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SUMMARIES OF THE 3<sup>RD</sup> CONGRESS OF THE EASTERN EUROPEAN SOCIETY OF ENDOMETRIOSIS AND INFERTILITY AND THE 6<sup>TH</sup> NATIONAL CONFERENCE OF ROMANIAN SOCIETY OF HPV

• Poiana Braşov, Romania, 1-3 July 2021 •

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• Sibiu, Romania, 23-25 September 2021 •

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Societatea Română de Ultrasonografie în Obstetrică și Ginecologie



Societatea Română de HPV



Societatea de Uroginecologie din România



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Societatea de Endometrioză  
și Infertilitate Est-Europeană



# AL III-LEA CONGRES NAȚIONAL AL SOCIETĂȚII DE ENDOMETRIOZĂ ȘI INFERTILITATE EST-EUROPEANĂ

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## Kisspeptin and implications in polycystic ovary syndrome

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**Introduction.** Kisspeptin is a hypothalamic peptide that plays an essential role in the upstream of gonadotropin-releasing hormones by mediating sex steroid feedback and metabolic regulation of the reproductive axis. Recent studies have shown its role in puberty onset, in the maintenance of normal reproductive function and in metabolic and hormonal disturbances leading to polycystic ovarian syndrome (PCOS). Encoded by the *KISS1* gene, it was first isolated from human placental tissue, but later on, its presence has been discovered in other numerous organs. PCOS is a common disorder characterized by polycystic ovaries, chronic anovulation and hyperandrogenism. Considering the existing evidence of kisspeptin regulating the hypothalamo-pituitary-gonadal axis, it is only a matter of time until this neuropeptide will play an important role in the diagnosis and management in PCOS. **Materials and method.** During January 2021 and May 2021, in the "Elena Doamna" Clinical Hospital of Obstetrics and Gynecology, Iași, a prospective study, showing the implications of kisspeptin in patients diagnosed with PCOS, was initiated. Sixty female patients were included in our study. They were divided into two groups, the control group consisting in

30 healthy patients with no evidence of PCOS or other endocrinological disorders, and a test group consisting in patients with PCOS. All patients were rigorously selected by respecting inclusion and exclusion criteria, and all of them gave their consent in participating in this study. Eight hormonal parameters were taken into consideration: kisspeptin, luteinizing hormone, follicular stimulant hormone, testosterone, estradiol, prolactin, insulin, and glycemic index. All laboratory tests were performed during follicular period. All patients benefited from clinical examination and pelvic echography. **Results.** When observing the results in our PCOS group, we encountered higher levels of kisspeptin, up to 200 pg/ml, and LH/FSH modified reports. The control group showed overall lower levels of kisspeptin, with values beneath 100 pg/ml. **Discussion.** Recent studies have clearly shown the involvement of kisspeptin and its receptors in the reproductive axis and in PCOS complicated by infertility. Further studies are needed in order to identify new and better therapeutic schemes for patients suffering from PCOS infertility.

**Keywords:** kisspeptin, polycystic ovary syndrome, infertility

## Implications of endometriosis on reproductive parameters in *in vitro* fertilization

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**Introduction/objective.** Endometriosis is common in infertile women. *In vitro* fertilization (IVF) is one of the therapeutic possibilities in infertility associated with endometriosis. Whether endometriosis has a suboptimal response to IVF is not clearly established. **Methodology.** We conducted a retrospective study in the MedLife Department of Maternal-Fetal and Reproductive Medicine. The medical data of patients with infertility of any causes who underwent IVF between January 2013 and August 2017 were reviewed. Only patients with all available data were included: age, causes of infertility, height, weight, dose of gonadotropins used for controlled ovarian stimulation, serum anti-Müllerian hormone (AMH) level, number of oocytes recovered, ovarian surgery data or anterior tubal. **Results.** A total number of 1708 patients were included in the study, 188 patients with endometriosis and 1520 patients without endometriosis. The patients had a mean age of 34.7 years old, an average serum AMH level of 2.92 ng/ml and an average BMI of 22.8 kg/m<sup>2</sup>. The patients

with endometriosis were younger ( $p=0.003$ ), had lower serum AMH ( $p=0.007$ ) and a lower number of recovered oocytes ( $6.68\pm 4.73$  versus  $7.46\pm 4.87$ ;  $p < 0.05$ ) compared with patients without endometriosis. In a multivariate regression model with AMH as a dependent variable, the presence of endometriosis was negatively associated with serum AMH ( $\beta = -0.093$ ;  $p = 0.001$ ) after adjusting for age, BMI and cause of infertility. In the subgroups of patients, the negative relationship between endometriosis and serum AMH level after adjustment was maintained at those of 35 years old and over ( $\beta = -0.107$ ;  $p = 0.008$ ) and under 35 years old ( $\beta = -0.082$ ;  $p = 0.05$ ) and in patients with normal ovarian reserve ( $AMH \geq 1.1$  ng/ml,  $\beta = -0.071$ ;  $p = 0.039$ ), but not in those with low ovarian reserve. **Conclusions.** Our study suggests that, although in endometriosis the AMH production appears to be low, serum AMH levels still overestimate the number of oocytes recovered after controlled ovarian stimulation for IVF.

**Keywords:** endometriosis, IVF, AMH

## Preoperative diagnosis of endometriosis – transvaginal ultrasound versus magnetic resonance imaging

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**Introduction.** Endometriosis is a common gynecological condition among women of childbearing age, associated with chronic pelvic pain, dysmenorrhea, infertility and impaired quality of life. Although the internationally accepted gold standard is the diagnostic laparoscopy, the preoperative noninvasive diagnosis methods – clinical examination, transvaginal ultrasound and magnetic resonance imaging (MRI) – are an important step in the correct preoperative diagnosis of endometriosis. The aim of this paper is to determine the ideal method of preoperative noninvasive diagnosis depending on the symptoms and location of endometriosis lesions, whether clinical examination and transvaginal ultrasound are sufficient or when MRI examination is necessary. **Methodology.** We performed, on a group of 96 patients diagnosed with endometriosis, imaging examination by transvaginal ultrasound and MRI before the surgical treatment of the lesions, with the collection of biological samples for histopathological examination. The results obtained after the intervention were observed, comparing the lesions identified preoperatively with those excised during surgery. **Results.** MRI provides accurate information for the staging of deep endometriosis, especially when the case does not allow

a transvaginal ultrasound examination – it is limited by chronic pelvic pain, *virgo intacta* or obese patient. MRI is used when the clinical examination and ultrasound do not identify lesions in symptomatic patients (parametric lesions, uterosacral ligaments). The association of MRI increases the sensitivity of transvaginal ultrasound in the diagnosis of endometriosis in these cases (70.3% compared to 11.3%). Large endometriosis lesions that can be easily identified on clinical examination and ultrasound do not require MRI (rectal nodules  $d \geq 2$  cm, endometriomas  $d \geq 4$  cm). For intestinal endometriosis, MRI and ultrasound have similar efficiency (83.78% and 87.75%). **Discussion and conclusions.** Although it is not a routine investigation in all patients suspected of having endometriosis, MRI is effective in identifying the lesions. It is necessary for the gynecologist to request an MRI investigation when the transvaginal ultrasound is insufficient or cannot be performed. The methods depend on the experience of the gynecologist and radiologist in making a preoperative assessment of the lesions, so that the surgical treatment is performed in the most complete way possible.

**Keywords:** endometriosis, transvaginal ultrasound, MRI

## Poor responders: what is new in 2021? Are we rising to the challenge?

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**Introduction.** In the field of human assisted reproduction, patients with low ovarian reserve are one of the main challenges for the infertility specialists. This is due to the low number of oocytes obtained after controlled ovarian stimulation cycles. **Materials and method.** As many studies reveal, the number of oocytes is directly proportional to the rate of blastocysts and the rate of pregnancy. This paper is a review of the literature, with the role of highlighting the news in the field. **Results.** What can we do for these patients to maximize their

chances of pregnancy? Dualstim, luteal phase stimulation, ovarian PRP and growth hormone therapy are just some of the latest options that poor responders seem to benefit from. **Conclusions.** As we well know, there are no effective methods to increase the ovarian reserve, so the poor responders are always in the center of scientific research, out of a desire to improve the pregnancy rate and the live birth rate.

**Keywords:** progesterone priming, controlled ovarian stimulation, freeze all

## Ovarian reserve after surgery of endometriosis cysts

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**Introduction/objective.** Endometriosis is one of the main causes of infertility in patients at risk. Surgical treatment – most often laparoscopic – leads, with the removal of the cyst lining and monopolar or bipolar coagulation of the remaining tissue, to a significant reduction of the ovarian parenchyma, with a significant reduction of the ovarian reserve. The aim of the study is to evaluate, through a retrospective study, the ovarian reserve after surgery for endometriotic cysts with bipolar electrocoagulation of the cyst implantation bed. **Methodology.** We evaluated 15 cases of patients with unilateral or bilateral ovarian cyst laparoscopically operated, with the removal of the cyst capsule and hemostasis by superficial bipolar coagulation to reduce the

depth of coagulation as much as possible. The ovarian reserve was evaluated in order to assess the severity of the decrease by monitoring two parameters: AMH and FSH values before and after surgery. **Results.** Ovarian cyst surgery is constantly followed by an increase in FSH levels and a decrease in AMH levels, more pronounced in bilateral ovarian cyst surgery. **Discussion and conclusions.** Electrocoagulation after the laparoscopic excision of ovarian cysts is associated with a significant reduction in ovarian reserve, which is partly a consequence of reduced ovarian parenchyma and the number of ovarian follicles and partly to the damage of the vascular system.

**Keywords:** ovarian cyst, laparoscopic ovarian cystectomy, electrocoagulation, ovarian reserve

## Dynamics of the influence of the coronavirus pandemic on the addressability of infertility patients

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**Objective.** The purpose of this paper is to highlight the extent of changes caused by the COVID-19 pandemic on the addressability and pathology of infertility patients. **Methodology.** In a retrospective study, we evaluated all consecutive patients who were referred to our hospital for hysterosalpingography between April 1, 2020 and March 31, 2021 (study group, n=12), compared to patients from the previous period, April 1, 2019 – March 31, 2020 (control group, n=116). **Results.** Variations between the two groups were highlighted, in terms of age, urban background, living in other counties, referring doctor outside the hospital (31.83 years old; 50%; 16.66%; 0% in the study group versus 32.5 years old; 68.1%; 26.72%; 26.72%

in the control group). Significant variations were observed in terms of uterine pathology: bicornuate uterus and endometriosis (8.33% in the study group versus 2.58% in the control group). The proportion of right hydrosalpinx (25% versus 7.78%) and left hydrosalpinx (16.66% versus 10.34%) also increased significantly. **Conclusions.** The coronavirus pandemic reduced the addressability of patients with infertility to 10.3% compared to the previous year, and significantly increased the proportion of patients discovered with bicornuate uterus, endometriosis and hydrosalpinx.

**Keywords:** hysterosalpingography, coronavirus, infertility

## Endometriosis-associated ovarian cancer

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Ovarian cancer is the gynecological tumor with the highest mortality, with a prevalence of 3.7% of malignant pathology in women. Over 90% of ovarian tumors have an epithelial origin, the rest coming from germ or thecal cells. In recent years, ovarian cancer has been divided into two subtypes – type I and type II, the first type including low-grade cancers and borderline serous tumors, endometrioid tumors, mucinous tumors, and clear cell carcinoma. The relationship between endometriosis and ovarian cancer was first discussed by Sampson in 1927, based on the coexistence of ovarian carcinoma with endometriosis in the same ovary,

similar histological pattern, and the absence of other malignancies with another location. In 1953, Scott highlighted the histopathological transition from benign endometriosis to cancer. Currently, the prevalence of ovarian cancer in people with endometriosis varies between 0.7% and 17%. Molecular medicine and genetics have allowed the understanding of the pathogenetic processes of endometriosis as a precursor to cancer. Currently, the malignant potential of endometriosis is recognized, thus leading to the need for proper long-term patient management.

**Keywords:** ovarian cancer, endometriosis

## Why do we fail the early diagnosis of endometriosis and adenomyosis?

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**Introduction.** Patients diagnosed in advanced stages of endometriosis and/or adenomyosis are still common in medical practice, although the advances in imaging are considerable. This delayed diagnosis is determined by a low degree of clinical suspicion. **Materials and method.** For this reason, we consider appropriate to review the diagnostic criteria, starting from the anamnesis data (personal and heredocolateral history, menstrual history, gynecological and obstetrical history) and the clinical and imaging examination. **Results.** In patients with endometriosis, the main symptom is pelvic pain, in its various forms (dysmenorrhea or dyspareunia). The characteristics of pelvic pain (diffuse or crampoid) must be correctly differentiated from that of pelvic inflammatory disease, with which it may coexist. From the anamnesis, we can insist on the characteristics of dysmenorrhea, which can occur frequently one to two days before menstruation, persists and lasts after its end. Urinary or digestive symptoms accentuated during menstruation are also suggestive (dysuria, diarrhea, dyschezia). The detailed clinical examination and the imaging investigations reveal the diagnosis. In

the case of adenomyosis, the anamnesis reveals dysmenorrhea, most often primary, to which is added the progressive increase of the amount of menstrual blood lost (up to menorrhagia). The patient may also report chronic pelvic pain, and in 10% of cases there is dyspareunia. The patient may have a history of diagnoses and treatments for endometriosis, endometrial polyps or even endometrial hyperplasia, with which there are associated. One of the most common associations is with the fibromatous uterus/uterine fibroids. There may be a history of infertility or failure of assisted human reproduction procedures. **Conclusions.** The early diagnosis in endometriosis allows the early adoption of a conservative medical attitude, with a beneficial impact not only on pain control, but especially on the patient's fertile prognosis. The early diagnosis in adenomyosis allows a better control of uterine hemorrhagic pathology, with the timing of a potential surgery and a better quality of life of the patient (for example, by avoiding anemia).

**Keywords:** endometriosis, adenomyosis, early diagnosis

## Preneoplastic alterations in abdominal wall endometriosis

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**Introduction.** Abdominal wall endometriosis is a frequent pathology, more and more common due to the increase in the percentage of births through caesarean section. The endometrial tissue can suffer certain structural and functional changes which can be detected by the immunohistochemical examination. These changes may lead to normal cell transformation in some patients with preneoplastic alterations (hyperplasia, dysplasia) and then evolving to neoplasia. **Objective.** The evaluation of how the inflammatory system is involved in cellular alteration and the observation of the preneoplastic (hyperplastic) transformation of areas of interest. **Experimental part.** This is a retrospective study of 20 patients admitted in the Obstetrics-Gynecology II Clinic, Emergency County Hospital of Craiova, between 2016 and 2021, which presented a history of caesarean section. The diagnosis of abdominal wall endometriosis was presumed due to the accentuated symptoms and the presence of a mass at the caesarean section scar level detected by ultrasound investigation. The patients were then biopsied and the excision of the endometriotic nodules was performed. The histopathological examination

established the final diagnosis. **Results and discussion.** The patients included in the study were between 17 and 56 years old. We noticed that preneoplastic cellular changes (endometrial hyperplasia) occur more frequent in older aged patients. Cytokeratin 7 (CK7) is found in both normal and neoplastic endometrial cells and can be used as a differential diagnosis marker, as it is negative in ovarian or digestive carcinomas. Anti-B-cell lymphoma-2 (Bcl-2)/phosphatase and tensin homolog (PTEN) antibody reveal immunolabeled ectopic endometrial cells, which may have suffered preneoplastic alterations. Anti-tryptase/Cluster of Differentiation 68 antibody demonstrates the presence of many mast cells/macrophages involved in the immune reaction around the endometriosis foci. **Conclusions.** A multitude of inflammatory, hormonal and mechanical factors are involved in the development of endometriosis. The presence of cellular apoptosis inhibiting genes increases the cell division rate, and the strong immune response can influence the malignant transformation of endometriosis.

**Keywords:** endometriosis, preneoplastic alterations, immunohistochemistry

## Endometriosis and subfertility: a systematic review

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**Introduction.** Endometriosis causes adhesions and lesions of the uterine tissues, resulting in the fallopian tubes not functioning properly. It creates cysts in the ovaries, which are the very cause of ovarian damage. It is not only the cysts that wear out the ovaries but also the surgeries that are performed to remove them. In fact, the more surgeries there are, the more damage is caused to the ovaries (Wei et al., 2020). Endometriosis depends on estradiol (E2) for its development, a hormone to which the success of pregnancy is due. In addition, endometriosis stops progesterone (P4) signaling (Houshdaran et al., 2020). This is due to chronic inflammation, lesions and deformities of tissues, but also to epigenetic changes in chromatin that determine cellular responses to mitogens and differentiation signals (Houshdaran et al., 2020). **Materials and method.** A recent literature search was conducted on the basis of PubMed with the keywords: “endometriosis”, “fertility”, “endometriosis and infertility”, “inflammatory reaction in endometriosis” and “endometriosis and epigenetics”. Based on the articles of Houshdaran et al., 2020, Wei et al., 2020, Qi et al., 2020 and Rasheed and Hamid, 2020, we try to find the answers to questions about the endometriosis and its effect on

fertility. **Results.** The development of endometriosis is dependent on estrogen, to which the endometrial tissues are hypersensitive. Although estrogen is required to initiate and promote the reproductive cycle, however hypersensitivity in women with endometriosis adversely affects reproductive function (Rasheed and Hamid, 2020). Endometrial lesions are present in an inflammatory microenvironment with higher local concentrations of cytokines, such as tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) (Kocbek et al., 2016; Qi et al., 2020). TNF- $\alpha$  increases the expression of phosphorylated IKKB, an important protein present in multiple signaling pathways that affects gene transcription, proliferation and apoptosis (Kocbek et al., 2016; Qi et al., 2020). Inflammation in the endometrial environment affects the quality of oocytes indirectly by cytokines in the peritoneal fluid, modifying ovulation and oocyte spindles, thus affecting both oocyte maturation and fertilization (Singh et al., 2016; Rasheed and Hamid, 2020). **Conclusions.** Inflammation and its derivatives negatively affect the quality of oocytes and make the environment of the uterus inhospitable to the implantation of the fetus.

**Keywords:** endometriosis, subfertility, inflammation

## Pathogenesis and pathophysiology of endometriosis: a systematic review

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**Introduction.** Endometriosis has been shown to be caused by abnormalities in molecular cataracts involving estrogen, progesterone and several prostaglandins (Günel et al., 2019). Three theories have been proposed to establish endometriosis (Chantalat et al., 2020). Retrograde menstruation is the most prevalent. Other studies show that we need to study endometriosis following in the footsteps of cancer and metastatic transcription factors (Eychenne et al., 2019; Chantalat et al., 2020). This review describes a summary of the molecular, metabolic and immune changes that occur during endometriosis, these changes contributing to its promotion and establishment. **Materials and method.** Articles were searched in PubMed, and articles from the last five years were selected. The pathogenesis of endometriosis remains unclear, however three theories have been proposed for the cause of endometriosis. **Results.** Retrograde menstruation, in which the epithelial and stromal cells of the uterus migrate and implant in the peritoneal cavity through the fallopian tubes, is the most accepted mechanism for the pathogenesis of endometriosis (Chantalat et al., 2020). However, retrograde menstruation does not explain the occurrence of endometriosis in extrapelvic areas. A second theory about the mechanism of initiation of endometriosis suggests that the epithelial peritoneal lining can be transformed into endometrial tissue under the influence of stimuli: this is the theory of colonic metaplasia (Chantalat et al., 2020). Another theory, for benign lymphatic or hematogenous metastases, proposes the extraperitoneal proliferation of endometrial tissue through the lymphatics and suggests that ectopic endometrial cells have migratory capabilities (Eychenne et al., 2019; Chantalat

et al., 2020). The transcription factor Specificity protein 1 (Sp1) promotes ectopic endometrial proliferation and is directly regulated by miR-25-3p (Shen et al., 2020). It is noted that the Sp-1 gene has been found to interact with many regulatory miRNAs that promote carcinogenesis and the development of various cancers. Hence, we need to focus on the study of genes that cause cancer metastasis or to hub genes such as Sp-1 that activate carcinogenic pathways. Glutamine/glutamate metabolism has been found increased in many types of cancer, such as in endometriosis, and several studies have correlated glutamine concentration with cell migration (Berkes et al., 2013; Zhang et al., 2017; Murgia et al., 2021). An increase in glutamine in specific areas of the brain in women with chronic pelvic pain associated with endometriosis suggests a role in the onset or worsening of pain in patients (As-Sanie et al., 2015; Murgia et al., 2021). Finally, estrogen and estrogen receptors play the most dominant role. During endometriosis, estrogen levels are dramatically increased. The dominance of estrogen does not necessarily mean that a woman has extremely high levels of estrogen, but that the ratio of estrogen to progesterone is very high, and there is no balance (Chantalat et al., 2020). **Conclusions.** Endometriosis is accompanied by changes in gene expression and many of them involve transcription factors that cause carcinogenesis and invasion of cells such as Sp-1. Also, it is accompanied by changes in metabolic pathways. Increased glutamate metabolism is observed, which contributes to the severity of symptoms and pain.

**Keywords:** endometriosis, pathophysiology, hormones, estrogen receptors, glutamine



## Research on the effect of endometriosis on fertility in an animal model

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**Introduction.** Endometriosis is a condition of female reproductive age where endometrial tissue (glands and layer) grows outside the uterus. Endometriosis is characterized by many researchers as an enigmatic disease and remains, even today, a serious condition that affects the quality of a woman's life and her reproductive capacity. Endometriosis can be surgically induced in rats, which exhibit similar symptoms to humans.

**Materials and method.** In our research, which was carried out at the Laboratory of Experimental Surgery and Surgical Research N.S. Christeas, 24 female rats of Sprague Dowley® type, aged 3 months old and weighing 170-200 grams, were used for the development of an animal model for the study of endometriosis. Living and handling conditions were in line with Presidential

Decree 160/91, which governs the protection of animals used for research purposes. All rats were deprived of food 12 hours before surgery. On the day of surgery, they were randomly divided into four groups, consisting of six rats each. Group A consisted of healthy female rats (control group). Group B consisted of rats with ovarian endometriomas. Group C consisted of rats with disseminated intraperitoneal endometriosis, while Group D consisted of rats with extraperitoneal endometriosis. In groups B, C and D, the disease was experimentally induced by transplanting fragments of endometrial tissue into ectopic sites. **Conclusions.** In our experimental model, we observed that endometriosis affects fertility by reducing the number of follicles.

**Keywords:** endometriosis, subfertility, rats

## Surgical induction of endometriosis in rats. A systematic review

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**Introduction.** Endometriosis can be surgically induced in rats, which exhibit similar symptoms to humans (Günel et al., 2019). **Materials and method.** The data were taken from PubMed and included studies from the recent years. In the studies we selected, the researchers induced endometriosis by transferring endometrial tissue from the uterus to extrauterine areas. **Results.** In their study (Cuevas et al., 2018), the researchers induced endometriosis in female rats. In endometriosis areas, still degenerated mast cells were observed. Mast cell secreted proteases play an important role in fibrinogenesis and endometrial tissue migration (Cuevas et al., 2018). Free radical scavengers, such as melatonin and erythropoietin, have been found to reduce endometrial lesions by their antioxidant properties (Yildirim G, et al., 2010; Günel et al., 2019).

In their study (Günel et al., 2019), the authors caused endometriosis in rats and after induction they administered estrogen to cause greater damage. In the group of rats administered by erythropoietin, endometrial foci and histopathological scores were both found to be reduced. After 20 days of erythropoietin treatment in rats, the lesions were further reduced (Chadha et al., 2008). **Conclusions.** Rats have been widely used in endometriosis models, as they show similar symptoms to humans. The accumulation of estrogen, the innervation of the hypothalamus and the oxygenation of the area through the development and differentiation of erythrocytes play an important role in the manifestation of symptoms.

**Keywords:** rats, endometriosis, estrogen, stress, erythropoietin

## Alternatives in endometriosis: myth or reality?

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**Introduction.** Endometriosis is considered an enigmatic malady with chronic symptomatology, having a negative impact on patients' quality of life. Surgical interventions and hormonal substitution therapy represent the current treatment for endometriosis. Adopting a long-term strategy may require a combination of surgical treatments, medical treatments and alternative therapies, in order to suppress the painful symptomatology and to control the other symptoms associated with endometriosis. **Methodology.** The research and the analysis of articles published in the specialized literature to assess the main options for the alternative treatment in endometriosis and the suppression rate of symptomatology. **Results.** The efficiency of conventional endometriosis treatment is currently limited. Consequently, it is necessary to exploit complementary and alternative strategies of therapy, to minimize the adverse effects of ongoing treatments. Several studies have shown that people suffering from endometriosis who have adopted a gluten-free diet have presented an improvement in ameliorating the painful symptoms and, at the same time, it has been concluded that an

increased intake of antioxidants has decreased the oxidative stress, responsible for the inflammation. Various medicinal plants have been investigated for their pharmacological properties in endometriosis therapy, their effects being linked to different compounds such as flavonoids and phenolic acid, reporting antiinflammatory, proapoptotic, antioxidant and immunomodulatory functions. Furthermore, some substances have been linked to a powerful effect ascribed to phytoestrogens which modulate estrogen-related activity. **Discussion and conclusions.** Women suffering from endometriosis are interested in using complementary and alternative medicine. The majority of female patients have used at least one CAM method to relieve the symptoms associated with the disease. Although promising, the available evidence is based on a limited number of well-conducted clinical studies. Therefore, properly conducted clinical studies are mandatory to get conclusive results regarding the promising role of complementary and alternative methods in endometriosis.

**Keywords:** endometriosis, complementary and alternative medicine, phenolic compounds, oxidative stress

## Parietal endometriosis

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**Introduction.** Endometriosis of the abdominal wall is a condition defined by the presence of endometrial tissue in the subcutaneous adipose tissue and in the muscles of the abdominal wall. The diagnosis can be difficult due to the fact that the symptoms are not specific. The patients present with catamenial abdominal pain and palpable abdominal tumor. Endometriosis of the abdominal wall usually affects women of fertile age and most commonly occurs on the post-caesarean scar. The diagnosis can be made by ultrasound or magnetic resonance imaging, correlated with medical history and clinical examination. The treatment of choice is surgical resection of the endometrioma. **Methodology.** During 2019 and 2020, 146 patients diagnosed with endometriosis were treated in our clinic. Eleven of these cases were diagnosed and treated for abdominal wall endometrioma. **Results.** 16.06% of the patients diagnosed with endometriosis were diagnosed with abdominal wall endometrioma. Of the 11 cases of parietal endometriomas, 45% also associated deep endometriosis lesions of the pelvic peritoneum,

unilateral or bilateral endometriotic cysts, deep endometriosis nodules in the parameters or uterosacral ligament or intestinal nodules. The average age of patients was 35 years old. The results of the histopathological examination confirmed in all cases the diagnosis of parietal endometriosis. In two of the 11 patients with abdominal wall endometrioma, polypropylene mesh was used to close the aponeurotic defect. **Conclusions.** Endometriosis of the abdominal wall is usually manifested by palpable tumor formation accompanied by cyclic abdominal pain. Ultrasound together with a correct clinical examination and the patient's history can guide the diagnosis. MRI is nonspecific but it can help diagnose node extension and the deep pelvic endometriosis lesions. In our experience, abdominal wall endometriomas occur quite frequently, with or without deep endometriosis. The number of cases diagnosed with parietal endometriosis is increasing, in line with the increase in the number of caesarean sections.

**Keywords:** deep endometriosis, abdominal wall endometrioma, surgical resection, cyclic abdominal pain

## Use of autologous hematopoietic bone marrow stem cells to improve fertility

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**Objective.** Hematopoietic autologous stem cells are undifferentiated cells with the potential to multiply and differentiate into different types of mature cells, which are obtained by harvesting bone marrow from the iliac crest, for example, from the same patient, in the same intervention as the treatment. The goal is to rejuvenate the ovaries in patients with premature ovarian failure and endometrial regeneration in pathologies such as Asherman syndrome. This treatment can give women the chance to have a pregnancy without donated oocytes, improves the quality of life of women suffering from premature menopause and restores fertility. **Materials and method.** We performed an analysis of studies in the literature on the results of treatment with hematopoietic autologous stem cells in improving fertility. **Results.** Studies that have evaluated patients who want a pregnancy but have been advised to use donated oocytes (due to a poor ovarian response to controlled ovarian hyperstimulation for *in vitro* fertilization or due to low ovarian reserve and low oocyte quality) show promising results.

Laparoscopic injection of stem cells proved superior to transvaginal injection. The use of autologous bone marrow stem cells has proven superior to the use of adipose tissue stem cells and is a minimally invasive technique with low associated risks. After the procedure, studies show follicular growth, improved vascularity, increased follicular and stromal cell proliferation and also reduced apoptosis and cell atresia. In refractory cases of Asherman's syndrome or endometrial atrophy for various reasons, studies reveal that the instillation of hematopoietic autologous stem cells has had favorable results in endometrial regeneration and the reappearance of menstruation and fertility. Studies also include obtaining spontaneous pregnancies after stem cell treatment in patients with a history of IVF failure. **Conclusions.** Stem cell therapy may provide solutions for dozens of women suffering from ovarian failure, poor oocyte quality, premature menopause, infertility or endometrial pathology such as Asherman syndrome.

**Keywords:** hematopoietic autologous stem cells, premature ovarian failure, AMH

## Bowel endometriosis – Bucharest endometriosis centre experience

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**Introduction.** Endometriosis is a chronic, inflammatory, estrogen-dependent condition which affects approximately 10-15% of reproductive-aged women. It is classified as genital versus extragenital. Affecting up to 37% of women with endometriosis, bowel endometriosis is the most common site for extragenital endometriosis and may present as deep dyspareunia, dyschezia, diarrhea or constipation, bloating, blood in the stool, pain with sitting, and chronic pain. It can line the bowel serosa or the subserosal area, or it can deeply infiltrate the muscularis or the mucosa. We present our three-year experience conducted in the Bucharest Endometriosis Centre, which proudly gathers multiple laparoscopic specialists who provide patient-targeted multidisciplinary treatment of bowel endometriosis. **Methodology.** Our team consists of three gynecologists, two general surgeons, one urologist, one consultant radiologist and five ART (assisted reproduction techniques) specialists. In three years, we managed 557 endometriosis cases in women with ages between 21 and 52 years old. All surgeries were done laparoscopically. **Results.** Among all

our cases, 414 patients proved to have deep infiltrating endometriosis and 226 patients had bowel endometriosis. We emphasize the chosen types of excision, their location and association pattern of the lesions, along with the intraoperative incidents and complications. **Discussion and conclusions.** The benefits of excisional surgery are undeniable, including not only pain relief, but improvement of the quality of life, potential increase of fertility and cancer prophylaxis. The surgical approach of the bowel endometriosis splits into three categories: shaving, disc resection, and segmental resection. It is influenced by the location of the bowel lesion, the depth of infiltration, the presence/absence of stricture and the number of lesions. Based on our extensive experience in conjunction with constant reviewing of the literature, we strongly advise that bowel endometriosis should be managed only by a multidisciplinary endometriosis-specialized team, which is able to diagnose and treat it accordingly, in a minimally invasive fashion.

**Keywords:** bowel endometriosis, laparoscopic surgery, multidisciplinary team

## Ureteral and diaphragmatic deep infiltrating endometriosis – surgical management in two challenging cases

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**Introduction.** Deep infiltrating endometriosis (DIE) represents infiltrative lesions with a depth more than 5 mm beneath the peritoneum surface. Besides the typical involvement, DIE can also impact the ureters and the diaphragm. We have encountered ureteral and diaphragmatic DIE more often than expected. We present two videos to demonstrate how we surgically managed this endometriosis phenotypes. **Methodology.** In our three-year experience, from a total of 557 managed cases of endometriosis, we encountered 57 cases of ureteral endometriosis and 47 cases of diaphragm endometriosis. **Results.** The first case is about a woman who was diagnosed in a urology department, with grade 3-4 uretero-hydronephrosis. After the placement of ureteral catheter (double J), she was hospitalized in our center for surgical treatment. The complete removal of the stenotic lesion was performed, with preserved integrity, against all the odds in favor for ureteral re-implantation. The second video displays the case of a patient who was operated one year before for bowel endometriosis with colorectal resection and diaphrag-

matic minor endometriosis lesions which were excised. Subsequently, the patient underwent ovarian stimulation within an ART (assisted reproduction technique) protocol. After this treatment, the patient accused severe pain localized in the chest, interscapular and in the right shoulder. Magnetic resonance imaging revealed infiltrative endometriosis lesion in the right hemidiaphragm that required excision and suturing of the diaphragm. **Discussion and conclusions.** Ureteral DIE incidence is cited as 0.1-1% and usually involves the lower one-third of its segment. Diaphragmatic endometriosis is a rare disorder. In 95% of cases, the lesions occur on the right hemidiaphragm. In contrast with ureteral endometriosis, which is mostly indolent but dangerous, the symptoms in diaphragmatic endometriosis may vary from intense chest pain to thoracic endometriosis syndrome (TES). Decompressive surgery is mandatory in ureteral endometriosis, as well as the full excision of diaphragmatic lesions.

**Keywords:** ureteral endometriosis, diaphragmatic endometriosis, DIE

## Endometriosis – a benign pathology with malignant potential

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**Introduction/objectives.** The capacity of endometriosis for malignant transformation is well known: either endometriosis implants can directly undergo malignant transformation, or both processes share a common precursor mechanisms and predisposing factors. Endometriosis-associated ovarian cancer (EOC) occurs in 60-80% of cases in association with atypical endometriosis and is represented by clear cell carcinoma (CCC) and endometrioid carcinoma (EC). The study seeks to identify atypical changes developed in endometriosis lesions as precursor lesions of ovarian carcinomas, as well as their association. **Methodology.** A retrospective analysis of 31 cases of endometriosis and 19 cases of CCC or EC was performed. Immunohistochemical markers were used to assess the existence of stem-like cells (BMI-1), and also the alteration of intercellular adhesion mechanisms (E-cadherin, beta-catenin) and of apoptosis and cell proliferation (CK18, Bax, Bcl-2, p53, Ki-67). **Results.** The progressive loss of BMI-1 expression with stage advancement demonstrates that BMI-1 can be considered as a prognostic factor in EOC. The

staining index of E-cadherin is intense in endometriosis and gradually decreases with the gradual evolution of cases diagnosed with malignancy. CK18 showed a high staining index in endometriosis, and in the malignant group a progressive reduction of the staining index was correlated with the stage progression. P53 expression in endometriosis was significantly lower compared to the expression in tumor tissue, indicating less aggressive behavior of endometriosis compared with malignant lesions. The Ki-67 index in tumor cells was reduced in more than half of the cases and was lower or even absent in endometriosis, as an indicator of less proliferative activity in the pathogenesis of endometriosis compared to malignant tumors. **Discussion and conclusions.** Endometriosis can be considered a precursor lesion of EOC, demonstrated both by their coexistence and the identification of intermediate lesions, and by the progression of various markers (of TEM, apoptosis and cell proliferation, respectively).

**Keywords:** ovarian cancer, clear cell carcinoma, endometrioid carcinoma, endometriosis

## The fate of frozen embryos: their destruction, adoption or donation?

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**Objectives.** *In vitro* fertilization (IVF) includes a complex set of procedures used to improve fertility, prevent genetic problems, and help conceive a child. In most cases, this procedure results in more than one embryo. The couples have a major problem after IVF regarding the remained cryopreserved embryos and what should happen with it. **Materials and method.** We performed a research on the international studies about the fate of frozen embryos after obtaining the number of pregnancies desired by the patient. **Results.** There are some principles of bioethics that are very important for both patients and medicine: respect for autonomy, non-maleficence, beneficence and justice. There are specific laws that must

be respected, laws stipulated by the Societies of Human Reproduction and Embryology, the Declaration of Human Rights and various civil and criminal codes available, which differ in each country and state worldwide, and also the beliefs of the Christian religion. The couples can opt for donation or adoption meaning they can transfer the embryos to another couple. Another option is the destruction of the surplus embryos. **Conclusions.** This article provides a complete picture of patients, as well as doctors in general, in terms of justice, religion and bioethics on surplus frozen embryos remaining after obtaining the desired number of children.

**Keywords:** embryos, fertility, conception, bioethics

## Therapeutic aspects of symptomatic adenomyosis

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**Introduction.** Adenomyosis is a benign uterine disease. It is represented by the presence of endometrial glands in the structure of the myometrium. It has become a common pathology. The symptoms are intense and usually affect the patient's daily life. Adenomyosis can be suspected based on the clinical and ultrasound aspects, and diagnosed by histopathological exam. It has multiple morphofunctional aspects, and sometimes it has important consequences on the patient's life. **Methodology.** This is a retrospective study, conducted between 2018 and 2021 in the Obstetrics-Gynecology Clinic II of the Craiova County Emergency Clinical Hospital, on a group of 40 patients, aged between 21 and 58 years old. The patients presented menometrorrhagia and pelvic-abdominal pain. The usual blood tests frequently revealed a certain degree of anemia, and the ultrasound examination showed suggestive aspects of adenomyosis. For some patients, a symptomatic treatment was necessary and in other patients, the surgical treatment. The samples were sent to the pathological anatomy department for the histopatho-

logical examination. The diagnosis of adenomyosis was confirmed by histopathological examination. In the classic hematoxylin-eosin staining, we observed areas with fibrocollagen tissue in full myometrium, groups of dilated cystic glands and endometrial stroma, with acute periglandular inflammation. The differential diagnosis with a possible metastasis with a digestive starting point was made using the immunohistochemical study with anti-estrogen receptor (ER) antibodies – positive reaction, anti-progesterone receptors (PR) – positive reaction, anti-cytokeratin 7 (CK7) – positive reaction, and anti-cytokeratin 20 (CK20) – negative reaction. **Conclusions.** The histopathological examination confirmed the existence of endometrial glands, positive for hormonal markers, and cytokeratins that are specific for the endometrial epithelium. The ultrasound examination proved to be a useful tool in the diagnosis of adenomyosis. It also helped us to guide the treatment and follow up the results.

**Keywords:** adenomyosis, pelviabdominal pain, ultrasound

## Endometrial polyps and infertility – the experience of our clinic

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**Introduction.** Endometrial polyps are often discovered in subfertile women. How polyps contribute to subfertility and pregnancy loss is uncertain, and the possible mechanisms are poorly understood. **Materials and method.** A prospective cohort type 1 study based on STROBE statement was designed. The study group included women diagnosed with endometrial polyps and infertility in the "Bucur" Maternity, "Sf. Ioan" Clinical Emergency Hospital, Bucharest, Romania, between January 2016 and December 2019. The diagnosis was established by ultrasound and hysteroscopy and confirmed during hysteroscopic procedure. **Results.** We performed 278 hysteroscopies during the study period. The study included 56 (20.14%) patients, aged between 28 and 46 years old (mean age: 29.57 years

old; standard deviation: 9.79) who associated infertility and endometrial polyps. The hysteroscopy confirmed the diagnosis of polyps made by ultrasound in 99.5% of cases. The main characteristics of the study group were as follows: urban area citizens (82%), non-smokers (73.2%) and obese women (65%). These women were diagnosed with primary (67.3%) and secondary infertility (32.7%). They had associated gynecological pathologies: uterine myomas in 1.7% of cases and adenomyosis in 2.3% of cases ( $p < 0.001$ ). **Conclusions.** Patients diagnosed with endometrial polyps may associate infertility. Future extensive randomized studies are required to prove our associations between endometrial polyps and infertility.

**Keywords:** infertility, endometrial polyps

## Deep endometriosis: when do we operate?

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**Background.** We define deep endometriosis as the peritoneal invasion of endometrial tissue more than 5 mm in depth. Frequently affected areas include the rectovaginal septum, the rectus, the sigmoid colon, the urinary bladder and the ureters. Usual symptoms include cyclical or noncyclical abdominal pain, infertility, dysmenorrhea, dysuria and dyschezia. The diagnosis is obtained mainly clinical, laparoscopy being considered the gold standard, since the direct visualization of the lesions is possible, as well as correlation with the histopathological examination. The treatment can be medical or surgical. Setting aside the established indications for surgery – unresponsive pain and infertility, there are certain aspects that need to be considered more thoroughly, such as the progressiveness of the disease, as well as the functional impact on the affected organs. **Materials and method.** We present a systematic review in which we included articles regarding the surgical treatment of deep endometriosis and the right time when surgery is indicated. We will also present several cases of severe deep endometriosis, in order to emphasize the progressive character

of the disease and the consequences of late surgical treatment. **Results.** Endometriosis should be viewed as a chronic disease which affects the quality of life. Certain localizations of the disease can lead to irreversible damage, going as far as organ function loss. For example, parametrial nodules can obstruct the ureter, develop ureterohydronephrosis and lead to kidney failure. Intestinal endometriosis can cause bowel obstruction, as well as the destruction of the nervous plexus within the intestinal wall, that will lead to functional disturbances. The goal of laparoscopic surgery in deep endometriosis is to completely excise the lesions, reducing the risk of recurrence and reintervention as much as possible. **Conclusions.** The surgical treatment of deep endometriosis is a challenging task. The failure of treatment is correlated with the surgeon's experience, case complexity and the anatomical localization of the disease. Endometriosis is a chronic disease and the goal of surgery is to stop the lesional progression and to restore the normal anatomy and function.

**Keywords:** deep endometriosis, surgical treatment, laparoscopy

## Impact of endometriosis on women's quality of life

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**Introduction.** Endometriosis is one of the most common gynecological diseases and affects approximately 10% of women of reproductive age. The most common clinical signs of endometriosis are menstrual disorders, chronic pelvic pain, dysmenorrhea, dyspareunia and infertility. The symptoms of endometriosis often affect the psychological state and also the women's socio-familial behavior. For this reason, endometriosis is considered a disabling condition that can significantly compromise social relations, sexuality and the quality of life. **Materials and method.** A review of the literature on the impact of endometriosis on women's quality of life has been carried out. The strategy involved the use of keywords such as "endometriosis", "anxiety", "depression" and "chronic pelvic pain", with the selection of articles and the narrative description of the data obtained. **Results.** The psychological factors play an important role in determining the severity of symptoms, and women suffering from endometriosis report high

levels of anxiety, depression and other psychiatric disorders. In addition, endometriosis is one of the most important causes of chronic pelvic pain. Several studies have highlighted the influence of chronic pelvic pain on the quality of life of women with endometriosis and their psychological well-being. High levels of anxiety and depression have been shown to increase the severity of pain. In addition, women with endometriosis report significantly more sexual dysfunction compared to healthy women. **Conclusions.** The negative impact of endometriosis on women's quality of life has been widely demonstrated by the literature, along with the fact that the presence and severity of pelvic pain are associated with anxiety and depression. An individualized, couple-centered approach, that integrates psychosexual and medical management for endometriosis, is considered optimal.

**Keywords:** endometriosis, chronic pelvic pain, anxiety, depression



Societatea de Endometrioză  
și Infertilitate Est-Europeană



# A VI-A CONFERINȚĂ NAȚIONALĂ A SOCIETĂȚII ROMÂNE DE HPV

1-3 Iulie 2021, Poiana Brașov - Hotel Alpin





## Implications of human papillomavirus infection in infertility

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**Introduction/objective.** Human papillomavirus (HPV) infection is one of the most common sexually transmitted infections worldwide. Reproductive function and pregnancy could be affected by HPV infection. The presence of HPV was reported in semen, and chronic viral infection determines the inflammation of low urethra, which provokes infertility. HPV in sperm was associated with miscarriage. Regarding fertility, this infection has also a negative impact in women. **Methodology.** Articles published in Web of Science Core Collection databases were reviewed. Only articles published in English until April 2020 were included. The research was performed using the following keywords: "HPV infection", "infertility", "semen". **Results.** In his study on 70 infertile men, Mohimi found a 11.4% prevalence of HPV infection. In men with HPV infection, sperm motility was lower and sperm morphol-

ogy was poorer than in control group. In his study on 729 infertile men, Boeri found a prevalence of 15.5% for HPV infection. The semen in HPV patients had a higher DNA fragmentation and poorer reproductive outcome. HPV infection during treatment for *in vitro* fertilization (IVF) or intrauterine insemination (IUI) was associated with poorer outcome. Spandorfer found a 50% lower pregnancy rate in IVF for women with HPV infection. Infected spermatozoa could act as a carrier of viral genome in oocyte during conception. HPV infection could alter the development of the embryo, especially in two cell phases. **Conclusions.** A multidisciplinary approach of infertile couple affected by HPV infection is very important, in order to improve not only the reproductive outcome, but also the overall health.

**Keywords:** infertility, HPV, semen

## Impact of HPV infection on cervix transformation zones in young patients

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**Introduction.** There are many types of human papillomavirus, and 14 of these types are commonly associated with cervical cancer. Approximately 70% of the cervical cancers and preneoplastic lesions are caused by types 16 and 18. Preneoplastic cervical lesions can be treated, and HPV infection can disappear under the action of the immune system. Persistent infections can progress to neoplastic lesions. **Materials, method and results.** This is a retrospective study, conducted in the period 2018-2019. This study included a group of 30 young patients, aged 17-29 years old. All the patients included in this study had cytological and colposcopic changes of the cervix and HPV HR+ genotyping. Some of the patients complained of vaginal bleeding after sexual intercourse, leukorrhea and vaginal discomfort, but most of them were asymptomatic and were diagnosed with HPV during a screening exam. For the patients with low-grade lesions on the cytological exam or colposcopy, it was decided to apply local treatments and a follow-up after six months. For the patients with high-grade lesions, we performed an excision of the cervical

lesions. The excised fragments were sent to the anatomic pathology department for microscopic study. Using the immunohistochemical study, we proved the presence of HPV in the excised tissue (positive anti-p16 antibody) and an increased degree of intraepithelial cell proliferation (CIN1-positive reaction to anti-Ki67 antibody in the basal layer, CIN2-positive reaction in the basal and intermediate layers, CIN3-positive reaction in the basal, intermediate and superficial layer). Seventeen patients presented high-grade lesions on the microscopic examination for the excised tissue. **Conclusions.** Untreated HPV infection leads to the transformation of normal cervical cells into premalignant and later malignant cells. These lesions were identified by histological and immunohistochemical studies that proved the degree of the intraepithelial lesions, by the presence of cells in the proliferation phase. The influence of HPV infection, demonstrated immunohistochemically, highlighted the prognosis and the evolution of the patients.

**Keywords:** human papillomavirus, colposcopy, microscopy

## Means of increasing HPV vaccine adherence

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Human papillomavirus can lead to cancer in both men and women. Almost all HPV-related cancers can be prevented by HPV vaccination (99%). HPV vaccines are recommended for adolescents between the ages of 11 and 14 years old, but adherence remains suboptimal and many adolescents do not receive the vaccine. A few strategies to ensure that many teens get vaccinated include using vaccination information systems and sending reminders to patients by their general practitioner. Educational interventions aimed at advising parents and adolescents to increase vaccine

coverage must become a priority. Clearly, alternative approaches to increasing HPV vaccination are urgently needed. We, as gynecologists, ought to give counsel to adolescents' mothers during their annual gynecological consultation. The aim is to improve, among parents, one by one, the level of knowledge on the effectiveness and efficiency of the vaccine, if we want to promote favorable attitudes, intentions and behaviors towards HPV vaccination.

**Keywords:** HPV, anti-HPV vaccine, education, counseling

## The influence of vaginal pH on the progression of HPV lesions

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Cervical cancer is the most common malignancy in the gynecological field, with the highest death rate. Most cervical cancers are diagnosed at the stage of intraepithelial neoplasia (CIN), being caused by the HPV infection. In general, the body has the ability to heal spontaneously following infection with various HPV viral strains. Under certain conditions, pathology or exogenous factors may influence the persistence of the infection and the further progression to cervical injury and cancer. Several factors that would influence the change in vaginal pH and therefore alter the immune function were evaluated. These factors were mostly represented by vaginitis with various infectious agents, vaginal candidiasis, *Trichomonas vaginalis* infection, oral contraceptive treatments, age and pregnancy. Bacterial vaginosis is characterized by the imbalance of normal vaginal flora with the increase of vaginal pH above 4.5. In relation to HPV infection, it was as-

sumed a possible correlation of the fact that the normal flora, mainly composed of lactobacilli, would produce hydrogen peroxide as a defense mechanism of tissues against pathogenic conditions. If the normal microflora of lactobacilli is destroyed for various reasons, the local defense is low, creating a favorable ground for the persistence of HPV infection. The vaginal HPV infection is caused by some biological interaction between these factors, or both can occur in a certain group of females which present some risk factors that are still unknown. It is known that the presence of vaginitis can be associated with HPV infection – a strain with a high oncogenic risk. Additional molecular studies are needed to demonstrate the synergic interaction between viral factors represented by HPV strains and infectious or environmental factors.

**Keywords:** HPV, vaginal microflora, vaginitis, vaginal pH

## Etiopathogenesis of premature birth in patients with HPV genital infection

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**Objectives.** Literature analysis of the influence of HPV genital infection on the pregnancy outcome. **Methodology.** A series of studies and literature data were evaluated regarding the risk of human papillomavirus infection in pregnancy and the implication in premature birth. **Results.** Six studies were included in the paper. HPV alone or surgical interventions due to HPV infection were analyzed as a risk factor in the outcome of the pregnancy. The results of the studies varied. The three studies that analyzed HPV-related disease of the cervix concluded that HPV is incrimi-

nated in poor pregnancy outcome. Three studies of the PPRM and HPV had different results. One study showed that HPV is not involved in pregnancy outcome, while the other two studies offered data, concluding that HPV is involved in premature birth. **Conclusions.** Research on the HPV involvement in premature birth offer precious data that may lead to new research area in the near future, with valuable results and influence in the pregnancy outcome.

**Keywords:** HPV, genital infection, pregnancy outcome

## Consistencies and discrepancies in preneoplastic cervical lesions

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**Introduction.** The goal of cervical cancer screening is to rapidly detect and treat severe preneoplastic lesions, which would otherwise have the real potential to develop a neoplastic lesion. The diagnostic approach includes individualized algorithms, and the treatment consists in removing the suspicious lesion within healthy margins, with confirmation by histopathological examination. **Materials and method.** We analyzed the diagnostic methods that we use and the degree of correlation with the results of the histopathological and immunohistopathological examination. We insist on frequent situations in gynecological practice, which move away from the ideal cases of perfect concordance between cytology, HPV genotyping, immunocytology, colposcopy and histopathological examination. **Results.** From the case studies focused on the preneoplastic pathology of the cervix, we note:

- Patients with repeated negative cytology, but with a rich inflammatory background, who on opportunistic examinations receive HPV HR16, 18 or 45

positive results; positive colposcopic examination, major grade histopathological result (CIN 2+).

- Patients with repeated ASCUS cytological results, HPV HR negative, suspicious colposcopic lesions, with either minor or major histopathological results.
- Young patients without positive cytology, but with HPV HR positive, in which the interventional attitude is untimely taken, the histopathological result being negative.
- Young patients with AGC cytological results, in whom colposcopy and histopathological examination confirm a high-grade result for a squamous, not glandular lesion.

**Conclusions.** We advocate for a more personalized attitude, which takes into account individual risk factors (onset of sexual life, number of sexual partners, smoking, other associated persistent genital infections). Consulting recent ASCCP guidelines, with an extremely pragmatic approach, can be very useful in this regard.

**Keywords:** consistencies, discrepancies, preneoplastic cervical lesions

## Giant *condyloma acuminatum* – case presentation

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**Introduction.** *Condyloma acuminatum* is a clinical manifestation of human papillomavirus infection. This pathology is characterized by the presence of fleshy, pigmented papules, located in the anogenital region. The most common types of HPV which cause these anogenital warts are HPV 6 and HPV 11. **Case report.** A 31-year-old patient, with a caesarean birth in the obstetrical history, came to the hospital's ambulatory service with several giant tumors/warts in the anorectal region. The tumors started to develop four years ago and have grown ever since. It was decided to apply the surgical treatment with the excision of these formations and to send the excised pieces to the pathological anatomy department. The histopathological result proved the presence of HPV infection (positive immunostaining with anti-p16 antibody), an increased degree of cell proliferation (intensive immunostaining with anti-Ki67 antibody), an abundant vascularization

of warts, and cauliflower-like formations (intense immunostaining with anti-cluster of differentiation 34 antibody). All of this proves the ability of the condylomatous tumors to grow and develop very fast. The negative reaction on the immunostaining with the anti-p53 antibody demonstrated the benign character of the tumors. **Conclusions.** The surgical treatment does not cure the HPV infection, but it does help improving the patients' quality of life. Histopathological and immunohistochemical examination helped us prove that the clinical development of the tumors was determined by the presence of HPV, and the accelerated development of warts was achieved from a large number of dividing cells, supported by an intense vascularization. The absence of oncoprotein p53 confirmed the benignity of cauliflower formations.

**Keywords:** anogenital region, human papillomavirus, surgical excision

## The impact of age and HPV status on the prevalence of CIN3+ lesions in patients with HSIL and ASC-H cytology

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The ASCCP 2019 guidelines stratifies the risk for a high-grade CIN3+ lesions, not only based on current screening test results, but also based on age and individual history. The aim of this study is to analyze the prevalence of CIN3+ lesions according to age and oncogeneity of the HPV genotypes in patients with HSIL and ASC-H cytological changes and to analyze the importance of colposcopy in the management of these cases. **Methodology.** The study includes a retrospective analysis performed on a group of 126 patients with HSIL and ASC-H cytology, who addressed the colposcopy department of the "Panait Sîrbu" Clinical Hospital of Obstetrics and Gynecology, Bucharest, between January 2018 and February 2021, who were tested for HPV and in which a surgical electroexcision procedure was performed. **Results.** 64.3% of the 70 patients with

HSIL and 21.4% of the 56 patients with ASC-H had a CIN3+ lesion. The prevalence of CIN3+ lesions was inversely proportional to the age of the patients and was maximum (83%) in the group of patients with HSIL cytology and infection with HPV 16/18 genotypes. In most cases, these patients had major colposcopic changes. **Conclusions.** Age over 50 years old, infection with HPV 16/18 genotypes, HSIL cytology and the severity of colposcopic impression were important predictive factors in the diagnosis of CIN3+ lesions. The results of the study support the calculation of the risk for a CIN3+ lesion according to the ASCCP 2019. The colposcopic impression had a decisive role in the management of these patients.

**Keywords:** HSIL cytology, HPV genotype, CIN3+ lesion, age, colposcopic impression

## HSIL management. Correlations between colposcopy and histopathological examination

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High-grade squamous intraepithelial lesion (HSIL) includes the entities formerly called intraepithelial cervical neoplasia (CIN 2, CIN3), moderate and severe dysplasia, and *in situ* carcinoma. Although not all high-grade lesions will progress to cancer, HSIL is considered a preneoplastic lesion. The aim of our study was to compare colposcopy changes associated with the diagnosis of HSIL (high-grade squamous cervical lesion) cytologically and histologically confirmed and the role of the

interprofessional team in the prompt evaluation and management of these lesions. We evaluated cytological/histological diagnoses of HSIL and colposcopic diagnostic elements. The cytological and histological diagnoses were reported according to the Bethesda system. Out of the total of 1180 PAPS collected in 2020, a number of 27 presented HSIL results, these being the ones evaluated in the present paper.

**Keywords:** HSIL, colposcopy, cervical dysplasia

## Conceptual shift in cervical cancer screening: from cytology to biomarkers

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By detecting abnormal cells, cervical cytology or the Babeș-Papanicolaou smear proved to be an effective cervical cancer screening tool, although it has a rather low sensibility. The recognition of the link between sexual activity and cervical cancer led to the idea of a sexually transmitted pathogen as a cause of cervical cancer. Persistent HPV infection is the trigger for almost all cervical cancers, allowing the development of new diagnostic and triage tools, in the form of biomarkers. The most important viral biomarker is HPV DNA, already in use for primary screening, triage or post-treatment

follow-up. E6/E7 mRNA and viral methylation are appropriate methods for identifying persistent HPV infections. Among cellular biomarkers, dual staining of p16INK4a/ Ki-67 on cytology reveals the presence of a CIN2+ lesion. On the other hand, the absence of E4 is a strong proof of a transforming HPV infection, making these biomarkers strong candidates for the screening of pathological specimens. Newer technologies include the detection of the amplification of the TERC gene, which plays a role in carcinogenesis and microRNAs.

**Keywords:** HPV, biomarker, cervical cancer screening

## HPV-induced alterations in the squamous epithelium – lesions in the ENT and genital area

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Human papillomaviruses have been the subject of numerous studies related to cervical cancer. But the tropism of these viruses for the squamous epithelium does not stop at the cervical level. Histologically similar lesions can be identified in other epithelia, including those in the ENT sphere. Although HPV-induced squamous cell carcinomas are not as frequent as the

cervical ones, when compared to the non-HPV-induced oral carcinomas, they have different clinical and phenotypic features and have a better prognosis. Also, in these cases, the possibility of prevention by vaccination is discussed.

**Keywords:** HPV, squamous epithelium, squamous cell carcinoma

## Cytohistological correlations in HPV infection

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Cervical carcinomas can be prevented by detecting and treating precancerous lesions early. Although the cytological screening has decreased the incidence worldwide, the results obtained must be integrated in a clinical context in order to avoid false-positive diagnoses. Persistent infection with high-grade HPV is the leading cause of preneoplastic and neoplastic lesions. Although the Babeş-Papanicolaou cytological examination, performed both conventionally and liquid-based, is the

most efficient method in terms of quality/price ratio, and the histopathological examination is often considered the gold standard, in some cases there are inconsistencies between the two. In our study, we aimed to retrospectively evaluate Babeş-Papanicolaou smears and post-biopsy results in order to determine the incidence of false-positive and false-negative cases.

**Keywords:** Babeş-Papanicolaou smear, cervical biopsy, squamous neoplasia

## Dermoscopic findings and HPV genotypes of genital keratotic lesions: bowenoid papulosis, seborrheic keratosis and *condyloma acuminatum*

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**Introduction.** Gynecologists and dermatologists often encounter keratotic lesions in the genital area. Although making a clear diagnosis can be difficult, it is important for the treatment and prognosis closely related to the patient's quality of life. Dermoscopy has proven to be a useful, noninvasive tool. However, there is still a lack of dermoscopic data comparing bowenoid papulosis (BP), seborrheic keratosis (SK) and *condyloma acuminatum* (CA). More than 40 human papillomaviruses genotypes infect the genital area and manifest as various intraepithelial neoplasms. **Methodology.** This paper is realized to describe the distinctive dermoscopic features and HPV genotype distribution of BP, genital SK and CA. **Results.** Dermoscopically, BP presents glomerular vessels, CA presents hairpin vessels and SK is the least

vascular-patterned disease. SK shows cerebriform and CA has a knob-like or finger-like appearance and a whitish halo. BP and CA have positive results at the HPV DNA detection, but studies have shown that more than half of SK have positive HPV results. For the high-risk genotype, mainly HPV 16, BP shows the highest detection rate, and for the low-risk genotype, mainly HPV 6 and HPV 11, CA presented the highest detection rate.

**Conclusions.** Dermoscopy can be useful for differentiating the entity of genital keratotic lesions ahead of an invasive method and a physician should consider the morphologic plasticity of HPV-related keratosis in the genital area or the genital wart in the expanded concept.

**Keywords:** dermoscopy, bowenoid papulosis, seborrheic keratosis, *condyloma acuminatum*

## HPV infection in pregnancy and prematurity

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**Introduction.** Epidemiologically reassessed, human papillomaviruses (HPVs), especially oncogenic genotypes (HPVhr), contacted by both partners in pre-conception and/or periconception, require the effective management of the possible risks of maternal-fetal complications and negative pregnancy outcomes. In recent years, multiple studies have evaluated the possible link between HPV infection and prematurity. Prematurity is one of the greatest challenges for obstetrics, both through increased incidence, at least 15 million babies being born preterm every year, and through the impact it has. The objectives of this paper were the review of the data on the HPVs etiology of prematurity in pregnant women, as well as the related maternal-fetal medical consequences. **Materials and method.** A review of the literature was carried out regarding the impact of HPV infection in pregnancy and the link between the presence of this infection and prematurity. The strategy involved the use of keywords such as "HPV infection", "high-risk HPV", "prematurity" and "pregnancy compli-

cations", with article selection and narrative description of the data obtained. **Results.** Simultaneously with the oncogenic effect on the female genital tract, the evolutions of HPVs infected pregnancies, especially HPVhr, are explored. The prevalence of HPVs detection in cervical and/or placental sites in pregnant women with complications and negative pregnancy outcomes varies between 2% and 70.4%. The prevalence of cervical HPVs in pregnant women varies between 15.9% and 67.1% in cases completed with preterm birth and between 18% and 27.3% in cases of preterm rupture of membrane. The prevalence of placental infection with HPVs varies between 18% and 50% in pregnancies completed with preterm birth. **Conclusions.** Gestational HPVs, especially HPVhr, induce a high risk of prematurity with related maternal and fetal medical consequences and requires routine preconceptions and/or periconception investigations of HPV for both partners.

**Keywords:** prematurity, HPV infection, high-risk HPV, pregnancy



# AL 9-LEA CONGRES AL SOCIETĂȚII ROMÂNE DE ULTRASONOGRAFIE ÎN OBSTETRICĂ ȘI GINECOLOGIE

## CURS DE ECOGRAFIE GINECOLOGICĂ

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## Arnold-Chiari syndrome and semilobar holoprosencephaly in two successive embryo transfers after intracytoplasmic sperm injection (ICSI)

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**Introduction/objective.** Current data indicate a slight increase in the incidence of congenital malformations in children obtained by *in vitro* fertilization (IVF) with intracytoplasmic sperm injection (ICSI). **Methodology.** We analyzed the congenital malformations that appeared in the period 2011-2019 following IVF procedures in our clinic. During this period, 3115 IVF procedures were performed, the incidence of congenital anomalies being 1.8% (56 cases). The percentage of brain abnormalities in the total number of congenital anomalies was 5.3% (three cases), two of them occurring in the same couple, after the same controlled ovarian stimulation. We present the case of a 28-year-old patient who was evaluated in our clinic for male infertility, the concentration of sperm in the semen being 3 million per ml, with a progressive motility of 25%. **Results.** IVF was performed with ICSI, obtaining ten oocytes, of which eight were mature, seven embryos resulted from ICSI, from which two blastocysts of very good quality

were selected. The first embryonic transfer with fresh blastocyst resulted in a clinical pregnancy, but unfortunately, in the morphology of the second trimester, the fetus was diagnosed by ultrasound with Arnold-Chiari syndrome. Amniocentesis showed a normal karyotype of the fetus, but the parents decided to stop the pregnancy. At the second embryonic transfer, this time with frozen blastocyst, the pregnancy was obtained again, but unfortunately this fetus was diagnosed with semilobar holoprosencephaly in the first trimester of pregnancy and the parents decided to stop the pregnancy. The karyotype of both parents was normal. **Discussion and conclusions.** Patients should be informed about the slightly increased risk of developing cerebral malformations in fetuses obtained by IVF with ICSI, a risk that, according to literature data, is maintained after adjustments made for maternal age and other risk factors.

**Keywords:** *in vitro* fertilization, congenital cerebral malformations, intracytoplasmic sperm injection

## The correlations between maternal-fetal Doppler parameters and the serum level of metalloproteinases in preeclampsia

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**Introduction/objectives.** Preeclampsia is a pregnancy-specific disorder which affects around 8 million pregnancies worldwide. While the pathogenesis of preeclampsia remains unclear, poor placental perfusion is accepted as a major mechanism of preeclampsia; however, prior studies suggest that matrix metalloproteinases (MMPs) are involved into the pathophysiology of this syndrome. MMPs are zinc-dependent proteases that degrade extracellular proteins and their role is mostly connected to remodeling the endometrial tissue during the menstrual and estrous cycles. In preeclampsia, Doppler ultrasound evaluation is considered one of the most useful method for prediction and its parameters can reveal hemodynamic repercussions of preeclampsia. **Methodology.** Our research included publications from Google Scholar and PubMed related to the role of MMPs (MMP-9 and MMP-2) in preeclampsia, as well as Doppler parameters in all three trimesters of pregnancy. Studies ranging from January 2016 to May 2021 were selected by the following including criteria: full-text articles, written in English, human-based

studies, MMPs serum levels and Doppler parameters in patients with preeclampsia. **Results.** Most of the studies concluded that in preeclampsia the levels of MMPs – especially MMP-9 and MMP-2 – are decreased compared to normal pregnancy. When it comes to maternal-fetal examination, there was observed a significant decrease of uterine artery PI in all three trimesters. In patients with preeclampsia, uterine artery Doppler RI was significantly higher, which suggests an abnormal development of placenta. Considering the fact that the decreased Doppler PI of uterine artery in pregnancy indicates the process of trophoblastic invasion and MMP-2 and MMP-9 are related to the same process, the concentration of these serum proteases should be increased during the pregnancy. Most of the studies have not revealed a significant correlation between the plasma concentration of MMPs and maternal-fetal Doppler. **Conclusions.** MMPs could be used as markers for preeclampsia diagnosis, even though their interactions need further understanding.

**Keywords:** metalloproteinases, Doppler, preeclampsia

## The value of 3D ultrasonography in the diagnosis of congenital uterine anomalies

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**Introduction/objective.** Congenital uterine anomalies represent deviations of the normal anatomy that result from the maldevelopment of the embryological müllerian ducts. The estimated overall prevalence is approximated at 5.5-6.7% in the general population and about 7.3-8% in infertile women. Most up-to-date classification systems for congenital anomalies of the female reproductive tract were published by the European Society of Human Reproductive and Embryology (ESHRE) and by the European Society for Gynecological Endoscopy (ESGE) which proposed six main classes of anomalies of the reproductive tract, ranging from normal uterus to aplastic uterus and potentially unclassified cases. The endoscopic evaluation represented the gold standard for female genital anomalies, until the wide use of 3D ultrasonography, due to its accessibility, reduce cost and accuracy. **Methodology.** Our research included numerous cases presented to the “Dr. I.A. Sbârcea” Clinical Hospital of Obstetrics and Gynecology, Brașov, for numerous reasons, varying from mild discomfort to reproductive pathology. The patients were examined

using 2D echography and 3D echography. Using these diagnostic tools, they were diagnosed with congenital uterine anomalies ranging throughout the classes included in the ESHRE guidelines. **Results.** In this paper, we included numerous cases from our clinic that were diagnosed with congenital uterine anomalies using 2D echography as the first investigation method and 3D echography for the certainty diagnosis. Using strictly echographic methods, the patients managed to receive an accurate diagnosis regarding their congenital uterine anomalies whilst skipping invasive diagnostic tools such as endoscopic evaluation or exploratory laparoscopy, or the use of time consuming and expensive investigations such as MRI. The main goal was to assess the use of 3D ultrasonography in concordance to the ESHRE and the ESGE guidelines for diagnosis. **Discussion and conclusions.** 3D ultrasonography offers high accuracy rates in congenital uterine anomalies diagnosis, while having a widespread use, ease of accessibility and cost effectiveness.

**Keywords:** ultrasonography, uterine anomalies

## The use of transabdominal ultrasound in postoperative urinary retention

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Transabdominal ultrasound is highly used to detect postoperative urinary retention (POUR), which is often underestimated. Multiple factors and etiologies have been incriminated in the occurrence of POUR. These etiologies can be related to the type of anesthesia, surgery, comorbidities and drug used. Untreated POUR can lead to significant complications, such as extension of the hospital stay, urinary infection or detrusor muscle dysfunction. Transabdominal

ultrasound is considered a noninvasive technique, useful in detecting post-voiding residual. It allows the clinical decision-making regarding postoperative interventions. This article outlines the advantages of transabdominal ultrasound scanning in the diagnosis of POUR.

**Keywords:** transabdominal ultrasound, postoperative urinary retention, anesthesia, detrusor muscle dysfunction, decision-making

## The role of transperineal ultrasound in the treatment of female with prolapse mesh complications

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From the numerous surgical options available for the treatment of pelvic organ prolapsed (POP), the vaginal mesh can be assessed by transperineal ultrasound. Although commonly used, vaginal mesh presents some complications, such as mesh erosion or extrusion, infection, and incontinence recurrence. These complications can lead further to feelings of hopelessness or emotional distress. When these complications are not timely identified, they can negatively influence the patient's health. Different imaging techniques – including transperineal ultrasound – are nowadays available

in order to visualize the vaginal mesh placement and its complications. Moreover, polypropylene is echogenic on ultrasound and, therefore, it offers a better opportunity tool for the postoperative visualization of the mesh placement. This review article discusses the role of transperineal ultrasound in the visualization of synthetic implants used in the treatment of POP, including the operative planning in the surgical mesh reintervention.

**Keywords:** transperineal ultrasound, mesh, dyspareunia, emotional distress, prolapse

## Diagnosis and management of fetal malformations detected in the Department of Maternal-Fetal Medicine of the "Filantropia" Clinical Hospital, Bucharest

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In 2020, in the Department of Maternal-Fetal Medicine of the "Filantropia" Clinical Hospital of Obstetrics and Gynecology, Bucharest, approximately 5000 ultrasound examinations were performed on approximately 2500 pregnant women. Of these, in 91 cases, fetal malformations were diagnosed. We present the diagnostic and management in these cases. These malformations were either isolated or in plurimalformative or genetic syndromes. In the population examined, there were no significant prenatally undiagnosed structural malformations. The vast

majority of congenital malformations diagnosed were treated at the "Filantropia" Clinical Hospital. The cases with indication for medical or surgical therapy after birth were addressed by multidisciplinary (multi-institutional) teams coordinated by our department. In contrast to the classic series, our experience in the year 2020 shows that ultrasound examination ensures the diagnosis of most of the significant fetal malformations.

**Keywords:** ultrasound examination, fetal malformations, multidisciplinary teams

## Prenatal diagnosis of diastematomyelia associated with multiple fetal malformations – a case report

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**Introduction.** Diastematomyelia, also known as split cord malformation, is a form of spinal dysraphism characterized by a cleft in the spinal cord. This congenital malformation is the result of an abnormal development of the notochord between the 15<sup>th</sup> and the 18<sup>th</sup> day of intrauterine life. Diastematomyelia may be isolated and located in only one area of the spinal cord. In this case, it has a favourable prognosis. Or it may be associated with other dysraphisms or congenital anomalies, in this case having an unfavourable prognosis. Prenatal diagnosis is possible by ultrasonography or fetal MRI. The objective of this article is to present a case of fetal diastematomyelia associated with multiple congenital anomalies. **Methodology.** This presentation aims to illustrate the case of a 17-year-old primiparous, who presented to the emergency room of the “Dr. I.A. Sbârcea” Clinical Hospital of Obstetrics and Gynecology from Braşov for the first time during her pregnancy at 17 weeks, complaining of abdominal pain. The pregnant woman was examined using a Voluson E8 Expert ultrasound (GE Healthcare, Milwaukee, WI) and was diagnosed with

plurimalformed fetus. **Results.** The ultrasound examination revealed a live fetus, with biometrics corresponding to 17 weeks, anencephalic, with an obvious deformity of the limbs and a complex cardiac malformation, who presented diastematomyelia, which included all the segments of the spinal cord. The mother requested a therapeutic abortion, and after the expulsion of the fetus, the following morphological abnormalities were observed: anencephaly, cyclopia, proboscis, polydactyly, complete diastematomyelia and limb deformities. The mother refused to perform the fetal karyotype. **Conclusions.** Routine fetal ultrasound examination is mandatory throughout pregnancy in order to diagnose pathologies that may be disabling in the postpartum period or even incompatible with life. The peculiarity of this case consists in the detection of a plurimalformed fetus, presenting complete diastematomyelia, in a young primiparous patient, who refused to perform the fetal karyotype after the initiation of the therapeutical abortion.

**Keywords:** diastematomyelia, congenital malformation, anencephaly, proboscis

## The importance of ultrasound in postmenopausal bleeding evaluation

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**Introduction.** Bleeding in the period following the onset of menopause is a fairly common pathology found in medical practice. These cases must be approached with the utmost care in order to highlight the cause, if possible, and to apply the appropriate treatment measures. Transvaginal ultrasound (TVUS) is a common, easily accessible evaluation method that brings additional information and is therefore recommended and used most often. **Materials and method.** We conducted a retrospective study in the obstetrics-gynecology clinics of the “Pius Brînzeu” County Emergency Clinical Hospital from Timișoara, between 2017 and 2019. Patients admitted for menopausal bleeding during this period were included in the study. The patients were evaluated by TVUS to allow a more accurate assessment of the appearance of the uterus, endometrium and appendages. The pathological aspects of the uterine wall, the appearance of the endometrium in terms of homogeneity, the thickness of the endometrium and the existence of pathological

aspects in the uterine cavity, the appearance of the adnexa, respectively any other pathological aspects present in the pelvic cavity were noted. **Results and discussion.** The application of a diagnostic method by taking a sample of endometrial tissue by endometrial biopsy, classic curettage of the uterine cavity, hysteroscopy or by examination of the uterus after hysterectomy actually guarantees the certainty of diagnosis after histological examination. The management of cases with menopausal bleeding must be individualized and must take into account both the histological result, the results of other investigations and the patient’s age, condition and associated pathologies, in order to apply the appropriate therapeutic measures. All these improve the patients’ prognosis. **Conclusions.** Ultrasound is a noninvasive and safe method of investigation. TVUS remains the most sensitive investigation to be applied in patients with postmenopausal bleeding.

**Keywords:** menopausal, ultrasound, endometrium

## Multiple leiomyomatosis – case report

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**Introduction.** Also known as uterine fibroids, leiomyoma comes from the smooth muscle tissue, being the most common benign tumor in female genital pathologies and affecting approximately 70% of females. Transvaginal and abdominal ultrasonography is the mainstay in the diagnosis of leiomyomatous formations, being also a sensitive, cheap and easy to perform method. The objectives of this paper were to present the diagnostic possibilities and conduct aspects in these cases. **Methodology.** The article is a case presentation of a 30-year-old patient, nulliparous, who presented to the emergency department, accusing menorrhagia, pelvic-abdominal pain, dyspareunia and intermenstrual bleeding. The anamnestic data showed that the patient had numerous unsuccessful attempts to obtain a pregnancy. **Results.** Ultrasonography revealed numerous leiomyomatous formations with dimensions between 3 and 14 cm, well delimited, with increased echogenicity and peripheral vascularization in echo-Doppler, both submucosal and intramural. The patient was hospitalized in the Clinical Department of Obstetrics-Gynecology I of the

“Pius Brînzeu” County Emergency Clinical Hospital from Timișoara, for a specialized consultation. During the hospitalization, a pelvic MRI was performed, confirming the initial diagnosis and also providing a broader picture of the anatomical relationships to perform the surgery. With the patient’s desire to obtain a pregnancy in the foreground, it was decided to perform a rigorous multiple myomectomy, in the classic way, succeeding in the complete removal of nodular formations, thus fulfilling two basic desiderata: the removal of nodular lesions with the restoration of anatomical integrity of the uterus, accompanied by a favorable postoperative status. **Conclusions.** Although benign, leiomyoma can have a significant impact on the daily physical and mental well-being of the woman who suffering from this pathology. The magnetic resonance imaging (MRI) has the advantage of providing a broader picture of the size, number, vascularity and limits of the fibroid, in relation to the pelvic structures, the transvaginal ultrasound remaining the gold standard in the diagnosis of this disease.

**Keywords:** leiomyoma, ultrasonography, myomectomy

## Ultrasound monitoring in pregnant patients with Grave’s disease

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We consider the ultrasonographic examination of the fetal thyroid revealing fetal goiter in pregnant patients with Grave’s disease a late sign of fetal thyrotoxicosis. Clinical fetal thyrotoxicosis is a rare disease that complicates 1-5% of pregnancies with Grave’s disease. Although transplacental passage of maternal TSH receptor stimulating autoantibodies (TRAb) to the fetus occurs in the first part of the pregnancy, the fetal concentration is low until the end of second trimester. The mortality of fetal thyrotoxicosis is 12-20%, mainly caused by heart failure. We present a fortunate case of fetal and neonatal thyrotoxicosis which had a favorable prognosis and a further development in a 37-year-old woman, known with Grave’s disease with ophthalmopathy and thyroidectomy performed 12 years prior, with hypothyroidism, which had in history a complicated pregnancy with fetal anasarca, premature birth and neonatal death. The current pregnancy was monitored using maternal thyroid

laboratory assessment and ultrasonographic markers. The earliest signs of fetal decompensation have been fetal tachycardia and fetal hyperdynamic status. The ultrasound examination of the fetal thyroid was in the normal range for the gestational age throughout the pregnancy. The patient gave birth by caesarean section at 35 gestational weeks to a live 2530 g male, with an Apgar score of 6 at 1 minute, 8 at 5 minutes and with a normal development through the first year of life. In conclusion, ultrasound monitoring for early signs of fetal thyrotoxicosis is essential in pregnancies with Grave’s disease in order to assess the development of the fetus, the amniotic fluid index and the fetal vital parameters which could improve the fetal and neonatal outcome by adapting the case management based on the ultrasound findings.

**Keywords:** fetal thyrotoxicosis, TSH receptor stimulating autoantibodies (TRAb), Grave’s disease, fetal tachycardia

## An intriguing differential diagnosis of a neural tube defect

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Neural tube defects occur during the fifth or sixth week of gestation, when a part of the neural tube fails to close normally, affecting the spinal cord, vertebrae, cranium or even the brain. Neural tube defects (NTDs) can be open or closed. Meningocele is a rare open NTD with a decreasing incidence due to recommended folate supplementation before and during pregnancy. We present an atypical case of ultrasonographic suspicion of fetal meningocele in a 41-year-old pregnant patient, developed under preconception folate administration. The patient had received levomefolic acid, a type of folic acid that has a biologically active formula, with the aim to prevent the development of neural tube defects. A cystic tumor was firstly suspected at a routine 3D examination at 10 gestational weeks and it was further evidenced at the first ultrasound screening that took place at 15

gestational weeks, due to maternal SARS-CoV-2 infection, which delayed the classical screening scheme. The ultrasound examination revealed a caudal cystic sac of 1.5 cm length with absent vascularization, which hardened the differential diagnosis: was it a meningocele or a sacrococcygeal teratoma? The mother decided to terminate the pregnancy at 16 gestational weeks. The positive diagnosis of the cystic tumor was made using the pathology report. This case of fetal meningocele in a female receiving folic acid during pregnancy highlights the importance of the first-trimester ultrasonographic screening and the necessity of trained fetal pathologists in order to increase the accuracy of diagnosis in fetal-maternal medicine.

**Keywords:** meningocele, teratoma, folic acid, prenatal diagnosis

## Ovarian dysgerminoma associated with pregnancy – a diagnostic and management challenge. Case presentation

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Ovarian dysgerminoma is a rare malignant tumor that develops from the germ cells of the ovary. Its association with spontaneous pregnancy is extremely rare, with a reported incidence of approximately 0.2-1 per 100,000 pregnancies. Women in the reproductive age group are more frequently affected. The chance of fetal viability or full-term birth without maternal-fetal distress is low. We report a case of right ovarian dysgerminoma diagnosed in a 28-year-old young woman with a viable six-week intrauterine pregnancy that ended at term by caesarean section, with the birth of a normoponderal fetus, with an Apgar score of 9, during the intervention being necessary the right ovarian adnexectomy, with the removal of an ovarian tumor of about 15 cm, irregular, of increased consistency. The histopathological examination confirmed the suspicion of ovarian dysgerminoma. During pregnancy, many

factors played a role in its favorable evolution, including early suspicion of malignancy, ultrasound imaging and the involvement of a multidisciplinary team. Ovarian neoplasms may increase rapidly in size, may be slightly symptomatic or completely asymptomatic. This is a diagnostic challenge for obstetricians and oncologists. Thus, the role of ultrasonography in pregnancy in raising an early suspicion of ovarian dysgerminoma is extremely important. Patients with ovarian dysgerminoma during pregnancy may have favorable results. The treatment must be customized, being necessary to take into account many factors: the cancer stage, the previous reproductive history, the impact of the tumor on the fetus, the gestational age of the fetus at the time of diagnosis, and whether abortion can improve the mother's survival or morbidity.

**Keywords:** dysgerminoma, pregnancy, ultrasonography

## Polydactyly – the first or the last piece of a domino chain? Case presentation

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Isolated postaxial polydactyly, as a single defect, is a common malformation, characterized by an additional finger placed on the ulnar or fibular side of the limbs. The global prevalence is 1-2 cases/100,000. The genetic-ethnic background significantly affects the global prevalence and type of polydactyly. Among the general characteristics, it can be noticed that male sex is significantly more affected compared than the female sex, the upper limbs are more affected than the lower ones, and the left limbs more than the right limbs. We report a case of bilateral postaxial polydactyly in the upper limbs in a 23-year-old patient in her first pregnancy, in whom the diagnosis was established at the gestational age of 13 weeks. Although it is a malformation easily detected by ultrasonography,

polydactyly can be a diagnostic challenge in terms of establishing the status of an isolated abnormality or as a component of one of the 119 possible plurimalformations that can be identified by ultrasound. Detailed serial ultrasounds were performed which revealed the characteristic of isolated malformation, therefore no noninvasive or invasive genetic tests were required. Thus, the role of pregnancy ultrasonography in raising an early suspicion of a genetic syndrome is extremely important. Girls with postaxial polydactyly may have favorable results. The postpartum treatment must be customized, being necessary to take into account many factors that can improve the quality of life of the newborn.

**Keywords:** polydactyly, pregnancy, ultrasonography

## Late-onset coronary heart disease (CHD) – cardiomyopathies

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**Introduction/objective.** Cardiomyopathies are affections of the myocardium right, left or both ventricles, being usually associated with abnormal cardiac function, and are typically not the result of a structural cardiac malformation. The incidence of cardiomyopathies is less than 1% of all neonates with congenital heart disease. Two types of cardiomyopathies exist: dilated and hypertrophic. Ventricular dilatation can be quantified by cardiac measurements (cardiothoracic ratio, cardiac width). The ventricular wall contraction is reduced and can be objectively assessed by M-mode measurements, the characteristic being the reduced shortening fraction. The most important sign leading to the diagnostic is cardiac failure with hydrops. **Methodology.** Between January 2016 and December 2020, the patients were examined by performing examination, as well as the morphological ultrasound of the second and third trimesters. **Results.** Three cases

of cardiomyopathies in pregnancies were encountered: one case was a dichorionic diamniotic twin pregnancy, in 22 weeks, with TTTS-high output cardiac failure, one case with primary cardiomyopathies (CMPs) – hypertrophic and spongy anomalies, and the third case with gestational diabetes and cardiomyopathies developed in the third trimester. **Conclusions.** The final prognosis will depend upon: isolated versus associated conditions (syndromic, metabolic etc.), the degree of systolic cardiac function impairment by time of birth. Cardiomyopathies are evolutive lesions, with deterioration in late weeks or early neonatal period. For the next pregnancy, it is important that the familial history is investigated thoroughly, and the key factor is the storage of fetal/neonatal blood and heart biopsy (if deceased).

**Keywords:** cardiomyopathy, cardiac failure, fetal hydrops

## Heart tumors and rhabdomyomas

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**Introduction/objective.** Heart tumors have a low prevalence and represent 1-2% of all cardiac anomalies. The most common type of tumors encountered are rhabdomyomas (80-90% of cases), but there can also be encountered teratoma, fibroma, myxoma, hamartoma, rhabdomyosarcoma and others. The fetal outcome depends on tumor size, impairment of flow, and the occurrence of rhythm disturbances. However, rhabdomyomas tend to shrink after birth and even eventually disappear completely. **Methodology.** Rhabdomyomas are homogeneous circumscribed tumors (oval or circular), with an echogenic bright density (evaluation with high-resolution ultrasound), and in most of cases are multiple, variable in size and regarding the site, occurring in the ventricular free wall, the ventricular septum or the atrial free walls. **Results.** Occasionally they can become obstructive, if they become very large, and can

lead to fetal hydrops, arrhythmias or fetal demise. The interference with the coronary arterial system may cause spontaneous death as well. Usually, rhabdomyomas are detected in the interval between 20 and 30 weeks of gestation. The main concern following diagnosis is the strong association of multiple rhabdomyomas with genetic condition – tuberous sclerosis (genetic disorder with autosomal dominant inheritance). When tuberous sclerosis is diagnosed clinically after birth, in 50-80% of cases it is associated with rhabdomyomas. **Conclusions.** Rhabdomyomas are the main cardiac tumors, being detected between 20 and 30 weeks of gestation, and in 40% of cases intracranial lesions exist. Rhabdomyomas are commonly associated with tuberous sclerosis, and now is achieved by molecular genetic testing.

**Keywords:** rhabdomyoma, cardiac tumors, tuberous sclerosis

## Three-dimensional endovaginal ultrasound versus diagnostic hysteroscopy

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**Introduction/objective.** Three-dimensional (3D) endovaginal ultrasound offers an accurate and objective representation of the uterine cavity, surpassing the limitations of 2D sagittal images, by adding a coronal section. Hysteroscopy is presently considered the gold standard for diagnosing intracavitary pathology, with increased applicability due to its inclusion in the investigation protocol of infertile patients. The objective of this paper is the evaluation of diagnostic benefits of 3D endovaginal ultrasound compared to diagnostic hysteroscopy benefits in cases of intracavitary pathology or mullerian anomalies. **Methodology.** A total number of 72 patients, aged between 20 and 46 years old, were evaluated over a 12-month period. Three-dimensional endovaginal ultrasounds were performed on a minimum endometrial thickness of 6 mm, for all patients. Hysteroscopies were performed preovulatory, between the 8<sup>th</sup> and 11<sup>th</sup> day of the menstrual cycle. Three-dimensional endovaginal ultrasounds and hysteroscopies were performed on different menstrual cycles. For the selected cases, after performing the 3D ultrasound and before the hysteroscopy, 3D hysterosalpingosonography was performed, between days 8 and 11 of the menstrual cycle. **Results.** Of the 72 patients investigated

by 3D ultrasound, we detected 19 patients without any uterine pathological findings, 13 cases with myometrial pathology, 17 cases with intracavitary pathology and 23 patients with müllerian anomalies. Of the 27 patients examined hysteroscopically, in 24 cases there was a diagnostic consistency between the two types of investigations, and in 8 of the 13 patients with müllerian anomalies the diagnostic hysteroscopy became an interventional one. **Discussion and conclusions.** Three-dimensional endovaginal ultrasound and hysteroscopy are complementary explorations that cannot replace one another. In the case of müllerian anomalies, the usefulness of hysteroscopy is limited almost exclusively to its interventional purpose, 3D endovaginal ultrasound mostly offering an accurate diagnosis. Intracavitary pathology benefits from an informational addition to the diagnosis if, prior to hysteroscopy, both 3D endovaginal ultrasound and 3D hysterosalpingosonography are performed. In these cases, the rate of diagnostic hysteroscopy decreases and the collection of preoperative investigative data leads to an interventional hysteroscopic approach with shorter interventional time and a carefully prepared operating plan.

**Keywords:** ultrasound, 3D, hysteroscopy



## Spina bifida aperta – a case report

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**Introduction/objective.** Neural tube defects (NTD) are the second most common major congenital anomaly, after cardiac malformations. The live birth prevalence of NTD's changed dramatically in the 1980s with the introduction of maternal serum screening and the widespread use of prenatal ultrasound imaging. **Methodology.** A healthy 33-year-old patient, with a 23-week pregnancy, came for routine ultrasound in our clinic, on her own initiative. The pregnancy was previously monitored inconstant and random. The ultrasound examination reveals lumbar *spina bifida aperta*, myelomeningocele and Chiari II malformation. The MRI examination confirms the

ultrasound diagnosis. Amniocentesis is proposed and revealed increased AFP in the amniotic fluid and normal karyotyp. After prenatal neonatology and pediatric neurosurgery consultation, the patient decided the termination of pregnancy. **Discussion and conclusions.** Although prenatally detected, the myelomeningocele and its long-term complications (paraparesis and/or paraplegia, bowel and bladder dysfunction, hydrocephalus, developmental delay and learning disabilities) retains its reserved and even lethal prognosis.

**Keywords:** *spina bifida*, myelomeningocele, Chiari II malformation

## Fetal hydrothorax – small series of cases

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**Introduction.** Fetal hydrothorax is defined as unilateral or bilateral accumulation of abnormal fluid in the pleural cavities. It can be isolated or it can be associated with other fluid collections in abdominal and pericardial cavities, or it can be associated with subcutaneous edema and polyhydramnios. The general incidence described in the literature is between 1/1500 and 1/5000, and the main causes of fluid accumulation are intrauterine anemia, intrauterine heart failure and hypoproteinemia, associated with numerous other factors causing fluid accumulation. **Materials and method.** We present a series of three cases of nonimmune hydrothorax, somehow linked to the period of COVID-19 pandemic, with positive serology for SARS-CoV-2, who appeared in asymptomatic patients, with no illness history, but with unilateral hydrothorax in one case at 32 weeks of gestation and two cases with bilateral hydrothorax. All cases were finalized in a natural way, all of them with intrauterine fetal death. **Results.** Primary fetal hydrothorax presents with a wide spectrum

of severity, ranging from small, harmless effusions, to life-threatening thoracic compression. It is associated with high mortality, respiratory insufficiency and fast fluid accumulation after puncture. The usual investigations to be performed in fetal nonimmune hydrothorax are amniotic fluid CBC, complete blood count, cytomegalovirus antibodies, Doppler for middle cerebral artery and umbilical artery, mucopolysaccharidosis, quantitative PCR, TORCH (toxoplasmosis, rubella, cytomegalovirus, herpes simplex), varicella-zoster virus antibodies, and a variety of structural abnormalities that interfere with the fetoplacental circulation must be considered. Chromosomal anomalies (aneuploidy, deletion, duplication, genetic mutation) and skeletal dysplasia may also be associated. **Conclusions.** Fetal hydrothorax is a severe condition associated with pulmonary hypoplasia and respiratory insufficiency and with a high rate of fetal mortality.

**Keywords:** nonimmune fetal hydrothorax, small series

## Prenatal diagnosis of clubfoot – literature review and case report

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**Introduction.** Until recently, the diagnosis of fetal structural abnormalities was established in the second trimester of pregnancy. Currently, due to the evolution of ultrasound technical equipment, the tendency is for fetal malformations to be diagnosed as early as possible in the first trimester of pregnancy. Congenital clubfoot is one of the most common congenital anomalies, having an incidence of 1 in 1000 live births. There are cases in which congenital clubfoot is associated with other fetal malformations, such as myelomeningocele, cleft lip, cleft palate etc. **Objective.** The aim of this paper is to evaluate the importance of ultrasonography in establishing the prenatal diagnosis of clubfoot, as well as an update of the ultrasound criteria in establishing this diagnosis. The paper also contains a case presentation that illustrates the importance of establishing a prenatal diagnosis of bilateral congenital clubfoot. **Materials and method.** In order to obtain the data that interested us, we performed a literature review. We

chose to use PubMed as the database. Only articles in English were included. Also, another inclusion criterion was that the article is available in full text. Articles on clubfoot treatment, surgical techniques, instructional courses and letters to publishers were excluded. We used the following keywords to perform the search: "clubfoot", "ultrasound", "prenatal", "diagnosis". **Results and conclusions.** Out of a total number of 209 articles obtained from the combined use of the keywords "clubfoot", "ultrasound" and "diagnosis", only 70 works were available after we added the keyword "prenatal". Although clubfoot is a common pathology that can be treated, the psychological impact on the couple is major. Ultrasonographic evaluation remains the main method of prenatal diagnosis of clubfoot. There is no agreement regarding the performance of the fetal karyotype when the prenatal ultrasound shows fetal clubfoot without other associated abnormalities.

**Keywords:** clubfoot, ultrasound, diagnosis

## Ultrasound aspect of different ectopic pregnancies

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**Introduction.** Ectopic pregnancy, an important cause of maternal death, benefits of high-resolution vaginal probes and accurate and rapid serum human chorionic gonadotrophin assays, associated with a good quality vaginal examination, which have significantly decreased the mortality by early diagnostic treatment. A common issue is differentiating between different types of ectopic pregnancy, different types of ectopic pregnancy having different, specific, treatments, depending on the precise location of the pregnancy. Another common problem is the difficulty in differentiating between the various types of ectopic pregnancy. An accurate differential diagnosis is important in ectopic pregnancies, as the management often differs depending on the type and exact location of the pregnancy. Another common issue is the difficulty in differentiating between the various types of ectopic pregnancy. An accurate differential diagnosis is important in ectopic pregnancies, as the management often differs, depending on the type and exact location of the pregnancy. **Materials and method.** We present a series of cases of ectopic pregnancies located in the uterus in other abnormal locations. The

diagnosis was performed using transvaginal ultrasonography, serum HCG assays and, in rare cases, computed tomography and MRI were performed. **Results.** All the cases presented were diagnosed and treated in the First Obstetrics and Gynecology Department, Sibiu. In all the cases of ectopic pregnancy, there were used for diagnosis transvaginal ultrasonography and all the other methods in establishing the location or the evolution of the pregnancy. The treatment was performed using conservative methods, such as methotrexate, mifepristone, intramniotic ultrasound guided puncture with methotrexate injection or surgery, usually by laparoscopy. In selected cases, open laparotomy was performed. The main goal of the surgery was fertility preservation, whenever it was possible. **Conclusions.** Transvaginal ultrasonography for ectopic pregnancy is modality of choice for the diagnosis of different locations of the ectopic pregnancy with high sensitivity. There are certain sonographic criteria for the diagnosis of each tubal and non-tubal pregnancies, including cervical and caesarean section scar pregnancies.

**Keywords:** ultrasound, ectopic pregnancy

## Doppler ultrasound – Pandora’s box of the first trimester of pregnancy

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As the fetal and placental structures develop, their vascular network becomes more pronounced. Therefore, during pregnancy it is possible to observe three separate and yet united units: maternal, placental and fetal circulation. With the help of Doppler ultrasound, it is possible to identify and characterize, right from the first trimester of pregnancy, the vascular flow from the uterine artery, the arched, radial arteries, as well as from the spiral arteries. Vascular resistance is different in these territories, at the same gestational age. The first trimester of pregnancy allows the evaluation of fetal circulation at different levels: umbilical circulation, peripheral arterial vessels (descending aorta, intracerebral vessels), heart, venous structures (inferior *vena cava*, venous duct). The Doppler spectrum obtained from the central venous circulation of the embryo brings information regarding the physiological aspect of the right ventricle. Thus, specific information

related to myocardial compliance and the pressure at the end of diastole can be obtained by Doppler tracking of the ductus venosus (DV), as well as the inferior *vena cava*. Abnormal blood flow in the DV (reversal of the “a” wave or the “a” wave absent) during the first trimester of pregnancy suggests an association between chromosomal abnormalities (trisomy 13,18,21, monosomy X) and congenital heart defects. During the embryonic period, three weeks after conception, the primitive heart begins to pulsate. By transvaginal ultrasonography, the activity of the heart can be identified in real time in the 2D image from 5 weeks and 3 days of gestational age. After 6 weeks of gestation, spectral and color Doppler signals of pulsed blood flow to the fetal heart and large vessels can be detected. In the latter part of the first trimester of pregnancy, ultrasonography and Doppler recording can be performed transabdominally.

**Keywords:** Doppler, first trimester, pregnancy

## Screening for fetal anomalies during the COVID-19 pandemic – logistic and diagnostic challenges

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Our presentation will focus on two aspects: organization (preparing prenatal diagnosis clinics/private offices for the new challenges) and a medical one (a presentation of special cases that we met this last one year and a half). Organizing departments/clinics had a material side which included protection for medical personnel but also patients, possibilities and limits of screening patients, planning the program and the functioning of the prenatal unit (limiting access for family or visitors, limiting the examinations number), but also communication – counseling the patients was a challenge, especially in the beginning, due to the limited information about maternal prognosis, vertical transmission, fetal risks and, in the last months, about

the opportunity of vaccination during pregnancy. The protocol of examination of confirmed COVID-19 cases included for us only the examination of the pregnant women hospitalized in the intensive care unit, which included the daily biophysical score with special attention to the amniotic fluid index. Regarding the pathology diagnosed in this period, we have met interesting cases (that will be presented), without any increase in incidence. The two aspects we associated with COVID-19 were missed abortion in the first trimester of pregnancy and premature birth (often iatrogenic), when the maternal respiratory status required extraction by caesarean section.

**Keywords:** COVID-19, prenatal diagnosis

## Ultrasound aspects in endometriosis lesions

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**Introduction.** Endometriosis is defined as the presence of endometrial tissue in the body, elsewhere than its normal location in the uterine cavity. Thus, the aspect that can be highlighted with the help of transvaginal ultrasound (TVUS) is different depending on the form of presentation. Ultrasound evaluation of the pelvic organs can provide useful information in patients with suggestive symptoms of endometriosis. The final diagnosis is established by histological examination of a sample from the suspicious tissue. **Materials and method.** During 2017-2019, in the obstetrics-gynecology clinics of the "Pius Brinzeu" County Emergency Clinical Hospital from Timișoara, we conducted a retrospective study which included patients with histopathological diagnosis of endometriosis. The different aspects identified by TVUS were highlighted and classified. **Results and discussion.** Using TVUS, the internal genitals and the rectouterine pouch were evaluated. In these cases, a closer examination of the anatomical structures in the ante-

rior and posterior pelvic compartment was performed in view of identifying foci of deep endometriosis, and the mobility of the pelvic organs was also assessed. The TVUS results were processed and corroborated with the results of other imaging investigations and images from surgeries performed for tissue sampling for diagnostic or therapeutic purposes, where appropriate. Although ultrasound has its advantages, it also has some limitations related at least to the limiting penetration depth, the experience of the specialist who performs it, and to the location of the lesion. Magnetic resonance imaging may play a role in evaluating the areas that cannot be highlighted with TVUS. **Conclusions.** TVUS remains the first-line imaging tool for women under suspicion of endometriosis. The identification of an image suggestive of endometriosis leads to the continuation of investigations in order to establish the diagnosis and the therapeutic conduct.

**Keywords:** TVUS, endometriosis, rectouterine

## Fetal growth charts and preeclampsia – integrated diagnostic steps

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**Introduction.** Placental dysfunction underlies a spectrum of perinatal pathologies, including preeclampsia and fetal growth restriction, and require a referral decision to be made within a certain time period. **Methodology.** The key issues in the management of a pregnancy complicated by fetal growth restriction and preeclampsia are the identification of the fetus at the greatest risk for deterioration, using of the most appropriate surveillance approach and determination of the delivery. Fetal growth restriction evolves from a preclinical phase to clinically apparent growth delay and may progress to fetal deterioration. The recent fetal growth charts that are based on multiple populations should be the first choice for an area where no population-specific references exist. **Results.** The identification of the small fetuses that require close surveillance is based on the absence of congenital anomalies and an

estimated fetal weight below the 3<sup>rd</sup> centile or below the 10<sup>th</sup> centile, coexisting abnormal pulsatility index umbilical artery (UA), middle cerebral artery (MCA) or cerebroplacental ratio index. **Discussion.** The surveillance frequency should be primarily guided by these parameters. The goal of fetal surveillance is the accurate estimation of the risk for hypoxemia, prelabour acidemia or stillbirth, as well as the rate of clinical deterioration. The degree to which fetal deterioration may be tolerated is dependent on gestational age. The appropriate standards for the assessment of fetal growth and birthweight are central to good clinical care and timely diagnosis, and have become even more important, with increasing evidence that the adverse outcomes are potentially avoidable.

**Keywords:** preeclampsia, fetal growth cart, fetal growth restriction

## Fetal arrhythmias – prenatal diagnosis and obstetrical attitude

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**Introduction.** Fetal arrhythmias are a common phenomenon, with various complicated etiologies and different prognosis. Although most of them are benign and transient, some types are associated with maternal pathologies or structural cardiac defects and can cause heart failure and fetal hydrops, leading to intrauterine death. The detailed analysis of fetal heart rhythm is based on ultrasound, using M-mode and Doppler echocardiography. The optimal prenatal diagnosis and the perinatal management have represented a challenge over the past decades. **Methodology.** We present the case of patient with 28 weeks of gestation, referred to our clinic for a routine evaluation. The ultrasound scan revealed fetal bradycardia (fetal heart rate 75 bpm), with no other signs of fetal hypoxia or congenital structural disorders. M-mode and Doppler flow velocity showed a pattern with a 2:1 AV block. The patient was admitted in our department for investigation, therapeutic intervention and careful monitoring. Further investigations revealed no maternal pathologies, no autoimmune or connective tissue disorders, and the absence of maternal SSA/Ro

and SSB/La autoantibodies. We started dexamethasone treatment, which showed to be effective, increasing fetal heart rate by 20%. **Results.** An interdisciplinary team with pediatric cardiologists and regular screening by fetal echocardiography were made. Caesarean section was performed at 36 weeks of gestation and the patient delivered a 2800 g female infant, with an Apgar score of 9. Postpartum, the newborn was transferred in the cardiopediatric unit for evaluation. Pacemaker implantation was not necessary, as the fetal heart rate normalized and no cardiac abnormalities were found. **Discussion.** The outcomes of intrauterine therapy of fetal arrhythmias depend on the types, etiology and fetal conditions. Close interdisciplinary surveillance and individualized clinical treatment should be determined according to specific types. The most recent European Society of Cardiology (ESC) Guidelines recommend the assembly of a pregnancy heart team for the better management of pregnancy and adjudicate on the prognosis of both mother and fetus.

**Keywords:** fetal arrhythmias, bradycardia, autoantibodies

## Imaging diagnosis and legal implications of brain injury in survivors following single intrauterine fetal demise from monochorionic twins

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The increased addressability of assisted reproduction techniques led to an increased incidence of multiples. There is reason to believe the the number of monochorionic (MC) twins may be influenced by oocyte age, embryo cohort quality, assisted hatching techniques or prolonged embryo cultures. First-trimester fetal loss – the “vanishing twin syndrome” – is a common accident which happens regardless chorionicity and is generally followed by an uneventful course of pregnancy. The demise of one fetus later than 14 weeks of gestation is believed to prompt significant effects on the continuing pregnancy, including neurologic sequelae and cerebral palsy. In MC twins, single intrauterine fetal demise (SIUFD) occurs spontaneously or following an obstetric intervention – selective feticide or fetoscopic laser therapy for twin-to-twin transfusion syndrome (TTTS). The intrauterine demise of one fetus will lead to an increased risk of adverse events in the survivor twin from MC pregnancies, with fetal brain abnormalities reportedly found in up to 36% of cases. The increased risk of cerebral damage in survivors following SIUFD generated efforts to identify predictors of neurologic sequelae. There is no gestational age risk stratification regarding the occurrence of cerebral lesions in surviving fetuses following single stillbirth in MC twins. However, judging from previously published reports and supported by our own practice, we may speculate that the critical period would be 24-34 weeks of gestation, when the impact of cerebral lesions is amplified by the immaturity of the fetal brain in the context of prematurity. Predicting the neurologic outcome of the surviving fetus is the

mainstay for ensuring proper parental counseling and informed management planning. It is thus essential to be able to achieve a timely and accurate diagnosis and to discuss the fetal prognosis in a multidisciplinary team. Perhaps the main controversy lies in the potential fetal and neonatal capacity to correct and partially heal cerebral lesions, with a good later life prognosis and manageable sequelae. Prenatal ultrasound is the primary diagnostic imaging method for anomaly screening in pregnancy and the reference standard for neurosonography. It may identify gross atrophic and necrotic-cystic lesions resulting from fetal brain hypoxia-ischemia, but has little sensitivity in the earlier phases of brain injury. MRI examination of surviving co-twins has been demonstrated to have superior diagnostic accuracy across studies, allowing for a timelier and more accurate lesion detection and characterization. Conventional MRI could miss lesions during the first two weeks after SIUFD, with a growing body of literature suggesting the superiority of diffusion weighted imaging (DWI) sequences in the detection of acute ischemic lesions. One of the main concerns in pregnancies complicated by SIUFD is our capacity to predict the neurodevelopmental outcome of the surviving fetus with respect to the detected brain lesions and fetal brain maturity at the event onset. This is where DWI may play a key role in refining the diagnosis and orienting the decision-making. The risk of neurologic impairment is in most cases doubled by that of prematurity.

**Keywords:** twins, prenatal ultrasound, conventional MRI, diffusion weighted imaging

## Prenatal ultrasound diagnostic limitations of *spina bifida*

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With the advent of ultrasound, obstetricians have been concerned with an early and reliable diagnosis of fetal malformations. The early detection of neural tube defects has become an integral part of modern obstetric care. Many *spina bifida* cases can be diagnosed before 20 weeks of gestation, but this is not always the case. Fetal position, such as dorsal decubitus, may affect the quality of the image. The female skeletal system matures more rapidly, which makes male fetuses more difficult to assess in an early pregnancy. In the early diagnosis of *spina bifida*, classical

cranial and cerebellar signs are used, such as the lemon sign and the banana sign. Subsequently, markers such as intracranial translucency or the frontomaxillary angle – some of them outside the routine practice or difficult to evaluate – emerged. Magnetic resonance imaging has a lower performance than ultrasound in the diagnosis of vertebral and cranial injuries. These limitations should be made known in order to avoid accusations of malpractice.

**Keywords:** *spina bifida*, skeletal system, neural tube defects

## Significations of absent or reversed end-diastolic umbilical flow

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Doppler velocimetry has been extensively applied in the prenatal diagnosis of fetal status for more than two decades. Absent or reversed end-diastolic umbilical flow is a strong sign of placental insufficiency, because abnormal Doppler velocimetry in the umbilical artery is correlated with lesions such as arteriolar obliteration in the tertiary villi system of the placenta. These two types of Doppler patterns (absent and reversed) are commonly treated in the literature because they are not frequent. Abnormal umbilical Doppler is associated with intraventricular hemorrhage, bronchopulmonary dysplasia and perinatal mortality. It can also be associated with respiratory distress syndrome, necrotiz-

ing enterocolitis, and impaired neurological development in the long term. Some fetuses with intrauterine growth restriction and absent but not reversed end-diastolic flow might stay *in utero* longer without the risk of death. Identifying this subgroup could allow avoiding some of the neonatal risks of extreme preterm birth. Women with pregnancies with obstetric risk, such as preeclampsia, hypertension and intrauterine growth restriction, should be assessed by Doppler velocimetry in the umbilical artery in order to reduce perinatal morbidity and mortality.

**Keywords:** end-diastolic umbilical flow, Doppler velocimetry, intrauterine growth restriction

## Endometrial assessment in perimenopausal and postmenopausal women

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**Introduction.** The end of a woman reproductive years comes along with new health risks that seem to arise with the fall of estrogen levels. The assessment of the endometrium is becoming a routine part of healthcare for women of all ages and plays a special role in perimenopausal and postmenopausal women, targeting to diagnose premalignant and malignant changes. **Methodology.** Clinical cases with the purpose to provide evidence-based advice on endometrial assessment in peri- and postmenopausal women. **Results.** Following the clinical examination to exclude other pathologies, endometrial assessment methods are categorized as noninvasive and invasive procedures. Diagnostic and therapeutic approach should be based on age and clinical indications: hormonal status, presence or absence of uterine bleeding, ultrasound findings – endometrial thickness (ET). Noninvasive procedures include: *ultrasonography (US)* – simple, a cost-effective first line investigation, with high diagnostic performance (PPV 72-86%), that can place the patients in high-risk and low-risk cancer groups; *sonohysterography* can help in the detection of focal lesions and raise sensitivity and specificity of US in identifying focal lesions; *computered*

*tomography (CT)* – not reliable for the evaluation of ET; and *magnetic resonance imaging (MRI)*, which is considered the most accurate imaging technique in the preoperative assessment due to high soft tissue contrast resolution. Invasive methods, with the main purpose to obtain endometrial tissue for histological and cytological examination, include: *dilatation and curettage*, an old method and highly used, which has been replaced with office-based *vacuum methods* to obtain endometrial tissue and *hysteroscopy*. The hysteroscopic approach has the advantage of making guided biopsies possible and allows the identification and removal of intrauterine focal lesions, but comes with higher costs, sometimes required anaesthesia and day care in hospital. Hysteroscopy is considered the gold standard for the endometrial assessment of bleeding in perimenopause. **Conclusions.** Endometrial assessment in perimenopause is based on noninvasive and invasive methods, combined with endometrial sampling, each of them having its own value and investigator-dependent performance.

**Keywords:** endometrium, malignancy, perimenopause, menopause

## The role of ultrasound evaluation in prolonged labor

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**Introduction.** During labor, fetal positional changes are specific, deliberate and precise, as they ease the way of the smallest diameter of the fetal head to pass through a corresponding diameter of the woman's pelvic structure. The proper diagnosis and management of prolonged labor is mainly impaired due to the imprecisions of the clinical examination, which is a subjective, experience-dependent and inexact technique. In 1989, intrapartum ultrasound (IPU) was used firstly to confirm or correct the digital examination impressions of the fetal head position (FHP) considered critical to the route of delivery. Moreover, IPU has been proposed as a noninvasive new technique to properly assess the level and the progression of fetal head in order to predict potential obstructed labors and to ease the decision whether to attempt a vaginal or caesarean delivery. **Methodology.** We reviewed all current data from literature that include both linear methods of measurement such as fetal head-

perineum distance (HPD), progression distance (PD) and fetal head-symphysis distance (HSD) and angular methods, such as the angle of progression (AOP), the angle of direction (AOD) and rotation. **Results.** In nulliparous women with prolonged labor, we found a better reliability of IPU instead of clinical evaluations and a good correlation between sonographic measurements and labor duration and outcome. **Conclusions.** The use of IPU is not meant to change the classic algorithm of labor monitoring, but to provide objective and reliable evaluations of the traditional parameters of crucial importance when prolonged or arrested labor is suspected. As caesarean delivery rates are increasing due to fear of medico-legal liability, every little effort should be made to promote spontaneous vaginal delivery and to increase medical and patients' confidence that labor is objectively assessed, with no human error involved.

**Keywords:** primiparous, ultrasound, prolonged labor

## Antenatal echographic examination of the fetal aortic arch

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Anatomical variants and congenital anomalies of the aortic arch (AA) are important to recognize antenatally, as they may be associated with congenital heart disease or chromosomal abnormalities and may have important implications for the immediate or late prognosis. These abnormalities are considered biomarkers, a biological indicator of the presence of the disease. Extending the examination of the fetal heart to aortic arch allows the detection of the most common variants of AA from the end of the first trimester. The current presentation will update the knowledge, presenting variants of aortic arch

with two vessels, cases of aberrant left vertebral artery, aberrant right subclavian artery, aortic coarctations, transposition of the great arteries and variants of AA on the right, detected in standard examinations, accompanied by embryological and anatomical explanations. The familiarity with the spectrum and ultrasound imaging of aortic arch variants is essential for the accurate diagnosis of abnormalities and malformations and to guide the management.

**Keywords:** aberrant left vertebral artery, aorta on the right, Taussig-Bing malformation



## Ultrasound in gynecology – case reports

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Ultrasound is the preferred imaging modality in the study of the female pelvis and provides basic and important information for detecting and characterizing almost all gynaecologic pathologies. It is the first-line method in the assessment of abnormal uterine bleeding, acute pelvic pain, congenital genital malformations, female infertility and for pelvic masses of uterine, ovarian or adnexal origin, also providing useful criteria in predicting their benign versus malignant nature. This paper

presents several clinical cases of rare and uncommon gynecologic conditions where transvaginal ultrasound played an important role in diagnosis and follow-up: a congenital uterine malformation, an enhanced myometrial vascularity after retained products of conception, a uterine arteriovenous malformation and a case of an ovarian mass that posed challenges in the preoperative diagnosis due to its atypical ultrasound aspect.

**Keywords:** ultrasound, Doppler, malformation

## Key-points in the imaging diagnosis of pelvic inflammatory disease

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**Introduction.** Although patient history, as well as clinical and laboratory findings are highly suggestive for the diagnosis of uncomplicated or complicated pelvic inflammatory disease (tubo-ovarian abscess – TOA), pelvic imaging may help defining other causes of pelvic pain or may aid in the evaluation of the disease severity. Ultrasound is the method of choice in uncomplicated cases, but CT or MRI can be helpful in patients with severe disease or atypical clinical presentation. **Materials and method.** Uncomplicated pelvic inflammatory disease (PID) has rarely specific ultrasound signs (free fluid in the Douglas pouch, fluid-filled fallopian tubes). In more severe cases, we may see the "cogwheel sign" (a characteristic aspect of the tube on a cross-section), indirect and nonspecific signs of endometritis (heterogenous thickening of the endometrium, less well delimitation of the endometrial echo, fluid within the endometrial cavity). The tubo-ovarian abscess is characterized by a complex multilocular mass, with thick walls, with multiple fluid levels and/or internal echoes (due to in-

flammatory debris). They are frequently bilateral. The anatomy of the adnexa and of the Douglas pouch are often distorted. If the tube and ovary are separately discernible structures within the inflammatory mass, we describe a tubo-ovarian complex. Doppler studies reveal zones of increased blood flow, due to inflammation. If the abscess is ruptured, we may see free abdominal pelvic fluid and the abscess wall in the pelvis. The presence of an intrauterine device (IUD) is sometimes confirmed. **Results.** Several particular situations are often encountered in our emergency room: severe PID or TOA in adolescents, PID in patients with long time intrauterine contraception (IUD) – the abscess is often located in the right adnexa and is caused by *Actinomyces* spp., PID after recent IUD withdrawal. The association of malignancy especially in postmenopausal patients with TOS is rare. **Conclusions.** Imaging techniques are useful in diagnosing PID (both uncomplicated or complicated), the ultrasound being preferred in our clinical setting.

**Keywords:** pelvic inflammatory disease, ultrasound

## Ultrasound versus MRI in fetal CNS anomalies

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**Introduction.** Among all fetal abnormalities that can be identified during a routine prenatal ultrasound, the central nervous system (CNS) anomalies are the most complex and commonly encountered fetal malformations. Even though ultrasonography (US) is the primary method of prenatal diagnosis, magnetic resonance imaging (MRI) has demonstrated to be useful due to its superior soft tissue contrast which is known to offer an accurate diagnosis of detected fetal brain anomalies. The aim of our study was to provide an objective evaluation of the advantages and limitations offered by an US examination compared with a fetal MRI, particularly for fetal brain abnormalities. **Methodology.** For this purpose, we investigated 27 cases of CNS abnormalities, over a period of three years, using a Voluson E8 and E10 Expert System sonograph, with a 2-5 MHz transabdominal convex transducer and a 4-9 MHz transvaginal transducer. All patients included agreed to follow more complex investigations and were referred to an MRI evaluation of the fetal brain. Sixteen patients included in our study underwent MRI investigation with a 1.5-T superconducting magnet (Gyrosan Achieva Philips Medical Systems, Best, The Netherlands), using the synergy body coil in supine position. T2-weighted single-shot fast spin echo sequences were used for all cases. In some cases, T1-weighted sequence was performed. Eleven patients were not able to benefit from the MRI examination due to different reasons (obese patients with increased abdominal perimeter, metal prosthetics, claustrophobia, the impossibility to maintain a supine position, early labor or, for a short period of time during the pandemic,

being infected with SARS-CoV-2). **Results.** Maternal age in our study group ranged from 17 to 38 years old, with a median of 27 years old, and the gestational age at the moment of diagnosis was between 17 weeks and 6 days and 36 weeks, with a median of 28 weeks. Out of the 27 cases, we identified total (five cases) or partial (three cases) agenesis of *corpus callosum*, agenesis of the vermis with *mega cisterna magna* (three cases), hypoplasia of the cerebellum (five cases), 19 cases with ventriculomegaly with various forms of presentation (symmetric, asymmetric, mild or severe), one case of supratentorial hydrocephalus, two cases of cerebral tumor, two cases with *spina bifida* alongside banana and lemon sign, two cases with holoprosencephaly, and four cases that associated a choroid plexus cyst. The results of the two modalities of examination were compared in terms of diagnostic accuracy for the 16 patients who also received MRI imaging. MRI confirmed the ultrasound diagnosis, without additional findings in 37% of the cases, added information in 31% of cases, changed a diagnosis in 18% of the cases and inquired the suppositions in two cases (12%). **Conclusions.** Compared with ultrasound alone, fetal MRI could offer important additional information in order to provide a proper management of the pregnancy. From prenatal family counseling about the fetal development and possible postnatal outcome, to an adequate referral for delivery and treatment planning or pregnancy termination, the cumulative value of ultrasonography and fetal MRI offers significant advantages.

**Keywords:** nervous system, abnormalities, transabdominal

## Breast malignant adenomyoepithelioma: a challenge to diagnosis and management

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**Introduction.** Breast malignant adenomyoepithelioma is an unusual and rare tumor associated with biphasic proliferation of epithelial and myoepithelial cells, being characterized on the basis of histologic, immunohistochemical and ultrastructural features. **Methodology.** We report the case of a 47-year-old woman diagnosed at the "Cuza Vodă" Clinical Hospital of Obstetrics and Gynecology, Iași, who accused the presence of mastodynia for approximately two months and the self-detection of a tumor in the supero-external quadrant of the right breast which has grown rapidly. **Results.** Breast ultrasound showed a heteroechoic formation, imprecisely delimited, with atypical vascularization, with local modification of the glandular structure – suspicious of malignancy (BI-RADS 4). The breast biopsy (fine-needle

aspiration) was done, but the result was inconclusive. A mastectomy with excision of the axillary lymph nodes was performed (the anatomopathologic examination performed during the intervention suspected the diagnosis of adenomyoepithelioma). The lymph nodes included metastatic lesions. The histopathologic examination of paraffin embedded tissue and immunohistochemistry confirmed the diagnosis of malign adenomyoepithelioma. **Conclusions.** Breast malignant adenomyoepithelioma is an unpredictable and rare tumor, which is difficult to diagnose, very few cases being reported in the literature. The cytohistologic diagnosis is difficult and should be supported by immunohistochemical study.

**Keywords:** adenomyoepithelioma, breast, malignant, immunohistochemical

## Tanatophoric dysplasia type I – ultrasound criteria for prenatal diagnosis. Four case reports

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**Introduction.** Thanatophoric dysplasia (TD), characterized by severe micromelia and thoracic narrowing, lethal during the neonatal period, is the most frequently diagnosed prenatal bone dysplasia of the fetus. We present four cases with TD diagnosed in the second trimester of pregnancy. **Materials and method.** During the second trimester morphology, we examined the contour of the skull ("cloverleaf-shaped skull"), the appearance of the femur ("telephone receiver-shaped femora") and the appearance of the other long bones of the limbs. We measured the limb bones length and compared them with standard diagrams (Hadlock, 1982; Merz, 1996). We used the ratio between the femur length (FL) and the abdominal circumference (AC),  $FL/AC < 0.16$ , in order to predict lethal postnatal bone dysplasia. Prenatal genetic counseling was recommended. The obstetric management was established by the ethics committee. In cases with therapeutic abortion (TA), we recommended radiological and pathological studies of the fetus. Genetic diagnostic tests for the FGFR3 mutation have not been

performed. **Results.** Between the 1<sup>st</sup> of January 2001 and the 28<sup>th</sup> of February 2020, we diagnosed four cases of TD prenatally. The diagnosis was made at 16<sup>+4</sup> weeks of gestation, 21<sup>+5</sup> weeks of gestation, 26<sup>+4</sup> weeks of gestation and 27<sup>+6</sup> weeks of gestation. All cases presented severe micromelia, "telephone receiver-shaped femora" configuration of the femur and the FL/AC ratio below 0.16. The "cloverleaf-shaped skull" feature was not present. The diagnosis of type I TD was established based on the described ultrasound signs. In three cases, TA was performed. One case gave birth at 40 weeks of gestation, a live newborn, weighing 2900 g, who died at 7 hours postnatal due to respiratory failure. **Conclusions.** Skeletal evaluation is an important component of the second-trimester fetal morphology. The multidisciplinary approach of bone dysplasia cases can ensure increased accuracy of prenatal diagnosis. The prompt prenatal diagnosis of TD can reduce neonatal mortality by practicing therapeutic abortion.

**Keywords:** skeletal dysplasia, tanatophoric dysplasia, prenatal diagnosis

## HLHS – to treat or to let go?

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Hypoplastic left heart syndrome is one of the most severe forms of congenital heart disease and, still, one of the most difficult to treat. With an incidence of 160-360 cases in 1,000,000 of life births, in countries with national screening programs, its detection rate reaches 97%. *In utero* demise in these cases is rare, unless associated with other chromosomal or genetic anomalies. While in cases that are not operated, the mortality rate reaches 95% in the first month, for children who undertake the three-stage surgical treatment the survival rates may reach 52%. Studies developed during this last decade focus on *in utero* non-surgical treatment, such as maternal hyperoxygena-

tion during the pregnancy, but data are still insufficient, thus a new protocol for these cases hasn't been developed yet. We gathered up cases from the period 2019-2021, from the departments of obstetrics-gynecology from Târgu-Mureş, Craiova, Cluj, Bucharest, with a purpose to establish when it was made the ultrasound diagnosis and what was the counseling for this patients. Taking into consideration the mortality and morbidity rates, the quality of life for these patients, and still no other treatment other than the Fontan circulation, a valid question is whether “to treat or to let go”.

**Keywords:** hypoplastic, screening programs, ultrasound

## Ultrasound prediction criteria for placental implantation abnormalities: clinical case presentation

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**Introduction/objective.** Placental implantation abnormalities (PID) are focal, partial or total abnormalities of placental adhesion to the uterine wall, these translating clinically into a lack of spontaneous delivery of the placenta during the third period, and any attempt to separate the placenta causes abnormal bleeding. **Materials and method.** Our scientific paper represents a clinical case report of abnormally invasive placenta (AIP) monitored and treated in the OG1 clinic, County Emergency Clinical Hospital, Târgu-Mureş. **Results.** A 25-year-old patient, IIG IP, with a history of uterine curettage, had multiple placental gaps at the ultrasound examinations during the second and third trimester of pregnancy, myometrial focal line interruption and numerous placental vessels penetrating into the myo-

metrium (bridging vessels). The placenta acreta index (PAI) adds up to a value of 5, which corresponds to a probability of PID of 69%. The delivery took place at 39/40 weeks of amenorrhea, the labour was spontaneous, and it was complicated by the prolongation of the delivery period over 30 minutes, which led to a manual extraction of the placenta, associated with an estimated total bleeding at 400 ml. The macroscopic examination of the placenta revealed multiple areas of abnormal focal insertion. **Discussion and conclusions.** The ultrasound examination focused on clear criteria represents the gold standard in the diagnosis of PAI and contributes to an optimal management of the cases.

**Keywords:** placental implantation abnormalities, placenta acreta index, ultrasound examination

## The application of ultrasound in labor and delivery

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During the last decade, intrapartum ultrasound (IPUS) has been proposed to have an essential role in the management of labor. IPUS has been found to be more accurate in determining fetal head position, station and descend, as well as in estimating the interval time to delivery. In 2018, the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) issued guidelines recommending to performed IPUS in any delay in the second stage of labor and before instrumental deliveries. Ultrasound has several advantages over the clinical digital exam. Since this method involves the abdominal transducer, its use is not painful, causing less physical and mental discomfort to the woman. Ultrasound is an objective exam and has a

shorter learning curve compared to the digital exam. The ultrasound exam is not invasive and involves lower rates of chorioamnionitis. The use of ultrasound before pushing for visual feedback helps in optimizing the descend of fetal head during contractions and increases the bonding between the woman and her baby. Using ultrasound before instrumental delivery for fetal position and station may help in optimizing the decisions regarding the mode of delivery. Nevertheless, ultrasound use during labor has not proven to decrease the perinatal morbidity and a large multicenter randomized clinical trial is needed to test this issue.

**Keywords:** IPUS, ultrasound

## Placental mesenchymal dysplasia and maternal factor V Leiden – responsible for severe IUGR

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**Introduction.** Placental mesenchymal dysplasia (PMD) is an underdiagnosed placental anomaly which is potentially accompanied by severe fetal and/or maternal complications. The purpose of our paper is to present a rare association of PMD with genetic maternal thrombophilia, taking into account the paucity of the cases published in literature regarding this pathology. **Methodology.** We report the PMD case from our institution and we present the results of a systematic review of the existing literature. The inclusion criteria for the review were: the diagnosis of PMD as defined by placental pathology, the description of placental morphology on antenatal ultrasound and the reporting of pregnancy outcomes. Our patient had an abnormal result of the combined second-trimester screening, an enlarged, hydropic placenta in the second-trimester ultrasound examination and was diagnosed with homozygote factor V Leiden. The fetus had a XY normal karyotype and developed severe intrauterine growth

restriction (IUGR) which led to delivery at 27 weeks of gestation. Neonatal death occurred two weeks after birth due to complications associated with extreme prematurity. **Results.** The literature research revealed that the etiology of PMD remains uncertain. PMD is associated with fetal complications, such as growth restriction, preterm delivery, intrauterine fetal demise, hematologic disorders, liver tumors, Beckwith-Wiedemann syndrome and genetic anomalies. We have not found a similar case associating PMD and maternal genetic thrombophilia, which can both be responsible for severe early-onset intrauterine growth restriction (IUGR). **Conclusions.** Close surveillance with genetic evaluation, serial growth ultrasound examinations and third-trimester assessment of fetal well-being should be taken into consideration when suspecting a PMD diagnosis antenatally.

**Keywords:** placental mesenchymal dysplasia, thrombophilia, IUGR

## Abdominal ectopic pregnancy: a challenging diagnosis. Case report and review

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**Introduction.** Abdominal pregnancy represents a rare form of ectopic pregnancy, accounting for 0.6-4% of these. Due to delays in diagnosis and difficulties associated with optimal management, the risk of mortality is significantly higher than for uncomplicated pregnancies (the mortality rates are 7.7 times higher than in tubal pregnancy and 89.8 times higher than in intrauterine pregnancies). **Methodology.** The purpose of our paper is to present a case of ectopic abdominal pregnancy diagnosed at 12 weeks and localized in the Douglas retrouterine pouch. In addition, due to the paucity of this diagnosis, we will present the most recent data published in literature on this topic. **Results.** A 35-year-old gravida 7, para 2 patient, was admitted to our hospital accusing vaginal bleeding and pelvic pain and having a positive urinary pregnancy test. Following the ultrasound examination, she was diagnosed with 12 weeks abdominal pregnancy and

she underwent laparotomy. The fetus and placenta were removed successfully, without significant hemorrhage, and she had an uneventful recovery, being discharged on the third day. Although most of the cases of abdominal pregnancy reported in literature were diagnosed in the first trimester, there have also been cases of advanced pregnancies associated with fetal viability, which require a more complex approach. **Conclusions.** A high index of suspicion is of paramount importance in establishing promptly the diagnosis of ectopic abdominal pregnancy, and ultrasound and MRI examinations play a major role in this step. The mainstay of management is surgery, with focus on the precautions that must be taken when examining the extent of the placental attachment and avoiding massive bleeding and organ injury.

**Keywords:** abdominal pregnancy, hemorrhage, ultrasound

## Acute appendicitis in early pregnancy – a diagnostic challenge

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**Introduction/objective.** Acute appendicitis is the most common surgical emergency during pregnancy. The diagnosis is rather difficult to determine, due to the associated symptoms during pregnancy. Ultrasonography remains the most widely used imaging test in the diagnosis of clinically suspected appendicitis during pregnancy. Computed tomography or magnetic resonance imaging are usually avoided. The purpose of presenting this clinical case is to determine the diagnosis and establish an optimal treatment plan for women with early pregnancy and suspected appendicitis. **Methodology.** We present the case of a 31-year-old woman who presented herself to the obstetrics-gynecology department with 5 weeks of amenorrhea, pain in the right hypochondrium, nausea and vomiting, symptoms that began one day before the presentation. Even though the patient did not have fever, it was decided to hospitalize her for further evaluation, with the diagnosis of early pregnancy, dysgravida. **Results.** The obstetric ultrasound revealed a unique yolk sac present, embryonic echo without cardiac activity, and fine fluid blade in Douglas. During hospitalization, antispasmodic and an-

tiemetic treatment was administered, her general condition worsening. The next procedure involved a puncture into the bottom of the Douglas sac, with the extraction of 20 ml of purulent-looking liquid. Septic shock with abdominal source was recognized. Emergency exploratory laparotomy was performed, attempting to limit abdominal contamination. Generalized purulent peritonitis secondary to acute perforated appendicitis was found intraoperatively. Appendectomy and lavage of the abdominal cavity were performed. The patient was discharged on the fifth postoperative day and maintained obstetric monitoring for the uncomplicated pregnancy. **Discussion and conclusions.** The physiological symptoms of early pregnancy may complicate the diagnosis of acute appendicitis. Septic evaluation and additional diagnostic equipment are needed, beyond the standard clinical approach. In the present case, the delay in diagnosis was associated with the evolution to abdominal sepsis, which determined an increased obstetrical risk and an emergency surgical approach.

**Keywords:** acute appendicitis, early pregnancy, complications, appendectomy

## Intrapartum ultrasound – can we accurately predict vaginal delivery?

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Labor dystocia represents one of the most challenging aspects of obstetrics. The gold standard for the evaluation of the labor's progress is digital vaginal examination, a practice that bears as disadvantages the subjectivity, the risk of infection and the discomfort. The use of ultrasound (US) has been proposed to be added to the clinical examination in order to correctly evaluate the fetal head position and station and even to differentiate between the women who can deliver vaginally and those who are predisposed to operative delivery. Intrapartum ultrasound (IPUS) assesses a series of elements that includes fetal head position, fetal head station, angle of progression, fetal head di-

rection, head-perineum distance, midline angle, progression distance and head-symphysis distance, and this evaluation can give a more accurate prediction regarding vaginal delivery. There are two main situations in which ultrasound assessment is likely to be of particular use in labor, represented by suspected delay or arrest of first or second stage, and potential need for performance of operative vaginal delivery (OVD). Intrapartum ultrasound may offer a new perspective of the management in labor, even though there is no agreement regarding the parameters and their integration in the management of labor.

**Keywords:** pregnancy, labor, ultrasound, dystocia

## Ultrasound assessment of the uterine scar after caesarean section in the nonpregnant uterus

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The rate of caesarean section (CS) has been increasing both in developed and developing countries. The risk of obstetrical complications related to the uterine scar after CS is widely acknowledged and it depends on its morphological appearance of a "niche" at its level. Current evidence suggests that the impact of a niche on future pregnancies, patient's fertility or its involvement in the onset of gynecological symptoms are incompletely elucidated. For this reason, our aim is to review the current literature and to highlight the tools used in the evaluation of abnormalities of uterine scar. Ultrasonography (US) is a very accessible method in most settings and it allows the evaluation of a uterine scar using specific scoring systems. Both bidimensional and tridimensional US have been proven accurate in the detection of defects at the level of the uterine scar. Recently, techniques such as 3D saline contrast sonohysterography and sonography-based automated volume count software have been described as

promising in the assessment of the uterine cavity as well as uterine scars. Three main parameters are quantified on US scan: the presence of the niche, the thickness of the remaining myometrium and the ratio between the niche and the thickness of the remaining myometrium. Uterine scar niche assessment should include US evaluation along with the assessment of patients' risk factors. We acknowledge the variability in proposed cut-offs in different niche scoring systems and we suggest that these should be used in practice only once consensus on precise values is reached. We suggest that the visualization of the uterine niche on US would improve the reliability of morphological assessment of the uterine scar defects. However, the clinical relevance of specific features and the utility of any interventions should be confirmed by appropriate trials prior to implementation in practice.

**Keywords:** caesarean section, uterine scar, uterine niche

## Cervical insufficiency – role of ultrasounds and treatment

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**Introduction.** Cervical insufficiency represents, even nowadays, a major problem that complicates the development of a pregnancy. It could lead to either losing the pregnancy or to have a delivery before the due date, and the complications associated with this. Diagnosing this affliction is still difficult due to clinical nonspecific symptoms; however, it should be suspected in all cases having antecedents of miscarriages or premature delivery. Furthermore, the presence of a surgical cervix because of a conization or other surgeries performed at the cervix level could increase the risk of developing cervical insufficiency, so that the screening for this affliction should be rigorously performed. **Materials and method.** The literature review process was performed using the PubMed and Cochrane databases, considering the following key phrases and words: cervical insufficiency, treatment of

cervical insufficiency, echography used in the diagnosis of cervical insufficiency. Furthermore, there were considered only the studies that were meta-analyses or trials published in the past five years (the period between 2016 and 2021). The literature review was performed by two authors and any controversy was cleared by the input and opinion of a third author. **Results and conclusions.** Cervical insufficiency is considered an important complication occurring during pregnancies. Thus, the reason of performing a rigorous screening of the patient is to establish the course of action and the prophylactic treatment. It must be mentioned that, even with the correct treatment, there is a high percentage of cases where a premature delivery or miscarriage occurs.

**Keywords:** cervical insufficiency, ultrasounds diagnostic, cervical cerclage

## Ultrasound optimization for the detection of fetal structural abnormalities at the end of the first trimester

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**Objectives.** To optimize the detection of the fetal morphological abnormalities using an ultrasound protocol between 11 weeks and 13 weeks +6 days of gestation.

**Methodology.** Ultrasound data of the fetal morphological examinations were obtained using an E10 Voluson Machine. Unselected pregnancies were examined at the end of the first trimester. The ultrasound exam involved the examination of the fetal skull and brain, the examination of the chest and heart, abdomen and of upper and lower fetal limbs. **Results.** The ultrasound protocol used at the end of the first trimester detected a multitude of

fetal structural abnormalities that included abnormalities of the fetal face (profile, palate and upper lip), brain structures, fetal heart (atrioventricular septal defects and great vessel abnormalities), abdominal and limb defects. **Conclusions.** The detection of the major fetal structural abnormalities at the end of the first trimester is feasible using an extensive ultrasound examination protocol. The obtained data allowed a correct couple counseling and an early therapeutic attitude.

**Keywords:** ultrasound, fetal morphological abnormalities, first trimester

## Imaging-pathology correlations in cancers of the upper genital tract

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The role of imaging (US, MRI, CT) in patients with suspected cancers of the upper genital tract is to provide high-quality information in order to establish an accurate diagnosis and to recommend the best therapeutic solutions. The lack of good and personalized communication between gynecologic oncologist and imaging specialist diminishes the quality of expected information. Also, there is a need of sub-specialization of radiologists in the field of gynecologic oncology.

Ultrasonography is an excellent tool in the hands of gynecologists and plays a major role in the diagnosis of gynecological malignancies. The gynecologist and US examination are essential in orienting the diagnosis, while the role of imaging specialist (MRI, CT) has become central to confirm an accurate diagnosis and to evaluate the extent of the disease, providing better treatment options and planning.

**Keywords:** imaging, CT, malignancies

## Ultrasound input diagnosing patients with a pregnancy of unknown location

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**Introduction.** Ultrasound is the pelvic imaging modality of choice for all pregnant patients. Determining the location of the pregnancy is the priority in evaluating these patients, except for hemodynamic stability. Whether the pregnancy is intrauterine or ectopic, the precise extrauterine location guides the remainder of the evaluation and management. The early and accurate diagnosis of ectopic pregnancy is essential to avoid adverse sequelae of this potentially life-threatening condition. On rare occasions, ectopic pregnancy can occur in a nontubal location, making timely diagnosis even harder. Ovarian, interstitial, abdominal or rudimentary horn

pregnancies are rare findings, but must be considered when the gestational sac is not objectified intrauterine. **Methodology.** We present four cases of rare location of ectopic pregnancies sonographically diagnosed and the individuality of the images obtained in each situation. In all cases, the ability to accurately scan every patient early in the first trimester created the possibility to solve them with a laparoscopic approach. **Conclusions.** The sonographic diagnosis of an ectopic, nontubal pregnancy is difficult. The capacity to precisely examine the patient allows a prompt management and a better prognosis.

**Keywords:** intrauterine, ovarian



## Isthmocele – challenges of a new disease

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An isthmocele is a defect of the caesarean scar with a rising incidence. It is characterized by a myometrial discontinuity similar to a diverticulum located on the anterior isthmus of the uterus. An isthmocele is mostly asymptomatic, often remaining undiagnosed and untreated. The easiest, most reproducible and noninvasive method of diagnosing an isthmocele is by transvaginal ultrasound. It is most commonly diagnosed at a routine ultrasound examination, but it can be encountered in the first trimester of pregnancies. It remains a long-term complication of a caesarean section and has been recognized as a cause of abnormal uterine bleeding and represents a major risk factor for obstetrical complications in subsequent pregnancies, such as caesarean scar ectopic pregnancy or uterine

rupture. The management must be individualised, at present no consensus being available for the diagnostic and treatment of this disease. Treatment options must take into consideration the patient's desire for fertility preservation. Minimally invasive techniques remain an excellent option in case of failure of the medical treatment. We present a case of a uterine isthmocele on the caesarean section diagnosed on a patient with an intrauterine 9-week evolutive pregnancy. The patient opted for the continuation of the pregnancy and the correction of the isthmocele. The surgical procedure was performed by laparoscopy under ultrasound guidance. No complications were encountered during or after the procedure.

**Keywords:** isthmocele, caesarean, laparoscopy

## Management of atypical polypoid adenomyoma – case report

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**Introduction.** Atypical polypoid adenomyoma is a rare uterine tumour formed of atypical endometrial glands. There are known approximately 500 cases reported in literature, and mostly occurred at fertile age. The main symptoms of this disease are abnormal uterine bleeding, usually with severe anaemia. The diagnosis of this tumor is histological; however, the ultrasound appearance locates the tumor and its delimitation. **Methodology.** We present the case of a 41-year-old woman who came to the emergency room of the "Dr. I.A. Sbârcea" Clinical Hospital of Obstetrics and Gynecology from Brașov after three years from the last gynecological checkup, with uterine bleeding and severe anaemia. The patient was examined using a Voluson E8 Expert ultrasound and was diagnosed with an unusual uterine tumour with benign characteristics. **Results.** The patient was admitted to the hospital and

a hemostatic and diagnostic curettage was performed. The surprise was the histopathological result that revealed a rare tumor, an atypical polypoid adenomyoma. The diagnostic panel was completed with an MRI and repeated ultrasound examinations. Due to the location of the tumor, a hysterectomy was the elective treatment in this case. **Conclusions.** The ultrasound examination remains the best option in the routine diagnosis of uterine tumors, although is a rare tumour. The peculiarity of this case remains the histological type of the tumor, and the correlation with ultrasound image of this. The take-home message of this case is that every woman should perform an annual gynecological checkup with a transvaginal echography in order to avoid radical treatments.

**Keywords:** atypical polypoid adenomyoma, ultrasound, rare tumour

## The importance of emergency ultrasound for the diagnosis of ovarian hyperstimulation syndrome

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**Introduction.** Ovarian hyperstimulation syndrome (OHSS) occurs in female patients undergoing fertility treatments. Although rare, this is a potentially life-threatening, iatrogenic complication that needs prompt diagnosis and efficient management. Presenting symptoms such as abdominal bloating, weight gain or nausea (not uncommon for pregnancy) might be misleading if not properly combined with adequate clinical data. **Materials and method.** We present the case of a 34-year-old patient with a moderate form of OHSS and we emphasize

the relevance of emergency ultrasound for an immediate diagnosis and expedient management. Using ultrasound for surveillance, the case was managed successfully with a conservative approach. **Conclusions.** Since nowadays assisted reproductive techniques are largely employed, it is of paramount importance that severe complications are known and diagnosed even by specialists other than gynaecologists who can perform an emergency ultrasound.

**Keywords:** emergency ultrasound, ovarian stimulation syndrome, assisted reproductive techniques, IVF

## Ultrasound detection of fetal anomalies: how to inform the parents

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Ultrasound technology has improved rapidly in the last years and its increased availability has made ultrasound detection of miscarriage, fetal abnormalities and of other pregnancy complications more common. The physicians' knowledge of how to give pregnancy-related bad news is becoming progressively important. A compassionate and informative method of breaking bad news, particular to the type of news, the anxiety level of the woman, the capacity to process and under-

stand the news for the woman, the physicians' comfort level and the resources that are available for emotional support are essential. Although studied in oncology, the strategies for communicating abnormal ultrasound information during pregnancy are scarce. We suggest a therapeutic approach to giving bad news during or after an obstetrical ultrasound.

**Keywords:** prenatal ultrasound, fetal anomalies, obstetrician, bad news, protocol

## Closed *spina bifida* – challenging antenatal diagnosis

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**Introduction/objective.** Neural tube defects are the most frequent central nervous system (CNS) malformations and they amount to approximately one to two cases per 1000 births. Open (*aperta*) *spina bifida* can be reliably detected prenatally due the intracranial signs and the direct visualization of the spine defect. However, since absent intracranial signs and intact skin overlying the defect in closed (*occulta*) spinal defects, the diagnosis could be difficult before birth. The aim of the study was to describe the sonographic features useful for the antenatal diagnosis of *spina bifida occulta* (SBO). **Materials and method.** A retrospective review of six antenatally detected cases of SBO. Postnatal images and clinical and surgical reports were reviewed when possible. The sonographic assessment of the fetal CNS was performed according to the existing guidelines of screening examination and targeted neurosonography using the highest-frequency transducer possible. The relation between the *conus medullaris* and the last ossified vertebral body (the conus distance) was assessed. **Results and conclusions.** The diagnosis of SBO was possible starting from 14 weeks and 6 days of gestation. In all six cases, abnormally low (below L3 or renal pelvis level) *conus medullaris* (teth-

ered cord) was observed. The accurate location of closed spinal defects was possible. At the level of the vertebral osseous defect, the skin continuity was intact. The most common subcutaneous mass was lipomyelomeningocele (three cases), one case of terminal myelocystocele, one case of low conus with small skin-covered meningocele, and one case of low conus without any masses. There was no evidence of cranial, posterior fossa anomalies or ventriculomegaly, except one case of *corpus callosum agenesis*. Maternal serum alpha-fetoprotein was negative in all cases. On a retrospective review, in all affected fetuses the intracranial translucency was in normal ranges at the 11-13<sup>+6</sup> weeks scan. The prenatal diagnosis of closed spinal defects remains more challenging than the open ones, since intracranial abnormalities are not present and the spinal defect is not obvious. Moreover, some variations of *spina bifida* may be indistinguishable by sonography in pregnancy. Our study suggests that the main sonographic features of SBO are low conus/tethered cord and subcutaneous cysts or masses, while intracranial abnormalities are not present.

**Keywords:** neural tube defects, *spina bifida occulta*, *conus medullaris*

## Ultrasound aspects in the diagnosis of adenomyosis

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**Introduction.** Transvaginal ultrasound has become the main test in the diagnosis of adenomyosis. Adenomyosis is characterized by the presence of ectopic foci of endometrial glandular tissue and/or stroma in the myometrium. Adenomyosis results from the invasion of the endometrium into the myometrium, causing changes in the junctional area. These changes are frequently observed in imaging studies, such as transvaginal ultrasound and magnetic resonance imaging. **Materials and method.** A review of the literature on the accuracy of ultrasound diagnosis in adenomyosis will be presented, as well as a comparison between ultrasound signs and symptomatology, clinical evidence of the correlation between adenomyosis and infertility. Relevant articles were searched through MEDLINE and PubMed between 2010 and March

2021. The ultrasound characteristics of adenomyosis are reviewed, including the differential diagnosis between symptomatic and asymptomatic adenomyosis. The data available in the literature on ultrasound diagnosis of pelvic adenomyosis, its clinical relevance and its limitation are discussed. **Results and conclusions.** Adenomyosis has a great impact on both the quality of life and fertility of women. The preliminary results of color Doppler transvaginal ultrasound showed a high sensitivity and specificity for the differentiation between adenomyosis and fibroids (95.6% and 93.4%, respectively). Larger studies are needed to understand the different types of adenomyosis and their clinical impact.

**Keywords:** adenomyosis, diagnosis, transvaginal ultrasonography, ultrasonography

## Fetal brain tumors – case presentation and literature review

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Fetal brain tumors are a rare fetal pathology, with an incidence varying between 1.7 and 13/100,000 births, and with pathological characteristics different than that of the child and adult. It is estimated that the most frequent are teratomas, then astrocytomas (glioblastomas), craniopharyngiomas, neuroectodermal tumors, choroid plexus papillomas, meningeal tumors etc. The prenatal ultrasound scan allows the positive diagnosis for the second and third trimesters, but further explorations (especially MRI) are required to differentiate from benign pathologies which have other prognosis and therapies. Unfortunately, prenatal MRI could have conflicting results with those of the ultrasound and postpone the management to the postnatal stage when the outcome

is generally unfavorable for the newborn. We present a series of four cases recorded in our hospitals in the last 10 years, with two teratomas, one intracerebral rhabdomyoma and one glioblastoma. The ultrasound diagnosis was done in the second half of the pregnancy and was confirmed in three out of four cases by MRI. All cases had a poor prognosis, with therapeutic termination of pregnancy or neonatal death. In conclusion, fetal brain tumors are rare ultrasound findings, easy to spot but harder to evaluate and offer certitude for the parents, unless a multidisciplinary team could be formed for a proper assessment of the prognostic.

**Keywords:** fetal brain tumors, prenatal diagnostic, MRI

## The obstetrical ultrasound examination in obese patients – tricks and pitfalls

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The medicine of the last decades deals more and more with obese patients, which generates risks for associated pathology and technical difficulties. It is estimated that 15-20% of the population is affected by this condition, and the percentage for the pregnant women has doubled in the last decade. As ultrasound examination is an important part of prenatal care, we studied how the body mass index (BMI) affected the ultrasound examination in a specialised medical clinic. **Materials and method.** This is a longitudinal retrospective study on the second and third trimester ultrasound scan performed in the last five years on patients with BMI over 25 kg/m<sup>2</sup>. The repartition was done regarding the recommended categories: overweight (25-30), first-class obesity (30-35), second-class obesity (35-40), third-class obesity (>35). The statistical analysis regarded the number of ultrasound exams performed for each patient, the technical difficulties, if any correlation with the fetal weight percentile and Doppler indexes was mentioned. **Results.** There were 1101 ultrasound scans selected, performed for second- and third-trimester morphological ultrasound in 942

patients. These patients were distributed as overweight (69%), first-class obesity (22%), second-class obesity (6%) and third-class obesity (3%), respectively. In general, the number of repeated scans in the study was higher than in normal patients, although no statistical correlation to BMI could be established. In 58% of cases, the specialist marked technical difficulties in the fetal ultrasound assessment, mainly related to the abdominal maternal adiposity. Most frequently, the recommendation was for the scan to be repeated in 2-4 weeks time, as opposed to the usual 6-8 weeks interval in regular patients. No correlation to the BMI was found for fetal anomalies, Doppler parameters or estimation for fetal growth. **In conclusion,** obesity has become an important factor during pregnancy, both as associated pathology and as a difficulty in the antenatal care, especially regarding ultrasound. The new specialists for antenatal fetal morphology ultrasound evaluation should be trained to deal with the pitfalls and to know tricks for improving the accuracy of the exams, and to explain these limitations to the patient.

**Keywords:** obesity, BMI, morphology

## Placenta tells...

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Ultrasound placental screening is usually simplified to grading and localization. Placenta (exchange path) is an organ derived from maternal tissues – decidua, and fetal tissues – chorion, that's why we have to examine it carefully, thinking at the physiology and pathology of each gestational age, from the maternal point of

view and the fetal point of view, as well. Ultrasound aspects and changes in the placental structures during the pregnancy dynamic, sustained by images from the personal collection, will lead us to the associated pathology.

**Keywords:** placenta, pathology

## Tips and tricks in the prenatal diagnosis of aortic coarctation

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The embryological origin of aortic arch is still unclear. Thus, the pathogenesis of aortic coarctation has different paths, which will explain that an anomaly can occur at different stages of gestation. The embryologic cause is a wrong connection between branchial arches 4 and 6 towards the descendent aorta. Impaired placentation leads to hypoxic cause, with a decrease of aortic flow and increasing pressure in pulmonary

artery and ductus. The histopathological cause is due to an intertwining of elastic and muscular fibers from aortic and pulmonary structures, followed by isthmic constriction. We propose a diagnostic algorithm for each of these situations, documented with images from our personal collection, to an earlier prenatal diagnosis.

**Keywords:** aortic arch, coarctation

## Transvaginal ultrasound – the key to diagnosing caesarean scar pregnancy. Case report

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Pregnancy on the scar is an entity characterized by the development of a new pregnancy on the scar of a previous caesarean section. Its incidence is 1 in 1800-2500 pregnancies, being in a continuous increase due to the augmentation in the number of caesarean operations, the early use of ultrasound, the development and improvement of ultrasound. Scar pregnancy can cause serious complications; some authors consider that it is a precursor of the *placenta accreta* or *percreta*, or that it can even become a life-threatening entity. Transvaginal ultrasound is the first imaging tool used, being superior to abdominal ultrasound. Several features that suggest a pregnancy on the scar have been described, such as: the visualization of a uterine cavity and a cervical canal without contents, the visualization of a gestational sac/placenta close to the hysterotomy scar with the fetal/embryonic pole and/or vitelline vesicle with or without cardiac activity, a thin myometric interface between the gestational sac and the anterior uterine wall or bladder, positive Doppler ultrasound around the gestational sac. Another important aspect is that the

sac and the fetus ascend into the uterine cavity, but the placenta remains in the initial site, low implanted. The management and the treatment of this entity remain a controversy, a wide variety of therapeutic options being proposed: surgery, minimally invasive procedures, treatment with methotrexate, uterine artery embolization or even the continuation of pregnancy. Thus, we present the case of a 30-year-old patient, gravida 3 parity 1, with amenorrhea of 8 weeks, with a history of birth by caesarean section, who presented in our institution for vaginal bleeding. Transvaginal ultrasound indicated an empty uterine cavity, a gestational sac implanted at the level of the caesarean scar with embryo with cranio-caudal length of 3.9 mm, and cardiac activity present. An exploratory laparotomy with local excision of the pregnancy was decided. In conclusion, the diagnosis of this entity is of real importance. Any new pregnancy in patients with a history of caesarean section should be considered a scar pregnancy until proven otherwise.

**Keywords:** ultrasound, caesarean scar pregnancy

## Complementarity of the imaging evaluation in the management of *spina bifida aperta*

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**Introduction.** *Spina bifida* is one of the most common diseases compatible with life of the fetal central nervous system, and the precise imaging evaluation, as well as the early intervention (before the second trimester) are essential for improving the prognosis.

**Materials and method.** As this review aims to be an update, we searched the PubMed, Scopus, MEDLINE and Web of Science databases from 2017 to 2021 to shed light on the most suitable diagnosis methods and therapeutic options. **Results and conclusions.** Commonly, the diagnosis of *spina bifida aperta* (SBA) is achieved by sonography through the identification of indirect cranial and cerebellar signs such as the lemon and banana signs – a loss of the convex outward shape of the frontal bones and tethering of the spine with downward traction on the cerebellum (the Chiari II malformation), respectively. Recently, it has been found that first-trimester diagnosis is possible by intracranial translucency (examining the posterior fossa for obliteration or non-visualization of the fourth ventricle). Moreover, magnetic resonance imaging (MRI) helps

confirm the diagnosis and establish the type of neural tube defect. Although not superior to sonography, MRI offers a more precise visualization of the position of the defect. However, MRI techniques such as fetal diffusion or diffusion tractography can identify early neural changes and, together with sonography, are a valuable weapon for early diagnosis. Given the serious consequences of SBA, prenatal management is the recommended option. Although minimally-invasive techniques require advanced skills, maternal injury is minimal and less iatrogenic damage is caused to the neural tissue in contrast to open repair. Moreover, fetoscopic repair has no detectable effect on brain microstructure when compared to an open-hysterotomy technique. Although the ethical issues surrounding fetal surgery are complex, parents should know that advances in fetal therapy have made prenatal surgery the best option for SBA and the *in utero* repair showed better results compared to postnatal interventions.

**Keywords:** *spina bifida aperta*, imaging, early diagnosis

## Ultrasound aspects of the placenta in smoking patients

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This prospective study was performed at the Santerra Medical Center, Constanța, Romania, on two groups of 100 pregnant women, with gestational ages between 33 and 37 weeks. In the first group, all patients were smokers. They smoked between 3 and 30 cigarettes a day (i.e., filter cigarettes). The second group included only non-smoking patients. A careful anamnesis was performed on the patients, in terms of the number of cigarettes smoked daily, if the partner was a smoker, if she smoked indoors or outdoors, if she worked or lived in areas with high air pollution. The results were compared both within each group and between the two groups. An increased incidence of ultrasound-detected intraplacental calcifications

was observed in patients working in toxic environments (i.e., polluted air) versus patients not working in polluted air. Also, an increased incidence of intraplacental calcifications in patients who smoked more than 10 cigarettes per day was noticed. The incidence of intraplacental calcifications was very low in patients who smoked less than five cigarettes a day in the open space. In conclusion, the incidence of ultrasound-detected intraplacental calcifications increases in a direct proportion to the number of cigarettes smoked. It is also increased in patients who work or live in a polluted air environment.

**Keywords:** smoking patients, cigarettes, intraplacental calcifications, polluted air environment

## Correlations between fetal intestine hydroaerial images and increased maternal consumption of carbonated drinks

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**Background.** Past evidence has suggested a role of carbonated beverages in fetal intestine hydroaerial images at ultrasound, yet the evidence has been inconsistent. **Objective.** To examine the relation between the intake of carbonated beverages during pregnancy and the fetal intestine hydroaerial images during pregnancy. **Methodology.** This study was performed at the Santerra Medical Center, Constanța, Romania, on 110 pregnant women at two different gestational ages (i.e., between 33 and 36 weeks and at 38 weeks) during 2018 and 2020. All patients in the study consumed more than 1 liter per day of carbonated beverages (i.e., juices or mineral water). Pregnant women who had eaten foods that could cause flatulence were not included in the study.

**Results.** At 33-36 weeks of gestations, suspicious fetal intestinal hydroaerial images were detected. After two weeks of reevaluation (i.e., at 38 weeks), in which women were advised not to consume carbonated beverages, fetal intestinal hydroaerial levels were much lower at ultrasound compared to the previous examination. **Conclusions.** As we challenge with an unprecedented role of fetal intestinal hydroaerial images in mothers who often consume carbonated beverages, future studies should estimate the causal relationships between a higher maternal beverage consumption and the fetal intestine hydroaerial appearance.

**Keywords:** flatulence, carbonated beverages, fetal ultrasound, fetal intestine, hydroaerial levels

## The place of ultrasound in the diagnosis of breast cancer – two cases with synchronous bilateral breast cancer

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**Background.** The incidence of synchronous bilateral breast cancer (SBBC) is reported to range from 0.8% to 3%. **Methodology.** We used ultrasound for the evaluation of breasts and axillary area in two women (33 and 47 years old, respectively). **Results.** Both patients detected by self-palpation a tumor in the left breast. For the first woman, the breast magnetic resonance imaging (MRI) detected in the inferior external quadrant of the left breast a tumor of 27/15 mm, with probable benign characters. Core-needle biopsies of the suspicious areas were performed, revealing the presence of fibrosis, supporting fibroadenoma as diagnosis. The patient presented in our clinic for a second opinion. In the right breast, in the upper superior quadrant, the ultrasound exam found a hypoechoic mass, very well defined, homogenous, about 21/17 mm – fibroadenoma, and in the left breast, in the inferior external quadrant, a tumor with features suggestive of malignancy was revealed, but taking into consideration the core biopsies, we recommended reevaluation after three months.

Afterwards, both tumors increased in dimensions (the right one: 28/22 mm; the left one: 50/37 mm). Left axillary zone exam detected a big lymph node with increased cortical zone at 8 mm. For the second patient, we found only in the left breast a mammary architectural distortion of 30/15 mm. Mammography confirmed our supposition of malignancy and also detected in the right breast a malignant nodule of 15/14 mm. Our ultrasound reassessment of the right breast established smaller dimensions that were close with the ones from the histological exam. Both women wanted to undergo bilateral sentinel lymph node (SLN) biopsy. For the second patient, we chose a conservative treatment for the right breast (breast and axilla). Each patient had a different histological type for each breast, a fact that was compelling. **Conclusions.** Ultrasound is a complementary diagnostic method for breast cancer, but it has been shown to be very useful for detecting synchronous breast cancer.

**Keywords:** ultrasound, synchronous breast cancer

## Estimation of fetal weight at term using the ultrasound measurement of umbilical cord circumference

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**Introduction.** An accurate prediction of birth weight can prepare the labor suite staff for a fetus with growth retardation who may develop distress or for a macrosomic infant who may experience shoulder dystocia. **Objective.** We evaluated the relationship between umbilical cord circumference (UCC) and birth weight. We also compared the accuracy of abdominal palpation with that of ultrasound to estimate fetal weight. **Methodology.** This prospective study included 56 singleton pregnancies between 37 and 42 weeks of gestation planned for birth in the next seven days, in the First Clinic of Obstetrics, Iași. Fetal weight was estimated by Hadlock formula – the four ultrasound measurements: head circumference (HC), biparietal diameter (BPD), abdominal circumference (AC), and femur length (FL). Ultrasound measurement of UCC was obtained from cross sectional three-vessel view of a free loop, including the Wharton's jelly. We used the average value (millimeters) from three different measurements. Birth weight (g) =  $C^2 + 35 \times C$  (mm), where C is the UCC. Fetal weight was additionally estimated using Insler and Bernstein's formula (maternal abdominal circumference

at the level of the umbilicus) and Johnson's method (using the uterine fundal height). The fetal weight estimated by the aforementioned four methods was compared with the actual weight of the baby after birth. **Results.** The mean fetal weight at birth was 3428±441 g (limits: 2570-4400 g). Fetal weight depending on the UCC was 3401±451 g, and estimated by Hadlock formula, it was 3411±461 g. The difference between Johnson's formula or Insler and Bernstein formula and the actual birth weight is statistically significant (3621 g and 3685 g, respectively; p=0.001). The difference between Hadlock's formula or UCC estimation and the actual birth weight is not statistically significant (p=0.600, and p=0.428). The correlation between the average umbilical cord circumference and the birth weight was direct, moderate in intensity in female (r= +0.607; p=0.001) and male (r= +0.781; p=0.001) newborns. **Conclusions.** Umbilical cord circumference, measured by ultrasound prior to delivery, may be helpful in predicting birth weight.

**Keywords:** fetal birth weight, ultrasound, umbilical cord circumference



## The value of 3D ultrasound in the diagnosis of congenital malformations of the female genital tract

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**Introduction.** Three-dimensional (3D) ultrasonography is a diagnostic method in gynecological pathology, with increased accuracy and specificity of up to 100%, extremely valuable in diagnosing congenital uterine malformations. Three-dimensional ultrasound can render images with increased sensitivity, being able to accurately describe the outline of the uterus, as well as the shape of the uterine cavity, almost as well as an MRI examination. **Material and method.** Uterine malformations are associated with an increased risk of infertility, abortion, premature birth, fetal dystocic presentations, and with an increased number of births by caesarean section. An early diagnosis is vital in establishing the therapeutic behavior, as well as for fertility prognosis. The aim of our paper is to highlight the importance of 3D ultrasound in the diagnosis of congenital uterine malformations, by comparison with 2D ultrasound, but also with other imaging diagnostic methods, such as hysterosalpingography. We drew a parallel between the acquisition of images of uterine congenital malformations by 2D and 3D ultrasonography, comparing in certain situations with images obtained by hysterosalpingography, to determine which of the imaging methods have superior accuracy. **Results and discussion.**

Two-dimensional ultrasound and hysterosalpingography were the most commonly used diagnostic methods for diagnosing uterine malformations. They have the ability to provide accurate information about the uterine cavity, but they have a major disadvantage – namely, they cannot assess the external contour of the uterus. In addition, in the case of hysterosalpingography, the intervention is invasive, it requires the presence of a gynecologist and a radiologist, exposes the patient to radiation and can be painful. Another imaging investigation that obtains images with increased accuracy is represented by magnetic resonance imaging, but in this case, there are disadvantages: high cost, low accessibility. **Conclusions.** As we know, the gold standard in diagnosing congenital uterine malformations is exploratory laparoscopy performed simultaneously with hysteroscopy, but being an invasive method, with risks associated with surgery, the gynecologist must first opt for a noninvasive imaging investigation. Of all the methods analyzed, 3D ultrasound is the only one that is noninvasive, has an increased sensitivity and specificity, as well as low costs.

**Keywords:** 3D ultrasound, hysterosalpingography, congenital uterine malformations

## The impact of SARS-CoV-2 infection on umbilical and cerebral mid artery flow

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**Introduction.** The novel coronavirus is responsible for the production of viral infections with various clinical aspects, with polymorphic symptoms and an increased risk of morbidity and mortality. A particular situation is represented by the SARS-CoV-2 infection in pregnant women, as well as the degree of fetal damage *in utero*, but also the neonatal effects.

**Materials and method.** One of the markers of fetal distress that can be easily objectified by ultrasound is the cerebro-placental ratio, which consists in evaluating the blood flows in the umbilical artery and middle cerebral artery. We selected a series of 60 pregnant women admitted to our clinic since the onset of the pandemic, who presented a positive RT-PCR test for COVID-19. We checked up for associated pathologies, if the pregnancy was monitored, the place of origin, gestation and parity, the treatment administered during pregnancy, as well as the gestational age at which the SARS-CoV-2 infection was confirmed, but also the evolution of the newborn. **Results and discussion.** The vertical transmission of the new type of coronavirus could not be accurately demonstrated, nor could the effects of infection on fetal well-being. However,

the severe maternal forms, complicated by ARDS and an important systemic inflammatory response, have an important impact on the evolution of pregnancy, reaching a vital prognosis. Among these consequences, we can mention both the literature and the experience of the clinic effects, such as intrauterine growth restriction, the risk of premature birth and fetal distress. Fetal ultrasonographic evaluation, correlated with maternal biochemical markers, as well as with the non-stress test, can reveal the fetal distress. When observing Doppler indices measured at the level of the middle umbilical and cerebral arteries, only a moderate alteration of the velocimetric markers could be noted. This could not be strictly attributed to SARS-CoV-2 infection, taking into account the associated maternal pathologies. **Conclusions.** In mild or moderate forms of infection with the new type of coronavirus, in the absence of other associated pathologies, Doppler velocimetry remains unchanged, but tracking resistance and pulsatility indices in the fetal circulation remains an important method of monitoring acute fetal distress.

**Keywords:** SARS-CoV-2 infection, pregnancy, fetal circulation

## The outcome of structural heart defects diagnosed in the first trimester of pregnancy

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**Introduction.** We present the results of a detailed protocol of fetal heart examination in the first trimester, in a fetal medicine unit in Romania. **Methodology.** Since October 2009, in the "Filantropia" Clinical Hospital of Obstetrics and Gynecology, Bucharest, we have systematically assessed pregnancies at 11-14 weeks in order to screen for aneuploidies and for major fetal structural defects. The fetal anatomy examination protocol included the detailed assessment of the fetal heart. This was performed using the same principles as for the second-trimester examination, in the entire cohort. **Results.** Our population consisted of 7693 patients and 7816 embryos. The protocol for the ultrasound evaluation of the fetal heart was completed for 7597 embryos (97.2%). The outcome is known for 6912 cases (90.9%). We diagnosed 39 heart defects – 30 in the first trimester,

seven in the second trimester, and two postnatally. Twenty of the 39 heart defects were isolated cardiac malformations. Twelve of the isolated heart defects were diagnosed in the first trimester. The sensitivity of the first-trimester ultrasound in identifying major heart defects was 76.92%. The overall survival in cases of isolated congenital heart disease diagnosed in the first trimester was significantly lower than the survival in the cases diagnosed in the second trimester. **Conclusions.** Many (76.92%) of the significant heart defects can be diagnosed by ultrasound examination in the first trimester. Our study is an argument for developing the multidisciplinary approach needed for the management of early detected structural heart diseases.

**Keywords:** heart defects, first trimester, ultrasound, protocol, outcome



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