Original article

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CHARACTERISTICS OF OVARIAN TUMOR CHANGES IN THE PEDIATRIC POPULATION

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On average, a third of all adnexal masses in girls originate from the ovary. The clinical presentation is non-specific. The treatment trend is ovary-preserving surgery. The aim of the work was to present the characteristics of ovarian masses in the population of girls aged up to 18 years. This retrospective study was conducted by analyzing the medical records of female newborns and girls up to 18 years of age. In the neonatal group, aged up to 12 months, 44.4% had right-sided and 55.6% left-sided ovarian masses. Cystectomy was performed in 6 (66.7%), while ovariectomy and salpingo-oophorectomy were performed in 1 (11.1%) baby each. In the group of girls aged 1−18 years, there were 63% right-sided and 34% left-sided changes. One girl had bilateral. The largest number of girls underwent cystectomy 24 (63.2%). Of the non-neoplastic changes, there were 9 (23.6%) follicular cysts, 8 (21.1%)simple cysts, 6 (17.1%) haemorrhagic corpus luteum cysts, while of the neoplastic benign changes there were 11 (28.8%) mature teratoma, and 4 (11.4%) serous cystadenoma.

The incidence of ovarian tumor changes in the population of girls up to the age of 18 is very low. Non-neoplastic changes occur much more often.*Acta Medica Medianae 2023;62(3):32-41.*

***Key words**: tumor changes, ovary, neonates, girls*

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Introduction

Available literature data are scarce regarding ovarian tumour changes in pediatric population in comparison to adult population, and a lot still remains unknown. There are almost no official guidelines on the management of ovarian tumours in children, so more clinical studies are necessary in order to improve the treatment quality (1).

On average, one third of all adnexal masses in young girls originate from the ovaries, but they also may originate from fallopian tubes and other pelvic organs. These changes are predominantly non-neoplastic, with cystic changes being the most common ones. They are followed by neoplastic benign changes, while neoplastic malignant changes are extremely rare (2).

Clinical manifestation is nonspecific and may often mimic other pathological conditions with similar symptomatology, thus making diagnostic procedure more difficult. The most common presenting symptom is abdominal pain, although these tumours may be utterly asymptomatic. Imaging techniques are leading diagnostic methods in diagnosing these changes, while laboratory analyses, such as value of tumour markers assessment, may be useful in differentiating benign from malignant tumours (3).

From a historic perspective, the main principle in treating all adnexal masses was oophorectomy. Having in mind the fact that these tumours are predominantly benign at this age, oophorectomy was often not necessary, resulting in an increased risk of infertility and other complications. This is why the treatment trend in recent years has been ovarian-sparing surgery aiming at healthy ovarian tissue preservation (4).

Aim of the paper

The aim of the paper was to demonstrate characteristics of ovarian tumour changes in the population of girls up to 18 years of age, and to point out their specificities related to age.

Material and methods

This retrospective study was conducted by analyzing medical records of female newborns and girls up to 18 years of age, treated at the Clinic for Pediatric Surgery, Orthopedics and Traumatology, Clinical Center Niš, in the period from January 1, 2017 to October 10, 2022.

A criterion for study inclusion was the diagnosis of ovarian tumour changes. All the patients underwent a complete clinical, laboratory, ultrasound, radiological examinations and imaging, as well as nuclear magnetic resonance imaging (MRI) when surgical treatment was indicated after the tumour had been diagnosed and specimen sent for pathohistological analysis (PH). The patients were divided into two groups according to their age. The first group comprised infants (0–1 year of age), and the second group comprised patients aged between 1 and 18 years. Based on medical history, we analyzed the side and size of the tumour, type of tumour and performed surgical intervention as well.

Upon collecting data, a unique database was created in EXCEL, followed by statistical analysis and data processing by using SPSS software package. Descriptive statistics (mean value) and a measure of variability (standard deviation) were used in the study. The Student's t-test was used to analyze how significant the differences were. The results are shown in tables and graphs.

Results

The study included 9 babies who had a surgery intervention. The oldest baby was 80 days old, and the youngest 5 days old. Average age was 32.11±23.42, with the median of 30 days (Table 1).

In 4 (44.4%) babies, changes were located on the right side and in 5 (55.6%) babies on the left side (Graph 1).

Table 2 shows distribution of performed surgical interventions. In the majority of babies, i.e. 6 (66.7%), cystectomy was performed and one newborn baby girl underwent ovariectomy and salpingo-oophorectomy (11.1%). In one patient,autoamputation of the cyst was detectedintraoperatively (11.1%).

The most common pathohistological (PH) finding was simple cysts, in8 (88.9%) babies, while haemmorhagicpseudocyst was present in 1 baby (11.1%).

Girls up to 18 years

The study included 38 girls in whom surgery intervention was performed. The oldest girl was 17, and the youngest 5 years old. Average age of all the girls was 14.37±2.91 years, with the median of 15 years (Table 3).

The greatest number of changes was evidenced in 24 (63%) girls, located on the right side, while in 13 girls (34%) there were left-sided changes. One girl had a bilateral change (Graph 2).

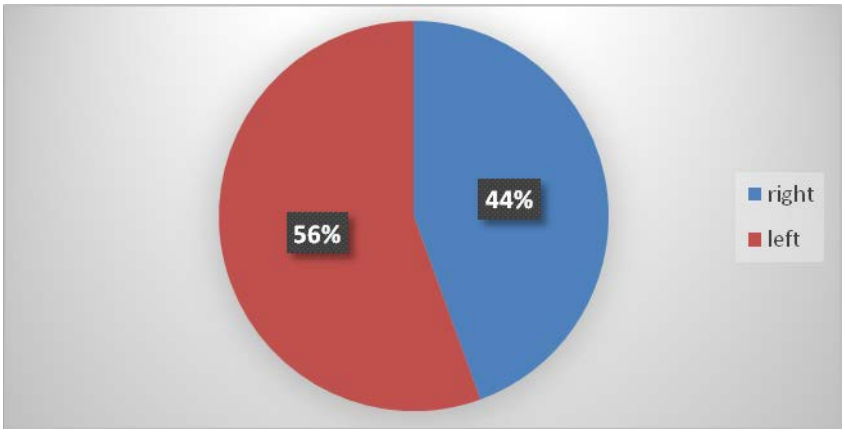
Table 4 shows the distribution of surgical interventions performed. In the majority of girls,i.e. 24 (63.2%), cystectomy was performed, a combination of ovariectomy and puncture in 4 girls (10.5%), adnexectomy in 3 (7.9%), partial ovariectomy in 2 (5.3%) patients, and there was autoamputation of the cyst in one girl.

A total of 21 girls had non-neoplastic ovarian tumours: follicular cysts in 9 (23.6%), simple cysts in8 (21.1%), haemorrhagic corpus luteum cystsfound in 6 (17.1%) girls, while, out of neoplastic benign lesions, the most common ones were a mature teratomain 11 (28.8%) and serouscystadenomain 4 (11.4%) girls (Table 5).

The cystswere divided into three groups according to their size. Small-sized cysts up to 5 cm were seen in 16 (47.1%), medium-sized 5–10 cm in 15 (44.1%), and big-sized over 10 cm in 3 (8.8%) girls (Table 6).

Table 1. Distribution of ovarian tumors according to age in neonatal population

Characteristics		
	Girls n (%)	9 (100,0)
Age	$\bar{x}$±SD	32,11±23.42
(days)	Me (Iq)	15 (29)
	Min-Max	5-80



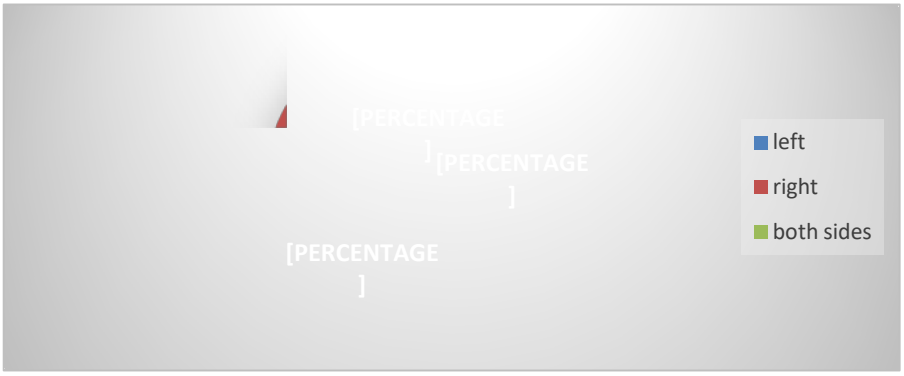
Graph 1.Distribution of ovarian tumors according to predominant side of occurrence in newborns

Table 2. Distribution of performed surgical interventions in neonatal population

Type of surgery	*n*	*%*
Cystectomy	6	66.7
Ovariectomy	1	11.1
Salpingo-oophorectomy	1	11.1
Autoamputation	1	11.1
Σ	9	100.0

Table 3. Distribution of ovarian tumor changes according to age in a population of girls aged from 1 to 18 years

Characteristics		
	Girls n (%)	38 (100,0)
Age	$\bar{x}$±SD	14.37±2.91
(years)	Me (Iq)	15 (3)
	Min-Max	5-17



Graph 2. Distribution of ovarian tumor changes according to the predominant side of occurrence in a population of girls aged between 1 and 18 years

Table 4. Distribution of performed surgical interventions in a population of girls between 1 and 18 years of age.

Type of surgery	*n*	*%*
Cystectomy	24	63.2
Ovariectomy	4	10.5
Partial ovariectomy	2	5.3
Puncture	4	10.5
Adnexectomy	3	7.9
Autoamputation	1	2.6
Σ	38	100.0

Table 5. Distribution of PH findings of ovarian tumor changes in a population of girls aged between 1 and 18 years

PH finding	*n*	*%*
Follicular cysts	9	23.6
Haemorrhagic corpus luteum cysts	6	17.1
Mature Teratoma	11	28.8
Simple cysts	8	21.1
Serouscystadenoma	4	11.4
Σ	38	100.0

Table 6. Distribution of ovarian tumor changes according to the size in a population of girls aged 1−18 years

Cysts	*n*	*%*
Small (up to 5 cm)	16	47.1
Medium (5−10 cm)	15	44.1
Large (>10 cm)	3	8.8
Σ	34	100.0

Discussion

Ovarian tumours are rare in the pediatric population. The literature data report the incidence of 2.6 cases per 100,000 girls, and they represent approximately 1% of all childhood malignancies. About 10−20% of all ovarian tumour masses have malignant potential (5,6). The World Health Organization has recommended classification of ovarian tumours into two big groups: non-neoplastic and neoplastic tumours. Non-neoplastic lesions, such as functional cysts and benign tumours, are most common tumour masses in the pediatric population (7).

The most frequent symptom of ovarian tumour is abdominal pain (in 57% of patients), while palpable abdominal or pelvic masses are present in 46% cases. They may be accompanied by nausea, vomiting, weight loss, obstipation, urinary infection and dysuria symptoms.

They may clinically be completely asymptomatic, or presented as the manifestation of acute abdominal pain caused by tumour mass torsion. Accompanying endocrine changes, such as precocious puberty, abnormal vaginal bleeding, virilization or masculinization, may also be the first manifestation of hormonally active tumours (3).

In every palpable abdominal mass in lower abdomen, the initial and gold standard in diagnostics is abdominal ultrasound which provides information on tumour mass size, localization, and the nature of tumour by distinguishing a cystic, solid or mixed tumour. Computed tomography and magnetic resonance imaging provide additional information on tumour nature and they show if the tumour has spread (8).

Neonatal ovarian cysts are most common abdominal masses in female newborns. The exact pathogenesis is still unknown. There are some data that point out the influence of maternal placental gonadotropins, especially in the third trimester, that stimulate fetal ovaries and thus ovarian cysts are formed (9). It has been reported that maternal risk factors, such as diabetes mellitus, Rh isoimmunization, and preeclampsia, are associated with an increase in gonadotropin levels, resulting in an increased risk of cyst formation (10). Most neonatal cysts cannot be diagnosed before the third trimester, because in this period the hypothalamic-pituitary-ovarian axis develops, so that fetal cysts identified before the third trimester are believed to arise from the other organ of origin (mesenteric cysts, meconium pseudocyst, simple hepatic cysts, ureterocele). There is no gold standard in the management of neonatal ovarian cysts. Since they are classified into simple and complex, based on ultrasound image, and since simple cyst may progress into complex cysts during pregnancy, or torsion in utero, some authors point out the significance of prenatal treatment of simple cysts by in utero aspiration in order to preserve ovarian tissue and prevent possible complications.Diguisto et al. in a randomized controlled trial emphasized the importance of in-utero aspiration and its association with increased incidence of in-utero involution of the cyst and a reduced neonatal oophorectomy (11). Also, an advantage of in-utero aspiration is a possibility of establishing the diagnosis by analyzing cyst content. Lecarpenof et al. in a retrospective study included a total of 42 newborns with intraabdominal cystic masses and analyzed biochemical content of the fluid sampled by in-utero aspiration of the cyst content. They concluded that estradiol levels of 1000ng/l or higher diagnostically confirm ovarian cyst with 100% sensitivity and 100% specificity in comparison to other diseases that cause intraabdominal cystic masses (12). On the other hand, there are some disadvantages of in-utero aspiration, such as re-accumulation of the cyst, infections, preterm delivery, and impossibility to perform some procedures because of fetal position or dry aspiration (11, 13). The most severe complication of the cyst is torsion with subsequent ischemia and necrosis, increased risk of the adnexa or ovary loss, and potential adhesions to surrounding tissues that may result in intestinal or urinary obstructions. In a large meta-analysis with 92 non-randomized studies, Tyraskis et al. reported that cysts measuring 40mm or more have higher risk of torsion, and surgical treatment

is required more in complex than simple cysts (14). In our study, during a five-year period, there was a total of 9 newborns with ovarian cysts, out of them there were eight cysts verified as simple cysts by ultrasound and one cyst was identified as hemorrhagic pseudocyst. Considering the size of abdominal cavity, each cyst larger than 30mm is believed to be large, so our opinion is that every cyst of 30mm in diameter or more should be treated surgically in order to prevent torsion and the loss of vital ovarian tissue. Literature data reveal the tendency of spontaneous regression of cysts measuring less than 20mm, so continuous ultrasound monitoring is necessary, as well as timely reaction if the cyst progresses in size. Since the diameter of all the cysts in our study was over 30mm, all the newborns were indicated for surgical treatment. In 6 of them cystectomy with ovarian tissue preservation was performed, in two babies torsion was reported, so oophorectomy, that is salpingo-oophorectomy, was performed, and in one patient a free auto-amputated cyst originating from the right ovary was found intraoperatively. The advantage of such a treatment is that surgery enables complete removal of the cyst with optimal preservation of ovarian parenchyma where possible and purposeful, and adhesion adhesiolysis as well if diagnosed. Also, timely diagnosis significantly shortens the parents' anxiety level (15).

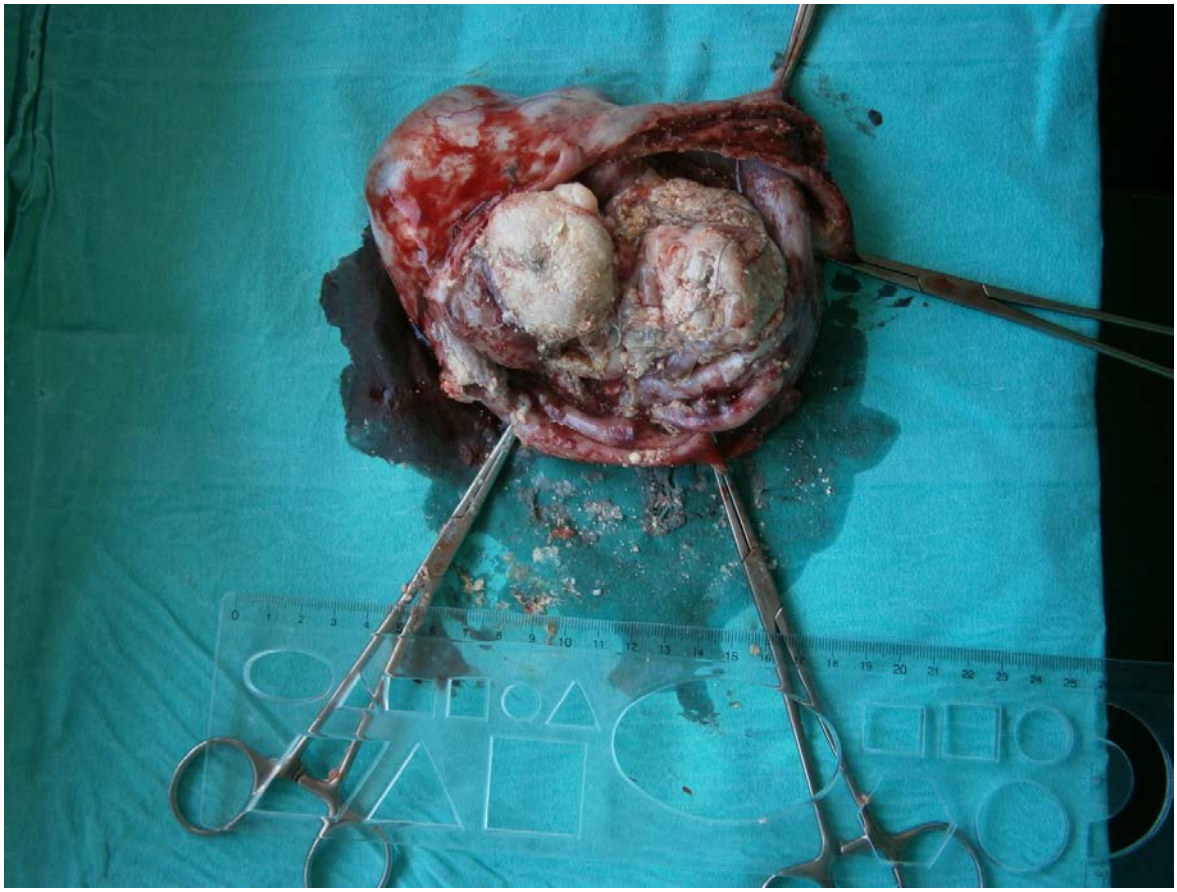
In another group of patients (1−18 years) ovarian tumour mass was diagnosed in 38 patients. Changes were mostly observed on the right ovary (63%), while in one girl both ovaries were affected. There is no logical explanation why the changes are mostly right-sided, but very often such a pain may imitate appendicitis, so ultrasound examination is of vital importance in establishing the diagnosis and in choosing optimal treatment option (that is, an incision on abdominal wall is made for both ovaries and uterus to be extracted).

Average age of girls was 14.37 years, so it can be concluded that the majority of already described tumour changes occur in puberty, with an important role of hormones in etiology (7). Most ovarian cysts occur during puberty and they are known as functional cysts. They may be classified as: a) follicular cysts that occur as a result of physiological fluctuation in hormone levels, they may produce estrogen, and they represent half of non-neoplastic ovarian tumors, and b) corpus luteum cysts that are formed following ovulation, they may be filled with blood and they are active in secreting hormones. Very similar to pathoanatomically functional cyst are simple cysts that are endocrine-inactive. There was a total of 21 (60%) girls with non-neoplastic ovarian changes, 7(20%) of them had simple cysts, 8 (22.9%) follicular cysts, 6 (17.1%) corpus luteum cysts, and in one girl the presence of both follicular and corpus luteum cysts was verified pathohistologically. It is known that the incidence of developing ovarian cysts in early childhood and pre-pubertal period is extremely low because of low hormonal activity (16). Our results are not in accordance with the results of Zhang et al. who analyzed a total of 521 patients operated at the Gyneacology Hospital of Fudan University, Shanghai, China, where 92 girls had non-neoplastic ovarian lesions, making up percentage distribution of 17.7% (17). On the other hand,Sadhegian et al. diagnosed non-neoplastic lesions in 76.9% patients in a smaller study population (18).

Out of neoplastic benign lesions, the incidence of mature cystic teratomas is the highest (Figure 1). They are neoplastic benign changes that contain elements from all three germ cell layers (endoderm, mesoderm, and ectoderm). They are commonly referred to as 'dermoid cysts' in cases when ectodermal component is predominant (19). They account for more than 50% of all ovarian tumours in pediatric population and are mostly asymptomatic, but abdominal pain or palpable mass may be present. Macroscopically, they are well-differentiated encapsulated masses filled with thick mass, usually unilocular, with characteristic protuberance within known as the Rokitanski nodule that may contain all elements of ectodermal origin (bones, teeth, hair, thyroid tissue, brain tissue, etc.) (20). There were 10 (28.6%) girls with pathohistologically (PH) verified diagnosis of mature teratoma, similar to the results of Cassa et al. who report percentage of mature teratomas in 39.6% patients out of a total of 102. Far less common are cystadenomas (2.8%), in our population they were present in 11.4% of patients. On the other hand, Zhang et al reported even 16.5% cystadenoma cases (17.21). Cystadenomas are mostly benign epithelial neoplasms, 75% of them are serous, and remaining 25% are mucous cystadenomas commonly seen in adult population, they very rarely occur in children (22).

Based on the size, tumour changes have been classified into 3 groups (small, medium, big). The distribution of small and medium tumours was similar, while there were considerably fewer changes regarding the size over 10cm. Some authors emphasize a positive correlation between big tumours and higher risk of malignancy, so in a retrospective study by Rogers et al., out of a total of 129 children treated at the Hospital for Sick Children in Toronto, Canada, the diameter of all malignant ovarian tumours was greater than 8 cm (23).Depoers et al. developed a predictive score system for detecting ovarian malignancies in order to avoid unnecessary adnexectomy, and this system may be applied in confirmed ovarian tumours with negative aFP and HCG. They classified patients into three groups according to the size of tumour (up to 65mm, 65−130mm, >130mm) and the presence of cystic tumour component: low risk, middle-risk, and high-risk patients. Patients at low risk could undergo ovarian-sparing surgery. Patients at middle risk require additional diagnostic procedures, such as an MRI, while patients at high risk should be proposed a radical surgical treatment (24).

Figure 1. Mature teratoma, nonneoplastic benign tumour change which in its composition can have elements of the all 3 germ layers



A fundamental imperative in treating all ovarian tumour masses is to preserve the remaining ovarian tissue (17,25,26). This was a leading principle in our study; in 24 (63.2%) girls cystectomy was performed, in 2 (5.3%) partial ovariectomy. In cases of torsion and subsequent necrosis with almost no healthy ovarian tissue left, and in suspected malignant neoplasms, there was no possibility for ovarian preservation, so in 4 (10.5%) girls ovariectomy was performed, and adnexectomy in 3 (7.9%) patients. Although ovariectomy was a basic option in treating torsion from a historic point of view, the importance of detorsion even in necrotic ovary has been emphasized recently, in order to increase the rate of fertility preservation, since follicular activity may be reestablished (27). Ovarian fixation for ovarian torsion is still being debated. Some authors believe that fixation may disturb ovaries-fallopian tubes relation, while others advocate ovarian fixation in case of the absence of contralateral ovary, recurrence, or an elongated ovarian ligament (28).

We believe that this study still has some limitations. All the cases are from one center experience only, the number of participants is low, and this can affect the final outcome of the study. Also, the study is a retrospective one, all the data were collected from existing medical records, so there was no adequate follow-up of operated patients. In the light of all aforementioned considerations, it is necessary to conduct a prospective study aiming at postoperative follow-up of patients to evaluate ovary function and its effect on fertility.

Conclusion

In conclusion, it can be said that the incidence of ovarian tumours in a population of girls up to 18 years of age is very low. In a neonatal population non-neoplastic tumour changes, that is follicular cysts, are most common. It is believed that placental gonadotropins play a key role in the pathogenesis of tumour changes. In a population of girls aged 1–18 years non-neoplastic lesions are predominant tumour changes, while mature teratomasare most common neoplastic benign tumours, but cystadenomasare not so common. The majority of these changes occur in puberty, with hormonal influence in their pathogenesis. The imperative in surgical treatment is healthy ovarian tissue preservation, and this should always be kept in mind

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KARAKTERISTIKE TUMORSKIH PROMENA JAJNIKA U DEČJEM UZRASTU

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U proseku, trećina svih adneksalnih masa kod devojčica vodi poreklo od jajnika. Klinička prezentacija je nespecifična. Trend lečenja predstavlja hirurgija čiji je cilj očuvanje jajnika.

Cilj rada jeste prikazati karakteristike tumorskih promena jajnika u populaciji devojčica uzrasta do 18 godina.

Ova retrospektivna studija sprovedena je analizom medicinske dokumentacije ženske novorođenčadi i devojčica uzrasta do 18 godina.

U neonatalnoj grupi, uzrasta do 12 meseci, bilo je 44,4% desnostranih i 55,6% levostranih promena. Kod šest beba (66,7%) urađena je cistektomija, dok je ovariektomija i salpingo-ooferoktimija urađena kod po jedne (11,1%) bebe. U grupi devojčica od jedne godine do 18 godina bilo je 63% desnostranih i 34% levostranih promena. Jedna devojčica imala je obostranu promenu. Kod najvećeg broja devojčica urađena je cistektomija – 24 (63,2%). Od neneoplastičnih promena bilo je devet (23,6%) *Cystis follicularis*, osam (21,1%) *Cystis simplex* i šest (17,1%) *Corpus luteum haemorrhagicum et cysticum*; od neoplastičnih benignih promena bilo je jedanaest (28,8%) *Teratoma maturum* i četiri (11,4%) *Cystadenoma serosum*.

Incidencija tumorskih promena jajnika u populaciji devojčica do 18 godina vrlo je niska; znatno češće se javljaju neneoplastične promene. *Acta Medica Medianae 2023;62(3):32-41.*

***Ključne reči**: tumorske promene, jajnik, neonatus, devojčice*