: rdom5@i.ua*
ORCID: 0000-0001-5401-3999

Рослік Ольга Анатоліївна – Запорізький державний медико-фармацевтичний університет. *E-mail: kosch.olga@ukr.net*
ORCID: 0000-0002-4729-5155

Рубльова Юлія Володимирівна – КНП «Міська дитяча лікарня № 5» Запорізької міської ради. *E-mail: nancyspagen@gmail.com*
ORCID: 0009-0005-5529-8144

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