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• 11-13 May 2023, Bucharest, Romania •
ABSTRACTS OF THE 5TH NATIONAL CONGRESS OF THE EASTERN EUROPEAN ENDOMETRIOSIS AND INFERTILITY SOCIETY and THE 8TH NATIONAL CONFERENCE OF THE ROMANIAN HPV SOCIETY
• 15-17 June 2023, Brașov, Romania •

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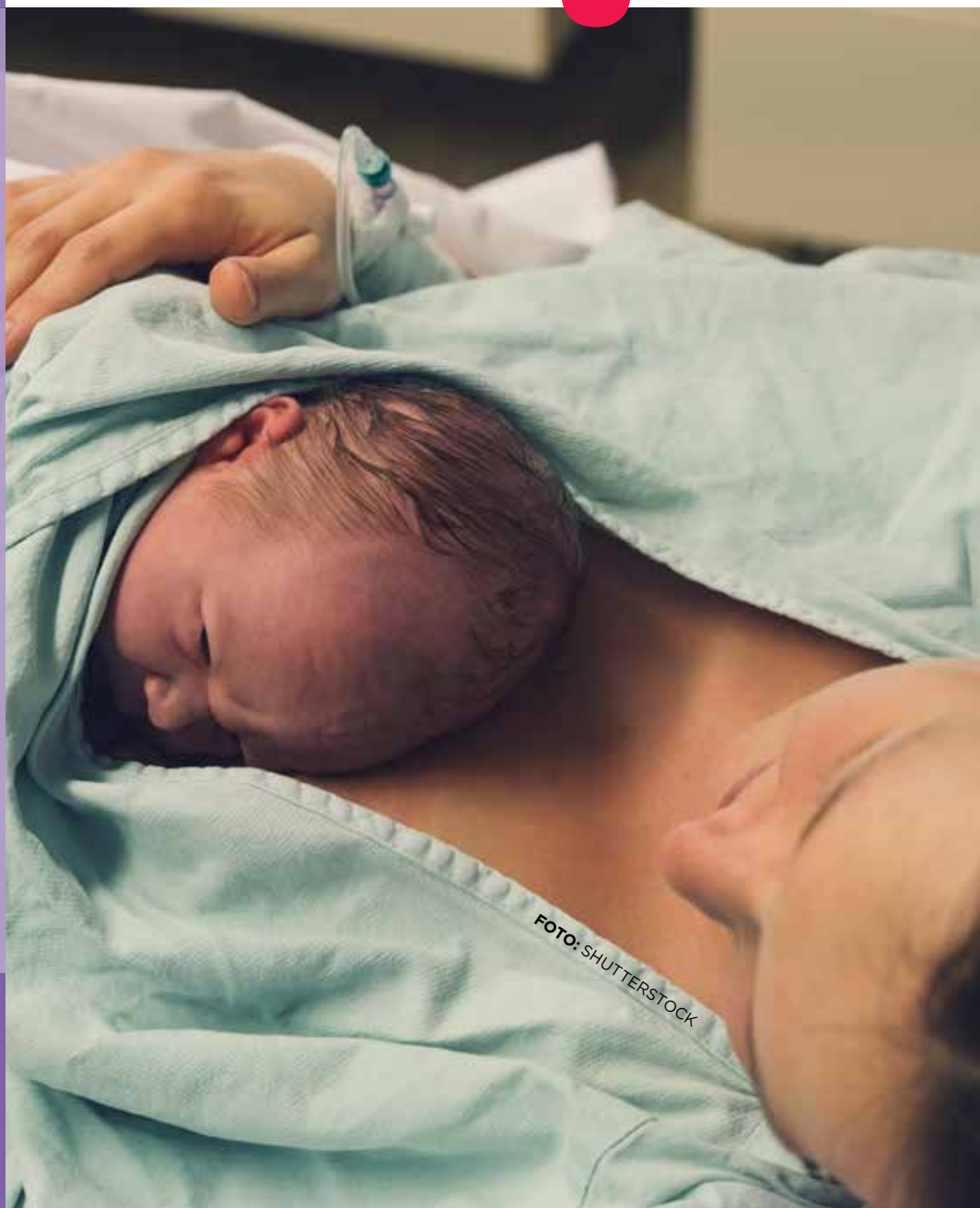

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ABSTRACT BOOK

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Management of uterine prolapse during pregnancy – a review

Diana Liliana Badiu, Roxana Penciu, Silvia Izvoranu, Dan Cozmei, Liliana Steriu, Corina Nour, Costin Niculescu, Vlad Tica

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Uterine prolapse during pregnancy is uncommon, with only a few cases reported in literature. Prolapse can lead to complications such as vaginal infection, urinary tract infections, abortion and preterm delivery, increasing both maternal and fetal morbidity. This review discusses the two types of management for uterine prolapse during pregnancy, conservative and surgical. Although conservative treatment of uterine prolapse during pregnancy represents the treatment of choice, women with severe prolapse have an increased probability of caesarean section. Therefore, obstetricians should be aware of the complications raised in pregnant women with prolapse, and the management should be individualized, depending on the clinical conditions of each patient.

Keywords: pregnancy, pelvic organ prolapse, preterm delivery, fetomaternal sepsis

Ultrasound risk evaluation in diabetic pregnancy

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Gestational diabetes mellitus (GDM), one of the most common metabolic complications in pregnancy, had a global prevalence of 14% in 2021, according to the International Diabetes Federation, Diabetes Atlas, 10th edition. The advanced maternal age, the sedentary lifestyle and the obesity, which is at worrying levels worldwide, make the prevalence of gestational diabetes to come as no surprise. Diabetes, gestational or preexistent, poses important risks to mother and the growing fetus if not managed correctly. Regarding the fetus, a plethora of short- and long-term complications can occur, from congenital anomalies, impaired intrauterine growth, perinatal morbidity and mortality to high rates of childhood and adulthood increased cardiometabolic risk. When it comes to maternal complications, these are also far from being negligible or a few, from preeclampsia, HELLP syndrome to complications during delivery, and in the case of those who develop diabetes for the first time during pregnancy, there are long-term additional risks of developing hypertension, metabolic syndrome and also type 2 diabetes mellitus. A profound understanding of the pathology, along with screening and diagnosis done right, as well as a good management help avoid some of the complications that accompany GDM. An important tool in the evaluation of the mother and the fetus is ultrasound imaging, providing vital information about their status. Ultrasound imaging is a noninvasive, easily available instrument used to evaluate the consequences of diabetes on the fetus, being used to monitor fetal growth and predict fetal weight, evaluate whether there are congenital abnormalities, monitor placenta and possible changes at its level. All of the aforementioned information helps guiding the maternal therapy and optimizing the mode and timing of delivery. The purpose of this paper is to review the role of ultrasound scan in the diabetic pregnancy, focusing on the effects of diabetes on the fetus and how it can be used to improve maternal-fetal outcome.

Keywords: diabetes mellitus, fetal weight, ultrasound

Evaluation and management of pregnancies with a history of venous thromboembolism

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Objective. Our aim was to present the management of pregnancies with a history of venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE). **Methodology.** A retrospective evaluation of maternal risk factors, previous and current pregnancies, as well as low-dose low-molecular-weight heparin (LMWH) prophylaxis in 77 pregnant women with a history of VTE (45 DVT and 32 DVT+PE cases). Prophylactic LMWH (enoxaparin, 1×2000 Anti-XA IU/0.2 mL/day) was prescribed as soon as the pregnancies were confirmed. **Results.** We have demonstrated that 87% of VTE cases were at least with one maternal risk factor for thrombosis and/or obstetric complications. Despite this, no significant difference was demonstrated between DVT and DVT+PE groups in terms of comorbidities, obstetric complications and adverse gestational outcomes ($p>0.05$). However, the rate of adverse gestational outcomes was significantly reduced in current pregnancies compared to previous ones ($p<0.001$). Additionally, the miscarriage ($p<0.001$) and preeclampsia ($p=0.022$) rates decreased in a statistically significant manner. We did not observe thrombosis-related complications under low-dose LMWH prophylaxis. **Conclusions.** The history of VTE should be searched in terms of thrombosis-related comorbidities and placenta-related obstetric complications. Low-dose LMWH prophylaxis is critical to have better gestational outcomes.

Keywords: venous thromboembolism, pregnancy

Early-onset fetal growth restriction

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Introduction. Intrauterine growth restriction (IUGR) affects 5-10% of pregnancies and represents the second cause of perinatal mortality. Early-onset IUGR is usually caused by placental dysfunction, but many other causes may be involved. **Case report.** We present the case of a 42-year-old woman, IIP, referred for amniocentesis for high genetic risk (trisomy 18) revealed by the noninvasive prenatal test (NIPT) for fetal aneuploidies. The amniocentesis performed at 16 weeks and 6 days showed a normal karyotype. A detailed second-trimester anomaly scan was repeated at 22 weeks and confirmed no signs of fetal structural abnormalities, an estimated fetal weight (EFW) at percentile (p) 16, and a pulsatility index (PI) within normal ranges for both uterine arteries and umbilical artery (UA). No signs of an active infection were found at the specific investigations, including extended TORCH complex, and thrombophilia was ruled out. During the following weeks, the fetus developed symmetric IUGR<8th percentile, with normal UA, MCA (middle cerebral artery), and *ductus venous* (DV) flows. At 30 weeks, the EFW was at percentile 5.2. At 32 weeks, we noticed a deterioration of the fetal well-being with a non-reactive nonstress test, absent end-diastolic flow in UA, but with normal DV Doppler. The patient was admitted for closer surveillance, corticotherapy and magnesium sulfate therapy. The CPR (cerebral-placental ratio) was <5th percentile, and PI-UA was above percentile 95. Two days later, the CPR reversed, the short-term variations on cardiotocography decreased at 3.1 ms, and an 1130 g fetus was delivered by caesarean section, with an Apgar score of 7. Overall, the outcome was favorable, with the newborn discharged after one month. **Conclusions.** In early-onset IUGR, optimal monitoring and delivery timing are crucial. Doppler scanning (uterine arteries, UA and MCA) and biophysical monitoring help prevent acidemia and stillbirth. Placental mosaicism must be considered in cases where NIPT results are not confirmed by invasive genetics.

Keywords: biophysical profile, Doppler ultrasound, intrauterine growth restriction

Polycystic kidney and congenital hydronephrosis – evolution and prognosis

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Introduction. Polycystic renal disease is nephrological, genetic, autosomal determined disorder that is characterized by the presence and uncontrolled growth of renal cyst due to a mutation occurring in one of PKD1 or PKD2 genes, with extrarenal manifestations, including hepatic, pancreatic, cerebral and aortic aneurisms, which require individual management and a complex approach. The basic characteristic of this condition is the presence of renal bilateral cyst. Cysts growth leads to degradation of renal function, the disease progressing to chronic stage, most often requiring substitution renal treatment (dialysis). **Materials and method.** We present the case of a 17-day-old male newborn, from a dispensary pregnancy, G-XI, P-VI, GA 38 weeks, BW 3100 grams, born in the Baia Mare Maternity. Diuresis was absent in the first hours of life, and renal ultrasound detected a polycystic right kidney, an undifferentiated left kidney, and a posterior urethral valve. At 3 days of life, the first surgical intervention was performed, exploratory cystoscopy for posterior urethral valve, later skin ureterostomy and peritoneal dialysis catheterization being performed. The patient's evolution worsened progressively, developing respiratory distress syndrome that required mechanical ventilation, and developing urosepsis and renal samples with significantly increased values. The patient had massive precranial, abdominal, upper and lower lymphedema. **Results and conclusions.** Hematological, biochemical and urine tests confirmed the acute kidney injury status. Peritoneal dialysis was instituted, but without a clinical and biological improvement. Genetic diagnosis brings benefits to the families and improve the clinical management of patients, which might be enhanced even further with upcoming therapeutic options. Polycystic renal disease induces acute renal injury if it involves pulmonary components. Polycystic kidney is a severe disease with evolution towards chronicity (requiring dialysis or kidney transplant for the survival of the patient), being associated with substantial mortality and morbidity.

Keywords: polycystic kidney, newborn, hydronephrosis

Neonatal cholestasis in preterm IUGR – diagnostic approach

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Cholestatic jaundice, defined as conjugated bilirubin level higher than 1 mg/dl, is a sign of a disturbance of bile formation and excretion, and it could be the expression of a severe disease. Its incidence is estimated at 1 case in 2500 live birth. In developing countries, it could be 19-33% of chronic liver disease. It occurs more frequently in biliary atresia (35-41% of the cases), but also in infectious diseases, endocrinological and metabolic diseases, Alagille syndrome, preterm birth and in IUGR newborns. Neonatal cholestasis is a frequent complication of parenteral nutrition. The incidence in premature newborns with parenteral nutrition is 23%, being closely related to the duration of parenteral nutrition and with birth weight. Other risk factors are low birth weight, the lack of enteral feeding and male gender. Intrauterine growth restriction interferes with the liver function and feeding tolerance and increase the risk for TPN associated cholestasis. Early diagnosis enables the early therapeutic intervention. We report a case of severe intrauterine growth restriction in a premature male newborn, with 30 weeks of gestational age and 800 g birth weight, born by caesarean section for meconium-stained amniotic fluid and "reverse flow" on the umbilical artery. The patient developed mild respiratory distress, hypoglycemia, meconial ileus and early cholestasis. Head ultrasound DOL 2 – cerebral venous infarction, anterolateral area of the horn of right ventricle, and microcystic images on the periventricular white mater. Complex hematological, serological and coagulation test were carried out. Cystic fibrosis or TPN associated cholestasis were suspected. The differential diagnosis was made with perinatal sepsis, TORCH syndrome, biliary atresia and α1-antitrypsin deficiency. Delta F508 – negative, low level of pancreatic elastase in feces and uncertain values of immunoreactive trypsinogen. The treatment with ursodeoxycholic acid was started. Three months later, transaminases, bilirubin and triglycerides were at normal levels. The final diagnosis was cholestasis in a severe intrauterine growth restricted preterm newborn and TPN-associated cholestasis.

Keywords: conjugated hyperbilirubinemia, cystic fibrosis, IUGR preterm

Managing gestational diabetes – importance of early detection and timely intervention

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During pregnancy, gestational diabetes is the most common metabolic disorder, characterized by altered glucose tolerance. The prevalence of gestational diabetes is increasing, which is linked to the rise in maternal obesity rates in recent years. Despite numerous large-scale studies on the topic, there is still ongoing debate about the screening and treatment of gestational diabetes. The fetal and neonatal complications associated with gestational diabetes include fetal macrosomia, hyperinsulinemia, hypoglycemia, hypocalcemia, neonatal hyperbilirubinemia, increased risk of respiratory distress, and shoulder dystocia, especially in macrosomic babies. Additionally, children born to diabetic mothers are at a higher risk of developing obesity and diabetes in adolescence and adulthood. Maternal complications of gestational diabetes include an increased risk of developing hypertensive syndromes and the likelihood of requiring a caesarean section. Screening and treatment of gestational diabetes are crucial in ensuring healthy outcomes for both mother and child. In this article, we will explore the importance of early detection and effective management of gestational diabetes, highlighting the benefits of timely intervention, and the potential risks of untreated gestational diabetes. Furthermore, we will present the latest international guidelines and recommendations for the screening and management of gestational diabetes.

Keywords: diabetes, screening, obesity, macrosomia

Predictive ultrasound signs for early nonviable pregnancy

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Transvaginal ultrasound and serum concentration of human chorionic gonadotropin are the main methods of prognostic evaluation of early pregnancies. Although these pregnancy investigation methods have proven their benefits, the interpretation is fundamental for a correct diagnosis, in order to avoid interventions that may affect pregnancies that would normally have had a physiologic course, as well as to apply an appropriate management in the case of nonviable pregnancies. Recent studies have shown the need to adopt rigorous criteria that minimize false positive results and thus decrease the frequency of diagnostic errors. Over time, a series of ultrasound features have been described which have proven effective in predicting nonviable pregnancies in the first trimester (cranio-caudal length in relation to the presence or absence of cardiac activity, yolk sac diameter, gestational sac diameter in relation to presence or absence of embryo with cardiac activity, embryonic heart rate, subchorionic hematoma etc.). In the context of the new prospects for the development of artificial intelligence softwares, the present work focuses on the description of the precise ultrasonographic aspects aboded by the latest studies that propose certain cut-off values dependent on the gestational age of the ultrasound parameters in the first trimester, increasing the sensitivity and the specificity of ultrasound in the diagnosis of nonviable early pregnancies, thus aiming to improve the reproductive prognosis of couples with recurrent abortions.

Keywords: ultrasound, nonviable pregnancy, CRL, heart rate, artificial intelligence

Echogenic content in the fetal gallbladder. Ultrasound features and clinical outcome

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Introduction. It is rare to detect echogenic content in the fetal gallbladder. The etiology, natural course and prognosis of this condition remain unclear. In addition to providing a systematic review of this topic, we suggest a plan for patient follow-up. **Methodology.** Of a total of 100 database entries identified in PubMed, EMBASE and ICTRP reviews, we selected 34 studies in which we investigated the ultrasound features and the outcome of this condition. **Results.** There were 226 fetuses with gallbladder echogenic content identified. Seventy-two fetuses were found to have biliary sludge; 30 cases had a single hyperechogenic focus and 100 fetuses had multiple foci in the gallbladder. There were 16 cases of distal shadowing, 37 fetuses with comet tail and twinkling, and 26 cases with no acoustic artefacts. Eight cases of spontaneous resolution before birth have been documented; nine fetuses exhibited no echogenic content at birth, and 136 cases of resolution of echogenic content within the first year of life have been described. **Conclusions.** Typically, the condition resolves spontaneously during the postnatal period. After adequately reassuring the parents, the patients should be monitored for spontaneous resolution; medical or surgical intervention is not indicated. Asymptomatic patients can be managed with a wait-and-see strategy.

Keywords: echogenic content, fetal gallbladder, prenatal diagnosis

The clinico-biological evolution of operated digestive tube malformations

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Introduction. Congenital digestive tract malformations are a significant cause of neonatal morbidity and mortality. Prenatal ultrasound detects a wide range of abnormalities of the gastrointestinal tract. The postnatal management of digestive malformations is exclusively surgical, and the results of surgical interventions depend on the knowledge and recognition of the disease. Neonates with congenital gastrointestinal anomalies have growth delays that persist beyond the neonatal intensive care unit. **Materials and method.** This singlecenter prospective study, performed over a period of two years (2021-2022), included a total of 58 newborns with gastric malformations admitted to the regional level III Neonatal Intensive Care Unit (NICU) of the "Louis Ţurcanu" Emergency Clinical Hospital for Children in Timişoara, Romania. Demographic variables and clinical data were collected (sex, gestational age, Apgar scores, admission weight and discharge weight measured in grams, length of hospitalization, pathological clinical sings, plain abdominal X-ray and dynamic follow-up of hematological, biochemical and coagulation balance). **Results and conclusions.** The prompt diagnosis of digestive malformations, before the first feeding, was an important factor in the postoperative evolution. Dynamic monitoring of biological samples helped to reduce infectious complications and shortened the length of hospitalization. CT and MRI examinations allow a better assessment of the malformation and associated anomalies, but require a long time and increase the risk of clinical instability. The cause of these malformations is still unknown, although some experts believe there may be a genetic link. The key to success is the specialized equipment, medications and trained staff available 24 hours a day in the neonatal intensive care unit.

Keywords: digestive malformations, postoperative status, evolution

Abnormal uterine bleeding in adolescence

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Background. Abnormal uterine bleeding in adolescence (AUBA) is a common gynecological issue. AUBA has a higher prevalence compared to adulthood (37% versus 10-20%), being determined by the menstrual disorders and influenced by hypothalamic-pituitary immaturity. **Objective of the study.** To assess the management of AUBA. **Materials and method.** The study included 60 adolescents, between 10 and 18 years old, admitted to Infant Gynecology Unit in the period 2021-2022. Gynecological and somatic anamnesis were determined. Clinical, ultrasound and laboratory examinations were performed. Pregnancy, iatrogenic causes, systemic and genital tract abnormalities were excluded from the study. The patients were informed, counseled and treated according to the national clinical guideline. Statistical data processing was performed using SPSS Statistics. **Results.** Sixty percent of the patients came from the rural area and 35% came from the urban area; 5% were refugees. The average age was 14.4 years old, menarche occurred at 11.8 years old, lasting in average 5.8 days. They had abnormal uterine bleeding for an average of 11.6 days. Coagulopathies, chromosomal abnormalities, and sexually transmitted diseases, including HIV infection, were determined in 11.5% of cases. Somatic diseases prevailed: anemia in 58.3% of cases, endocrine disorders in 10% of cases. The hormonal profile was performed in 81.6% of patients. The average admission was 8.6 days, and 35% patients were admitted for several times, 5% being treated in the intensive care unit. Patients received hemostatic (85%), anti-anemic (58.3%), hormonal (40%) and analgesic (11.7%) treatments. At the same time, the prolonged hormonal therapy (in 68% of cases) and anti-anemic treatment (in 50% of cases) were indicated after discharge. **Conclusions.** Abnormal uterine bleeding is one of the most important issues in adolescents' health, requiring careful diagnosis, long-term treatment and follow-up.

Keywords: abnormal uterine bleeding in adolescence, hormonal treatment, anemia

Fetal ovarian cyst – a scoping review of the data from the last 10 years and a case presentation

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Abdominal cystic masses are diagnosed during the intrauterine period and have a relatively low incidence. Fetal ovarian cysts are the most common form diagnosed prenatally or immediately after birth. The pathophysiology of the development of these types of tumors is not fully elucidated, with ovarian hyperstimulation caused by maternal and placental hormones being the most accepted hypotheses. We conducted a scoping review with the aim to map the current knowledge regarding the treatment of fetal ovarian cysts diagnosed in the intrauterine period. Focusing on the articles published in the last 10 years in the specialized literature, we tried to identify a conceptualization regarding the surveillance and treatment of these anomalies. We describe the case of a 38-year-old patient, in her second pregnancy, with a physiological course of pregnancy until 29 weeks of gestation, when a cystic mass of 52/48 mm was detected in the abdomen during the routine ultrasound examination. The most likely origin was established to be the right ovary. Applying the diagnostic criteria described by Nussbaum, the detected cystic mass was of a simple type, with a thin wall, transonic content, without the presence of septa, vegetations or the appearance of intracystic hemorrhage. We observed a linear growth trend from the time of diagnosis when the diameter measured 52 mm, until 38 weeks of gestation when it reached 76 mm. A female fetus was born, weighing 3570 g, with an Apgar score of 10, with a good postnatal adaptation. On the eighth day of life, the newborn was transferred to the pediatric surgery unit where ovarian cystectomy was performed. Intraoperatively, a cystic mass was found belonging to the right ovary, with a size of 80/70/70 mm. Ovarian cystectomy was performed, with the successful preservation of ovarian tissue. The postoperative recovery had a favorable outcome.

Keywords: fetal ovarian cyst, ultrasound, Nussbaum criteria

The particularities of menstrual cycle in women with primary infertility

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Introduction. The fertility rate is a fundamental and integral criterion in the socioeconomic well-being of a country. The fundamental mechanisms in pregnancy occurrence are represented by the quality of the embryo and the morphofunctional state of the endometrium, which represents the mirror of the pathological processes that occur in the pelvic organs. **Aim of the study.** To study the particularities of the menstrual cycle in patients with primary infertility. **Materials and method.** A prospective study was conducted, which included 96 patients divided into two groups. The study group (L_1) included 48 primary infertility patients and the control group (L_0) included 48 fertile patients. The patients were interrogated according to a questionnaire that included 130 questions. The study was approved by the Research Ethics Commission of the "Nicolae Testemițanu" State University of Medicine and Pharmacy, Chișinău, Republic of Moldova (No. 79/62 of 26.04.2017). The patients signed an informed consent to participate in the research. **Results.** Study groups were homogenous according to the following criteria: age of menarche, duration of menstruation. Patients in the study group had regular menstrual cycle in 70.8% of cases (n=34), and those in the control group, in 93.8% of cases (n=45), χ^2=8.649; p=0.003. Every fifth patient suffering from primary infertility reported hypomenorrhea, compared with the fertile patients – 18.8% (n=9) versus 2.1% (n=1), χ^2=7.839, p=0.020. The presence of intermenstrual and postcoital bleeding was reported only by patients in the study group, with a frequency of 14.6% (n=7), χ^2=7.551; p=0.006, and 4.2% (n=2), χ^2=2.043, p=0.15, in the control group. **Conclusions.** Patients suffering from primary infertility more often reported irregular and prolonged menstrual cycle, hypomenorrhea, intermenstrual and postcoital bleeding, algodysmenorrhea, dyspareunia and premenstrual syndrome, which indicates the existence of endometrial dysfunction based on the pathogenesis of infertility.

Keywords: primary infertility, menstrual cycle, algodysmenorrhea

Agenesis of the *corpus callosum* – a series of cases and literature review

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Introduction. *Corpus callosum* is a transverse tract of fibers that connects the two cerebral hemispheres. His role is to favor the exchange of information between hemispheres, being important in language, reading, writing, attention, memory, but also emotions. The *corpus callosum* may lack completely or only partially, causing a very various neonatal and pediatric symptomatology. **Methodology.** During the period 2020-2023, we registered in our clinic a number of six cases of partial or total agenesis of the *corpus callosum*. All cases were analyzed by systematic fetal morphological ultrasound, karyotype and fetal MRI. The data were analyzed prospectively and after birth, and were statistically correlated several parameters such as the anatomopathological appearance, ultrasound or MRI data, Apgar score, neonatal adaptation, neurological disorders or seizures. **Results.** The prevalence of *corpus callosum* malformations was 1.507 to 1000 births in our clinic, during the analyzed period. Isolated *corpus callosum* malformation was diagnosed in three of six patients (50%), and the associated cerebral malformations was diagnosed in four of six patients (66%). Prenatal diagnosis was correctly established in five out of six cases (83%). Overall, a normal outcome was found in one case and moderate or severe developmental delay was present in two of three children (65%). One of the survivors, to which a 6q27 microdeletion was discovered, presented microcephaly, muscular hypotonia and retinal lesions, being diagnosed with Aicardi syndrome. **Conclusions.** In our study, the mortality was 50% of the three survivors within three years. A single case (16.6 %) presented a good neonatal adaptation and a favorable neurological development. Even with the help of modern diagnostic methods, including simple genetic testing by karyotype or extended by WES/WGS, the diagnosis of certainty is difficult and counseling remains controversial. Large scale trials and pediatric tracking of cases are required to have statistically significant results in terms of neurocognitive adaptation of children with *corpus callosum* malformations.

Keywords: *corpus callosum*, Aicardi syndrome

Reviewing maternofetal results following vaginal birth after caesarean section in north-eastern Romania

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Introduction. As Romanian caesarean delivery rates rise, there is a need to evaluate the success of vaginal birth after caesarean delivery (VBAC) in public hospitals. **Results.** A total of 63 cases were analyzed, and relevant information on maternal and fetal parameters, including outcome of the present pregnancy, were retrieved. A total of 63 cases of VBAC were included in our study. The mean age of the patients was 30.52 years old. In our selected cases, 40 patients (63%) received prenatal care, 21 (33%) patients did not receive any prenatal care, and two patients (4%) were partially followed-up. The mean admission to delivery time interval expressed in days was 0.97. A total of 27 patients (42.8%) had ruptured membranes before VBAC. Prophylactic episiotomy was performed in 38 cases (60.3%), and instrumental delivery was indicated in eight cases (12.6%): seven vacuum extractions and one forceps application. The mean gestational age at birth was 37.25 weeks of gestation. The smallest gestational age was 27 weeks, while the maximum gestational age at birth in our cases was 42 weeks. A total of 15 preterm births were identified: three cases of extreme preterm births, five cases of very preterm births, and seven cases of late-term births. Only one case of post-term birth at 42 gestational weeks and four other cases of late-term births at 41 weeks were recorded. The male:female ratio for newborns was 1.73, with a mean birth weight of 2,956.03 g, respectively a mean Apgar score at 1 minute of 7.63. The main complications that followed VBAC were postpartum hemorrhage (10 cases) and uterine atony (five cases), which required manual removal of the placenta and instrumental and manual control of the uterine cavity. Postpartum transfusion of two units of blood were required in two cases. **Discussion.** The first objective of the present study was to retrospectively assess the VBAC cases that were admitted to a tertiary maternity hospital in Romania, between January 2014 and August 2020. An increasing trend in the number of VBACs was observed, from four births in 2014 to 17 births in 2019, but in this tertiary center, approximately 6000 births take place annually, so the VBAC rate is less than 1%.

Keywords: vaginal birth, caesarean delivery, VBAC

Acute coronary syndrome in pregnancy

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Introduction. The incidence of maternal mortality in developed countries is relatively low, but cardiovascular diseases represent a significant percentage of the causes of maternal mortality. Acute coronary disease and myocardial infarct during pregnancy are responsible for about 20% of all maternal death. Acute myocardial infarction in pregnant patients can occur first through an obstructive mechanism, especially in patients with advanced maternal age, or through non-obstructive mechanisms in young patients. The most common causes of acute coronary syndrome in pregnancy are: spontaneous coronary artery dissection, coronary embolism or thrombosis, coronary vasospasm, normal coronary arteries and atherosclerotic coronary artery disease. The most common risk factors are hypertension, hyperlipidemia and type 2 diabetes. Afro-American women and women with lower socioeconomic status seem to be at risk. Patients with preexisting cardiovascular diseases present a significantly increased risk and must be advised as such. The diagnosis is the usual one in acute coronary syndrome, based on suggestive symptoms and significant enzyme changes with elevated serum troponin. As the invasive investigation by coronary angiography is decided, the protection of the fetus for exposure to radiation is essential. The treatment must be carefully individualized and has as options medical treatment or interventional treatment with the placement of metal stents and drug-releasing stents. **Materials, method and results.** We present two patients with a pregnancy of 24 and 37 weeks of gestation, without risk factors, without cardiovascular pathology in the antecedents who presented acute myocardial infarction and were treated by interventional cardiology, both deceased by post-therapeutic cardiogenic shock. **Conclusions.** Acute coronary syndrome during pregnancy, including cardiogenic shock, must be identified early and promptly managed in order to reduce maternal and fetal adverse outcomes.

Keywords: acute coronary syndrome, pregnancy

The role of maternal attachment in the recovery of the hospitalized newborn

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Introduction. The natural process of parent-infant attachment can be interrupted due to diverse factors, such as the infant's illness, parental psychoemotional distress and NICU admission just after birth. Early maternal/infant separation can result in a series of traumatic emotional reactions from both the newborn and the mother. **Materials and method.** The study was conducted on 60 mothers whose newborn children were hospitalized in the Neonatology – Preterm Department of the "Louis Țurcanu" Emergency Clinical Hospital for Children, Timișoara. The mothers included in the study were divided into two groups: separated mothers/newborns and unseparated mothers/newborns. To conduct the study, a questionnaire was prepared and distributed to both groups. **Results and conclusions.** The study reported that the separated mothers/newborns group had an average hospital stay longer than 10 days compared to the group of unseparated mothers/newborns where the average duration of hospitalization was 7 days. In the group of separated newborns, 40% had a favorable evolution and 30% had complications. Regarding the behavioral changes occurred in the newborns, comparing the results of the two groups, it appears that the group of separated newborns had the most behavioral changes. The most common were crying (66.7%), followed by decreased appetite (13.3%), sleep disorders (10%) and weight loss (6.67%). The most common behavioral changes seen in mothers were decreased/loss of milk, anxiety states and sleep disorders. Maternal-infant separation has not only a negative impact on the child, but also on the mother, with both short-term and long-term effects.

Keywords: mother-infant separation, neurodevelopmental risk, breastfeeding, maternal separation anxiety

The effectiveness of early administration of erythropoietin in newborns

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Introduction. Neonatal hypoxic-ischemic encephalopathy is the leading cause of disability and infant mortality through its consequences on the central nervous system. It is estimated that approximately 2-4% of full-term neonates experience an episode of hypoxia during or immediately after labor, and an even greater percentage of preterm neonates are at even greater risks. Recombinant human erythropoietin (EPO) has been among the most successful therapeutic biologics and clinically important in different neonatal pathologies. **Materials and method.** A total of 72 newborns, with a gestational age of 30-34 weeks at birth, over a two-year period, were included in the study – a control group of 35 newborns and a study group of 37 patients. 1000 U/kg EPO was administered to the study group in the first 48 hours after birth. In the control group, it was administered after one week of life. Transfusion requirements and neurological development were followed during therapy. **Results and conclusions.** In the study group, compared to the control group, the number of transfusion of erythrocytes was reduced. There were seven infants in the erythropoietin group who needed transfusion (20%), compared to the control group, where transfusion was administered in 18 infants (51.42%). Regarding the neurological outcome, the group analysis indicated that, in the study group, erythropoietin improved long-term outcomes only for infants with moderate periventricular leukomalacia, but not in those with severe periventricular leukomalacia. The early administration of EPO reduced the risk of disability for infants with moderate periventricular leukomalacia and improved the evolution of preterm anemia.

Keywords: risk factors, neonatal anemia, periventricular leukomalacia

The value of proinflammatory cytokines in women with preterm and term birth

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Introduction. Preterm birth is the leading cause of neonatal morbidity and mortality. Although the underlying causes of pregnancy-associated complication are numerous, it is well established that infection and inflammation represent a highly significant risk factor in preterm birth. However, despite the clinical and public health significance, infectious agents, molecular trigger(s) and immune pathways underlying the pathogenesis of preterm birth remain underdefined and represent a major gap in knowledge. **Objective.** To estimate the value of the serum levels of proinflammatory cytokines such as interleukin-1β, interleukin-6 and TNF-α in women with preterm and term birth. **Methodology.** This prospective cohort study included 130 women, who were divided into two groups. Patients selected were divided into L_1 (65 women with premature spontaneous labor and newborns) and L_0 (65 women with term delivery and their newborns). The numerical values of the parameters were numbered in an Excel table, after which they were imported into the statistical analysis software R studio, using descriptive, variation and correlational analysis. Applied statistic tests used were non-parametrical Mann-Whitney test and p Spearman test, used as appropriate. P values less than 0.05 were considered statistically significant. **Results.** The results of this study demonstrated increased plasma levels of Interleukin-1β (minimum 0.99 pg/ml, maximum 10.6 pg/ml, median 3.99 pg/ml) in women with preterm birth compared to the control group, and in women with term delivery (minimum 0.05 pg/ml, maximum 3.13 pg/ml, median 1.08 pg/ml). At the same time, the study found an increased plasma levels of interleukin-6 (minimum 0.99 pg/ml, maximum 192.93 pg/ml, median 51.90 pg/ml) in women with preterm birth compared to the control group, and in women with term delivery (minimum 9.65 pg/ml, maximum 137.97 pg/ml, median 21.51 pg/ml). Also, the study found increased plasma levels of TNF-α (minimum 12.51 pg/ml, maximum 121.72 pg/ml, median 26.54 pg/ml) in women with preterm birth compared to the control group, and in women with term delivery (minimum 9.23 pg/ml, maximum 45.42 pg/ml, median 12.40 pg/ml). **Conclusions.** Proinflammatory cytokines (interleukin-1β, interleukin-6 and TNF-α) have a majore role in the imunophatogenetic mecanism of the preterm delivery. Thus, this ratio may be a promising diagnostic marker in prognosis of the preterm birth.

Keywords: preterm birth, inflammation, infection, proinflammatory cytokines

Hysterectomy role in abnormal placentation

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Introduction. Nowadays, the rate of abnormal placentation has increased. The high frequency of caesarean section has resulted in a high incidence of placental disorders such as *placenta praevia*, *accreta*, *increta* or *percreta*. Hysterectomy is the main treatment to control the blood loss. **Objective.** The management of patients with placental disorders and the evaluation of hysterectomy as a procedure of choice. **Materials and method.** The case series involves three patients, aged 30-42 years old, with abnormal placentation, at 35-39 weeks of gestation. Caesarean section was performed for the baby delivery and then two patients underwent hysterectomy. **Results.** One patient was ultimately diagnosed with *placenta increta* and two were diagnosed with *placenta accreta*. The actual invasive depth of the placenta tended to be deeper than had been diagnosed before surgery. All three patients were ultimately discharged from the hospital without any complications. **Discussion and conclusions.** Obstetricians must be aware of the complications of abnormal placentation. Hysterectomy may be taken into consideration based on the clinical findings, and the management of each case should be individualized.

Keywords: hysterectomy, placentation

Can obstetricians prevent the occurrence of necrotizing enterocolitis in newborns?

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Introduction. Necrotizing enterocolitis (NEC) is one of the most aggressive emergencies in neonates. Although the global incidence of NEC has not been systematically evaluated, it is estimated to affect 6% to 15% of preterm and very low birth weight infants. While preterm babies are particularly at risk, there have also been cases of NEC in term babies. NEC is characterized by variable intestinal inflammation, ranging from mucosal injury to full-thickness necrosis, which can lead to perforation and sepsis. The pathogenesis of NEC remains incompletely understood, but it is clear that intrauterine life and the peripartum period play an extremely important role. Studies have suggested a possible link between the occurrence of NEC and the alteration of the newborn's microbiome, which can result from the administration of antibiotics to the pregnant woman and their exposure during the intrauterine period. **Objective of the study.** To evaluate the effectiveness of reducing the administration of antibiotics during pregnancy in preventing NEC. **Materials and method.** A review of the literature was conducted for the period 2018-2022 by accessing PubMed and the Web of Science database. Additionally, cases selected from the clinics involved in the study over the last two years were analyzed. The cases were discussed and analyzed by a multidisciplinary team comprising obstetricians, neonatologists and pediatric surgeons. The diagnosis, etiology and treatment were evaluated by all the specialties mentioned before. **Results.** There is a clear connection between prolonged antenatal and postnatal exposure to antibiotics and the development of NEC. Our observations have shown that the majority of NEC cases were exposed to antibiotic therapy during pregnancy, with a higher incidence of NEC observed in newborns who were administered more antibiotics intrapartum. By highlighting the microbiota of the newborn, depending on their gestational age, and its sensitivity to certain antibiotics, the connection between NEC and antibiotic exposure becomes apparent. **Conclusions.** The administration of antibiotics during pregnancy is a double-edged sword. While it can significantly improve the pregnancy prognosis, it may also have long-term effects on the newborn. Therefore, the decision to administer antibiotics must be carefully evaluated and tailored to each individual case. It is essential to recognize that the cause of many neonatal pathologies, including NEC, lies in the intrauterine period. Hence, obstetricians must carefully consider the administration of antibiotics to pregnant women. The benefits of their use must be weighed against the potential long-term effects on the newborn. Treating infections during the gestational period is crucial, as they can lead to premature birth, neonatal complications, chorioamnionitis, sepsis, or even death. However, it's recommended to advise expectant mothers on how to prevent infections. Antibiotics should only be prescribed based on the antibiogram, and it's advisable to avoid using the latest generation antibiotics as much as possible, as these can significantly alter the microbiome of the newborn.

Keywords: necrotizing enterocolitis, antibiotics, pregnancy

Ankyloblepharon filiforme adnatum – bilateral interrupted type: illustrative clinical case and literature review

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This clinical entity, representing a rare congenital anomaly, is often benign, with a potential family trait, describing the congenital fusion of eyelids, partial or complete, an isolated finding or part of a well-defined syndrome. The AAP recommends the eyes examination of the newborn within the first 30 days of life and in most European countries case scenarios, it's being performed as part of discharge examination. A check-list could be of great help on busy wards in this regard. Emerging scientific data are supporting the theory of a shared etiology for a variety of clinical presentations at birth, such as: ankyloblepharon, ectodermal dysplasia, cleft lip/hard palate. TP63 gene 3q27 at AEC domain includes 42 mutation types, known so far. This clinical case might be the first one describing a bilateral interrupted type of congenital *ankyloblepharon filiforme adnatum*, and in our experience it was an isolated finding.

Keywords: *ankyloblepharon filiforme adnatum*, congetinal abnormality

Correlations between neonatal seizure etiology and long-term outcome

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Introduction. Neonatal seizures (NS) are a major challenge for clinicians due to discrete clinical signs and variable electro-clinical correlation. Most of the NS are caused by an acute illness or brain insult with an underlying etiology. EEG monitoring is absolutely mandatory to avoid undiagnosed or overdiagnosed NS, taking into account the frequent subtle semiology of seizures. A valuable and increasingly used method for the continuous monitoring of brain electrical activity in critically ill newborns in neonatal intensive care units (NICU) is amplitude-integrated electroencephalography (aEEG). aEEG background pattern is also an important predictor of the individual evolution of patients with NS. **Materials and method.** This prospective study followed the assessment of newborns with NS admitted to Preterm and Neonatology Department of the "Louis Ţurcanu" Emergency Clinical Hospital for Children, Timişoara, over a period of three years. In the neonatal period, patients were electroencephalographically monitored and clinically and biologically assessed for the etiology of NS. Subsequently, their neurological long-term outcome was monitored. **Results and conclusions.** Hypoxic-ischemic encephalopathy (HIE) was the most common condition that caused seizures in full-term newborns and intraventricular hemorrhage determined most seizures in preterm newborns. The increased incidence of unfavorable neurological outcome was observed in patients with HIE – 48.5%, followed by those with structural disorders (cerebral infarction, hemorrhage or malformations, hydrocephalus) – 30.3%. Of the patients who had an unfavorable neurological outcome, 60.6% were born prematurely. aEEG was very effective in detecting prolonged seizures and *status epilepticus*, being less invasive, easy to set up and allowing extended bedside recordings. Neonatal seizures are associated with a substantial risk of mortality and long-term neurodevelopmental disabilities and epilepsy. There is a continuing need for high-quality research in order to improve the outcome and long-term prognosis of these patients.

Keywords: neonatal seizures, etiology, aEEG

Open *spina bifida* with cervical meningocele and absent Chiari type II malformation

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Introduction. *Spina bifida* (SB) is a congenital anomaly caused by the incomplete development of neural tube. It can be further classified into SB occulta (closed) and aperta (open). The first type is the mildest form of the neural tube defects which involves a minimal neural involvement and a hidden vertebral defect. The second type defect allows the neural tissues to communicate with the external environment such as meningocele and myelomeningocele. A reliable prenatal diagnosis of open SB is feasible as early as the end of the first trimester, by means of direct or indirect signs. The severity of open *spina bifida* disease is associated with the size of the spinal defect. **Case report.** We present the case of a pregnant woman examined in our center from 18 gestational weeks with suspected encephalocele and recommendation for abortion. The ultrasound scan identified a tumoral formation in the cervical region with 15 mm in diameter and origin in the spinal cord central canal – suggestive for open *spina bifida* with cervical meningocele. Apart from the cervical spine malformation and the mild difference between lateral cerebral ventricles, the fetal development was normal and we didn't identify indirect signs suggestive for Chiari type II malformation. During the pregnancy, the cervical meningocele has increased from 15 mm to 30 mm until the third-trimester, when the fetus was born. The evolution of the newborn was favorable. Meningocele repair was performed successfully in the first weeks of life, and at the age of 1 years old the child had a good neurological outcome. **Conclusions.** Cervical open SB is difficult to differentiate from occipital meningocele at the first-trimester anomaly scan, as the spine is not yet fully ossified and the ultrasound findings are subtler. Cervical open SB accompanied by cervical meningocele can associate a normal brain morphology, with no Chiari type II structural determinations.

Keywords: *spina bifida*, meningocele, cervical spine

Urinary tract malformations: prenatal diagnosis and correlation between ultrasonography and MRI

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Introduction. Prenatal urinary tract malformations are a commonly observed condition during ultrasonography, posing a challenge for the physician, as they present a wide clinical spectrum and variable prognosis. Sometimes, the fetal anatomy may be difficult to investigate because of maternal obesity or the presence of oligohydramnios, which are commonly associated with urinary tract malformations. The aim of our study was to evaluate the value of MRI findings as a complementary investigation to sonographic diagnostic in cases with fetal urinary tract anomalies and to determine its possible benefits for the management of pregnancy. **Materials and method.** In our study, we report our two-year experience with nine cases of fetuses between 21 and 35 weeks of gestation with urinary tract anomalies in whom sonography couldn't provide a definite diagnosis. Ultrasonography was performed using a Voluson E8 and E10 Expert System sonograph, with a 2-5 MHz transabdo convex transducer and a 4-9 MHz transvaginal transducer. Subsequently, all patients were referred to an MRI evaluation using a 1.5-T super conducting magnet (Gyroscan Achieva Philips Medical Systems, Best, The Netherlands). These anomalies included fetal hydronephrosis grade 3 (n=3) and grade 4 (n=2), renal cystic lesions (n=2), renal agenesis associated with severe oligohydramnios (n=1), posterior urethral valve (n=1) and fetal megacystis (n=2). **Results.** In four out of nine fetuses, MRI and ultrasonography presented concordant conclusions and provided a final diagnosis that was afterwards confirmed by the postnatal evaluation or the postmortem examination. The addition of MRI to sonography modified or added significant supplementary information for the diagnosis in five cases. In a fetus where a suspicion of bilateral ureteropelvic obstruction was made, the diagnosis of bilateral ureterohydronephrosis associated with unilateral ureterovesical junction obstruction was established. In a fetus with an enlarged bladder at 32 weeks of gestational age, the posterior urethral valve was excluded and an ureterocel was observed. In a case with unilateral renal agenesis, an ectopic kidney was found. In a patient with suspected unilateral renal agenesis, MRI proved complete bilateral agenesis alongside pulmonary hypoplasia. In two cases, the addition of MRI to sonography led to a diagnosis that modified the decision to continue or terminate the pregnancy. **Conclusions.** Fetal MRI improves the diagnostic accuracy in anomalies affecting the fetal kidney in third-trimester fetuses. It may be a useful complementary tool which has the ability to detect additional extrarenal malformations, particularly in cases with inconclusive sonographic findings, especially in cases associated with pulmonary hypoplasia.

Keywords: urinary tract malformations, prenatal diagnosis, magnetic resonance imaging

Attempting to predict early-onset sepsis: the inconsistent role of traditional biomarkers

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Introduction. Timely diagnosis of early-onset sepsis (EOS; in the first 24 hours) is challenging, due to a lack of markers with acceptable sensitivity and specificity. Bacteriological confirmation by blood culture is possible only after 48-72 hours of life. **Materials and method.** We conducted a retrospective cohort study which included 1355 neonates with premature rupture of membranes (PROM) and postnatal age below 24 hours. Infants born at less than 23 weeks of gestation, with congenital anomalies, or absence/incomplete sepsis screening according to the unit protocol were excluded. The study population was classified into two groups: Group A (neonates with PROM longer than 18 hours before birth; n=826 patients) and Group B (PROM less than 18 hours; n=529 patients). For the secondary analysis, the neonates were stratified into three subgroups: subgroups A1 and B1 (proven EOS); subgroups A2 and B2 (probable EOS); subgroups A3 and B3 (absence of EOS – the control group). The intensity of the neonatal inflammatory response was compared by assessing the concentration of C-reactive protein (CRP), white blood cells count (WBC) and procalcitonin (PCT) in neonatal blood at three different determinations. **Results.** Increased CRP levels and leukocytosis measured at day 1 were identified in group B ($p<0.001$) and in subgroup B2 ($p<0.05$). Regarding the subgroups without neonatal sepsis, leukocytosis on day 1, CRP on day 3, and fibrinogen levels on day 2 were significantly higher in the B3 subgroup compared to the A3 subgroup ($p<0.05$). The procalcitonin serum levels were higher in the B2 compared to the A2 subgroup ($p<0.05$). **Conclusions.** Our results show that traditional biomarkers tested in common practice may be of more use in neonates with membranes ruptured for less than 18 hours, which are not necessarily included among those eligible for antibiotic prophylaxis. Early diagnosis would allow the initiation of individualized treatment, with the reduction of mortality and morbidity.

Keywords: early-onset sepsis, WBC, CRP

Neonatal COVID-19 pneumonia: is lung ultrasound the bridge between laboratory and clinical findings?

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Introduction. The pandemic caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has exposed vulnerable populations from the outset, yet the burden of this virus is spreading to the entire population. In addition to concerns about how the virus is transmitted from mother to fetus or newborn, there are concerns about the effects of the virus on the newborn. Thus, this study aims to highlight the importance of lung ultrasound in newborns with COVID-19 symptoms. **Methodology.** Based on inclusion and exclusion criteria, 23 neonates were selected for this study. The aim was to evaluate neonatal clinical and paraclinical characteristics following exposure to SARS-CoV-2, correlated with their imaging investigations. The lung ultrasound examination was performed using a Samsung ultrasound machine with a linear and a micro convex transducer. The chest wall was divided into 12 areas – six areas for each hemithorax. The nipple line was the demarcation between the upper and lower region. **Results.** Regarding the transmission of SARS-CoV-2, three of all newborns (13.04%) had vertical transmission and the rest had a postnatal infection (86.96%). The three most common symptoms described were psychomotor agitation, loss of appetite and rhinorrhea. Oral candidiasis was the most frequent comorbidity. The lung ultrasound findings varied: erasing A-lines and sparse B-lines were found in all cases, confluent or coalescent B-lines in 56.52%, pleural abnormalities in 69.56%, and white lung image in 43.47% of cases. **Conclusions.** Most newborns presented asymptomatic or mild COVID-19, but showed ultrasonographically detectable lung changes. Lung ultrasonography helps detect lung lesions induced by both SARS-CoV-2 infection and other lung diseases, having the advantage of being a non-irradiative method, easy to use and with the possibility of repeated measurements.

Keywords: lung ultrasound, COVID-19, neonate

Fetal morphology – more than standard

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The anomaly scan represents the most crucial imaging evaluation during pregnancy. Unfavorable visualization due to high fetal mobility, maternal obesity, and inter-observer variability or protocols limit the accuracy of clinical applications and outcomes. The addition of artificial intelligence (AI) techniques has the potential to optimize fetal ultrasound examination by shortening the evaluation time, reducing the workload, and improving the overall accuracy. So far, AI has been successfully applied to the automatic detection of fetal ultrasound standard planes, biometric measurements, and less for malformations detection, thus the improvement of the conventional imaging approaches is debatable. This study attempts to review and propose applications of AI in prenatal diagnosis and discusses the challenges of this innovative domain.

Keywords: fetal morphology, artificial intelligence prenatal diagnosis

Early diagnosis of twin-to-twin transfusion syndrome

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Introduction. Twin-to-twin transfusion syndrome (TTTS) is a severe complication in monochorionic multiple pregnancies, with high mortality rates. Early TTTS represents 7-23% of all TTTS and is defined as debut before 18 weeks of pregnancy. The early diagnosis of TTTS is not standardized at this moment, but Quintero staging, based on two-dimensional ultrasound and Doppler study, can be helpful even in the first trimester, although those assessment are appropriate for the second trimester. **Case presentation.** We present the case of a 29-year-old woman with no medical history who was referred at 8 weeks and 2 days of amenorrhea. The transvaginal ultrasound assessment revealed two GS (gestational sacs) with two embryos. A marked discordance was noted between the CRLs (crown-rump length) of the two embryos. At 11 weeks and 4 days, the patient was examined, and we observed the appearance of the "lambda" sign which suggested a dichorionic diamniotic pregnancy. The discordance in the development of the two fetuses was maintained. After a thorough morphological examination, a fetal cystic hygroma and a *ductus venosus agenesis* were noticed in the smaller fetus. Noninvasive prenatal testing was recommended, with normal results. At 13 weeks and 4 days of amenorrhea, the patient was examined, and a 21% discordance was noted between the two fetuses. Also, inside the GS of one of the fetuses, we noticed a thick amniotic band that was probably misinterpreted before as a "lambda" sign. The pregnancy was considered monochorionic/diamniotic. At this point, we suspected an early TTTS. The ultrasound aspect of cystic hygroma and *ductus venosus agenesis* was persistent. The patient requested medical termination of pregnancy. The forensic exam of the fetuses revealed a severe growth discordance between the two fetuses, a unique placenta and an amniotic band. The genetic exam revealed two female fetuses with normal karyotypes. **Conclusions.** The early diagnosis of TTTS is rare, and most of them remain undiagnosed, waiting for the fusion of the chorioamniotic membrane after 16 weeks of pregnancy. One amniotic band can be misinterpreted as chorioamniotic membrane and the "lambda" sign can be described in early pregnancies.

Keywords: twin-to-twin transfusion syndrome, early diagnosis, amniotic band syndrome

Comparative analysis of methods of artificial triggering labor for pregnant women at term at the First Obstetrics and Gynecology Clinic, Târgu-Mureş, Romania

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Introduction/objective. Artificial triggering of labor represents the induction of uterine contractions before they occur spontaneously for the purpose of obtaining a natural birth for those pregnant women who previously were not in labor. **Methodology.** This scientific paper represents a retrospective study carried out in the First Obstetrics and Gynecology Clinic of Târgu-Mureş, between 8 March 2021 and 8 December 2021. The methods used for the artificial induction of labor were vaginal device with dinoprostone (Propess type) and oxytocin infusion. **Results.** During this period, we had 57 cases of artificially induced labor. According to the randomization criteria, 10 cases were excluded, resulting in a final sample of 47 patients (16 cases using dinoprostone and 31 cases with oxytocin infusion). Maternal outcomes were approximately identical for both groups, the exception being the time from triggering labor to delivery, which was longer in the case of using oxytocin infusion. We had no cases of neonatal hemotransfusion, hypoxic ischemic encephalopathy, grade 3 or 4 intraventricular hemorrhage, necrotizing enterocolitis or need for neonatal hypothermia. Compared to deliveries triggered with dinoprostone, neonatal jaundice and serosanguineous edema at the level of the scalp were reported more frequently in deliveries triggered with oxytocin infusion. **Discussion and conclusions.** The use of dinoprostone and oxytocic infusion represent effective methods of artificial triggering of labor under conditions of compliance with obstetric indications and pharmacological characteristics.

Keywords: artificial triggering of labor, dinoprostone, oxytocin, birth

Fetal lower urinary tract obstructions

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Fetal lower urinary tract obstruction (LUTO) presents a wide spectrum of severity and affects 2-3 of 10,000 fetuses. LUTO is usually associated with a high mortality and postnatal morbidity, mainly due to lung hypoplasia and impaired renal function. Outflow obstruction of fetal urinary bladder during *in utero* development leads to progressive bladder dilatation, mural thickening, hydroureteronephrosis, parenchymal renal damage and oligohydramnios. This provokes fetal pulmonary hypoplasia, further increasing the risk of perinatal mortality and morbidity. Actual life expectancy and quality of life for fetuses with LUTO is difficult to predict due to many confounding factors. A high rate of termination of pregnancy, various degrees of severity of the obstruction and varying stages of development that the pathology arises contribute to this uncertainty. The most common causes of LUTO are posterior urethral valves (PUVs) and urethral atresia. Less common causes are represented by anterior urethral valves, megalourethra, cloacal malformations and prolapsing ureterocele. The differential diagnosis is highly dependent on fetal gender. For male fetuses, the most likely diagnosis is PUV; however, it is urethral atresia for female gender. Many of the consequential features aforementioned are visible under sonographic examination. A comprehensive anatomic survey, including fetal echocardiogram and amniotic fluid assessment, should be performed. Genetic counseling and diagnostic genetic evaluation are mandatory. The couple should be informed about the option of elective termination of pregnancy. For fetuses with favorable prognostic indicators, the advantages and disadvantages of fetal therapeutic interventions (vesicoamniotic shunting, valve ablation *via* cystoscopy, vesicostomy etc.) should be discussed with the family. The parents should meet with a pediatric nephrologist and a urologist to review the possible postnatal courses, including short- and long-term outcomes to ensure that realistic expectations are set. Although there is a lack of consensus upon the approach to fetuses with LUTO, especially in terms of *in utero* therapeutic interventions, there are some recent efforts by some clinician groups to provide a scientific set of recommendations. Still, further studies are needed to improve standardization of sonographic diagnostic parameters, validate prenatal biomarkers and improve staging systems to optimize prenatal care. These will help to provide a more accurate selection of patients who might benefit most from fetal interventions, in terms of long-term survival and renal function.

Keywords: fetal lower urinary tract obstructions, hydroureteronephrosis, renal function

Prenatal diagnosis and genetic confirmation of a fetus with Majewski syndrome

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Majewski syndrome – also called short-rib thoracic dysplasia 6 with/without polydactyly (SRTD6) or short-rib polydactyly syndrome type II (SRPS type II) – belongs to a group of autosomal recessive skeletal ciliopathies under the name of short-rib thoracic dysplasia (SRTD) with/without polydactyly. Ellis Van Creveld syndrome, Jeune asphyxiating thoracic dystrophy, Mainzer-Saldino syndrome etc. are other examples from this SRTD group. Although the main phenotypic characteristics, such as constricted thoracic cage, short ribs and shortened tubular bones, resemble, there is a wide range of phenotypic variability, especially in terms of nonskeletal visceral involvement. As the name itself implies, polydactyly is variably present and the phenotypic overlap is prominent among the patients. Some are compatible with life; however, others are lethal in the neonatal period. Majewski syndrome is a rare subtype of the aforementioned group, with an incidence of <1/1,000,000, caused by homozygous mutation in the NEK1 gene on chromosome 4q33. Hypoplastic thorax with short ribs, protuberant abdomen, micromelia with particularly short tibiae, pre-postaxial polydactyly, brachydactyly and dysmorphic craniofacial features (prominent forehead, low-set and malformed ears, short and flat nose, micrognathia, cleft lip/palate etc.) are common findings. Additional urogenital, gastrointestinal, cardiovascular and cerebral malformations have also been reported for this severe early onset condition, which is fatal in the neonatal period. Herein, a pregnant patient's fetus with genetically confirmed Majewski syndrome is presented in detail, starting from the first admission of the mother, at 18 gestational weeks, until his postpartum demise, with all sonographic and postpartum findings. The anomalies typical for SRTD group were accompanied by several nonskeletal visceral ones, which supports the diagnosis. WES analysis of fetal samples confirmed the syndrome by demonstrating c.3107 C>G (p.Ser1036Ter) homozygous mutation of NEK1 gene on chromosome 4. Consanguineous parents were later shown to be heterozygous carriers of the same mutation. Genetic counseling is provided and the avoidance of random natural conception without preimplantation genetic diagnosis is emphasized for future pregnancies. To conclude, careful and systematic sonographic examination of a malformed fetus leads to the detection and grouping of varying types of anomalies. Along with the genetic confirmation, these may enable the documentation of the pathology of index case, even for the rarest diseases. Thus, precautions can be taken to prevent recurrence, and these provide a chance of conception of a healthy fetus for the mother.

Keywords: prenatal diagnosis, genetic diagnosis, Majewski syndrome

Study of delivery type in two age groups in a five-year period (2018-2022) in the General Hospital of Chania "Agios Georgios"

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Introduction. Caesarean section has become a problem for Greece, having reached the level of 60%. On the other hand, the British newspaper *The Independent* states that Greece is one of the safest places for a woman to give birth. Our maternity ward is the second in Greece regarding the number of births, apart from large urban centers and non-university hospitals. With these thoughts, we studied the variation of vaginal delivery and caesarean section in two age groups in a five-year period (2018-2022). **Materials and method.** The type of delivery was studied in the delivery registry of our clinic (vaginal delivery [VD] and caesarean section [CS]) in women ≤18 years old (group A) and in women ≥35 years old (group B). Previous CS were excluded from this study. **Results and conclusions.** In the period 2018-2022, there were a total of 3244 births, of which 40 in Group A and 500 in Group B. In total, there were 1229 VD (40%) and 2015 CS (60%). In Group A, there were 27 VD (67%) and 13 CS (32%). In Group B, there were 283 ND (56%) and 217 CS (43%), with main indication of preeclampsia, complications of gestational diabetes, non-reassuring NST, and maternal desire. In the total of births, as mentioned in the introduction, there was a rate of 60% caesarean sections. Although the number of teenagers (Group A) is very small in our study, representing 1.2 % of the total, we notice that in relation to other studies, the rate of caesarean sections is very low. The results are recorded in group B according to the following percentages: VD 43%, CS 56%. A drastic reduction is required regarding the caesarean sections, because they represent a surgical procedure.

Keywords: delivery, caesarean section

Management of neonatal thrombocytopenia

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Introduction. Thrombocytopenia is defined as the platelets number below 150,000/mm^3. It is present in 1-5% of newborns at birth, and severe thrombocytopenia occurs in 0.1-0.5% of newborns. Approximately 8% of premature infants and 6% of newborns admitted to neonatal intensive care units have severe thrombocytopenia and are at an increased risk of hemorrhage, especially cerebral hemorrhage followed by subsequent neurological sequelae. Thrombocytopenia present in the first 72 hours of life is usually secondary to placental insufficiency and caused by reduced production of platelets. Thrombocytopenia occurring after 72 hours is usually secondary to sepsis or necrotizing enterocolitis and is frequently more severe and prolonged. Neonatal immune thrombocytopenia represents less than 5% of cases of early thrombocytopenia (early-onset, below 72hours post-delivery). Autoimmune and alloimmune thrombocytopenia have very different characteristics, including the treatment management. In fact, this treatment is based on platelet transfusion associated or not to intravenous immunoglobulin administration. **Materials and method.** We performed a prospective study in the Neonatology Department of the "Louis Țurcanu" Emergency Clinical Hospital for Children, Timișoara, for a period of 12 months, which included a group of 100 newborns with thrombocytopenia in the first 28 days of life. We divided the group into full-term and premature newborns and we analyzed the time of onset of thrombocytopenia, the average values of platelets, the establishment of the causes that determined thrombocytopenia, as well as the type of therapeutic intervention. **Results and conclusions.** Neonatal thrombocytopenia is a common clinical problem. Most episodes are mild or moderate and resolve spontaneously without apparent clinical sequelae. Higher percentages of newborns developed thrombocytopenia in the first 72 hours of life, in most of the cases associating intrauterine hypoxia. Premature newborns develop thrombocytopenia in a much higher rate than term newborns. The management consists in the platelet transfusion if the value of the platelets is less than 50,000/mm^3 or the patient is bleeding. Late-onset thrombocytopenia is often severe, with affected neonates often requiring platelet transfusions, in most of the cases being associated with sepsis or NEC, and these must be controlled, followed by a slow recovery in the platelet number over the following four to five days.

Keywords: thrombocytopenia, management, newborn, platelets transfusion

Neonatal pneumothorax – risk factors, evolution and prognosis

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Introduction. The presence of air in the pleural space between the visceral and parietal pleura leads to a pathological condition called pneumothorax. Neonatal pneumothorax is associated with significant morbidity and mortality. The authors aim to analyze the risk factors, evolution and prognosis in a lot of newborns diagnosed with pneumothorax. **Materials and method.** The study was carried out in the Neonatology Department of the "Louis Țurcanu" Emergency Clinical Hospital for Children, Timișoara, for a period of two years. The study included 35 newborns, and the inclusion criteria were: clinical signs of respiratory distress, sudden clinical deterioration, SaO_2 decrease, significant radiologic signs. **Results and conclusions.** The highest incidence of pneumothorax was observed in the 32-27 weeks group (41%) and in the >38 weeks group (41%), with a lower distribution at more than 32 weeks (18%). The gender distribution was: 42% female newborns and 58% male newborns. Pneumothorax appeared in 48.6% of cases in newborns who required invasive mechanical ventilation, 17% required noninvasive ventilation (nCPAP/Optiflow), 3% received free flow oxygen therapy, and in 31.4% of cases there was no supplemental O_2 requirement. Preexistent respiratory pathology included: idiopathic respiratory distress syndrome (RDS) in 63% of cases, congenital pneumonia (20%), transient tachypnea of the newborn (7%), and meconium aspiration syndrome in 10% of cases. In some cases, maternal-fetal infection and perinatal asphyxia were associated, thus increasing the risk of unfavorable results. In 75% of cases, the treatment consisted of chest drainage (average of three days), 25% requiring expectative management and positioning. The evolution was favorable in 85% of cases, with the complete resolution of pneumothorax, and in 15% of cases the evolution was unfavorable, followed by demise, this being influenced by the associated pathologies. In conclusion, pneumothorax is an important condition in neonatal pathology. Based on these risk factors, with adequate therapy, the mortality can be reduced.

Keywords: neonatal pneumothorax, risk factors, prognosis

Influence of perinatal factors on bronchopulmonary dysplasia incidence and outcome

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Background. The fetus can deploy an inflammatory response when exposed to microbes. The inflammatory process can be localized to an organ or become systemic when inflammatory mediators enter the circulation, often named as "fetal inflammatory response syndrome" (FIRS). Neonates born with FIRS have a higher rate of complications such as early-onset neonatal sepsis, intraventricular hemorrhage, periventricular leukomalacia and death than those born without FIRS. Survivors are at risk for long-term sequelae like bronchopulmonary dysplasia (BPD), neurodevelopmental disorders, cerebral palsy, retinopathy of prematurity and sensorineural hearing loss. The aim of our study was to analyze the correlation between perinatal conditions and the frequency of BPD and the outcome of BPD in preterm population. **Materials and method.** A retrospective observational study was performed in the Neonatology Department of the First Obstetrics Clinic, Cluj-Napoca. In the study group, there were enrolled 263 preterm newborns, admitted in our unit between 1 January 2014 and 31 December 2016, with gestational ages below 32 weeks and 6 days. **Results.** Of the study group, 73% were from single pregnancies and more than two-thirds of preterms (71.48%) were inborn patients. Thirty-five preterms developed BPD. We found a significant correlation between BPD and maternal chorioamnionitis severity ($p<0.001$). No significant correlation was found between gender and BPD, and the place of birth and BPD. Preterms with low Apgar scores and need of extended resuscitation had a higher incidence of BPD ($p<0.001$). The length of CPAP and the need of oxygen (FiO_2) significantly corelated with the incidence of BPD in the study group. A significant correlation between early-onset sepsis and BPD was found ($p<0.001$; OR=3.77; 95% CI; 1.8-7.91). **Conclusions.** Maternal chorioamnionitis correlates with BPD. Extended resuscitation increased the risk of BPD in study group. The length of CPAP and FiO_2 values correlated with BPD. Early-onset sepsis represents a risk factor for BPD.

Keywords: preterm birth, bronchopulmonary dysplasia, inflammation

Healthcare professionals' attitude towards the management of preterm delivery at the limit of viability – study protocol and preliminary results

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Introduction. Preterm birth is associated with the largest proportion of deaths in children younger than 5 years old and is a substantial contributor to adverse health outcomes in children and adults, despite considerable improvement in care. Ideally, professional guidelines indicate management strategies for active and palliative care among infants born at less than 26 weeks of gestation, involving collaboration between senior clinical staff from obstetric, midwifery and neonatal teams. Studies have highlighted different interpretations of such guidance, and wide regional variation in infant outcomes of mortality and morbidity suggests variable approaches and biases of healthcare professionals during high-risk delivery. Such variation has also tremendous implications for parental counseling in decision-making in situations in which the prognosis is uncertain. **Aim.** The aim of this study was to evaluate the attitudes of healthcare professionals involved in the counseling of parents facing extremely preterm birth, in order to understand how different factors associated with the management of extremely preterm infants are followed. **Materials and method.** Using a pretested 53-items questionnaire, anonymously distributed among midwives, obstetricians, neonatologists and ICU nurses involved in perinatal counseling of women and families at extremely low gestational ages (<25 weeks), we assessed the variation in attitudes, knowledge and beliefs regarding the management of extreme prematurity, using a qualitative, multicentric study design. **Results.** Based on preliminary pilot-study results, we found important variations in the approaches by midwives, obstetricians, neonatologists and nurses involved in perinatal counseling of women and families at extremely low gestational ages (<25 weeks). We also detected conflicting attitudes in areas such as parental involvement, initiation of treatment, and the perceived impact of disability on infants. Decision-making in these often rapidly developing scenarios, however, remains complex and emotionally challenging for healthcare professionals and parents. Previous research has explored the attitudes of neonatal healthcare professionals toward the treatment of extremely preterm infants and highlights conflicting attitudes toward areas such as parental involvement, initiation of treatment, and the perceived impact of disability for the infants. **Conclusions.** Variation in clinical care and counseling practices between the different professional groups involved in preterm delivery has been identified, highlighting the potential for ambiguity and confusion among parents having multiple conversations with multiple professionals. To our knowledge, such research has not been undertaken in Romania and we hope that after completion we will able to understand the differences in attitudes among healthcare professionals directly involved in the complex management of extremely preterm infants.

Keywords: extreme prematurity, survival, counseling

Current aspects in the management of SARS-CoV-2 infection in pregnancy

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Introduction. Because clinical studies on diagnosis, management, prevention and many other aspects of pregnancy and breastfeeding during COVID-19 have improved significantly since the beginning of the pandemic, a substantial amount of prior knowledge has changed, and previous publications may no longer be applicable. In addition, to reduce maternal, fetal and neonatal morbidity and mortality in the event of future pandemics, vaccination recommendations in pregnancy must be made early. **Materials and method.** This review of the literature seeks to offer a comprehensive update on the mutual effects of pregnancy and SARS-CoV-2 infection, debate current issues based on the most recent discoveries, and identify existing knowledge gaps. **Results.** Emerging studies indicate significant risks associated with SARS-CoV-2 infection during pregnancy, including preeclampsia, intrauterine growth restriction, preterm birth and the risk of birth malformations. Vaccination against COVID-19 is advised for women who are pregnant, trying to become pregnant, breastfeeding or who may become pregnant in the future. Vaccination during pregnancy is associated with the transmission of SARS-CoV-2 antibodies to the fetus. **Conclusions.** Additional clinical trials should investigate the long-term consequences, the results, the safety of vaccinations and the influence of the pandemic on the health of pregnant women.

Keywords: COVID-19, pregnancy management

Chorionic bump: an abnormal finding at the first-trimester ultrasound?

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Objectives. The aim of the study was to provide new information on the early diagnosis of chorionic bump pregnancies and to assess the impact of this diagnosis on pregnancy outcome. **Methodology.** The current study was conducted in two reference centers: Ginecho Clinic and the Prenatal Diagnostic Unit of the tertiary center, Emergency County Clinical Hospital of Craiova, Romania. A total of 823 first-trimester pregnancies were included, and ultrasound evaluation was performed transvaginally. Three cases of chorionic bump pregnancies were detected and their prognosis was evaluated. **Results.** A prevalence of 0.36% was found. Of the three cases, two had a favorable prognosis and the third case showed miscarriage at 13 weeks. In all cases, the genetic testing had a normal result. **Conclusions.** Chorionic bump is a phenomenon rarely seen at the time of first-trimester ultrasound, but it has a characteristic appearance and should be differentiated from an early embryonic demise. Although in our study the rate of pregnancies with a good prognosis was higher than that of pregnancies with an unfavorable outcome, we cannot draw any clear conclusions because of the small number of diagnosed cases.

Keywords: ultrasound, chorionic bump, prognosis

Transvaginal ultrasound in pregnancy after genital neoplasms

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Introduction. Genital cancers are the leading cause of death among women, mainly due to the absence of effective screening and advanced disease at the diagnosis. An important percentage of genital cancers occur in women younger than 40 years of age (cervical cancer; about 8-12% for ovarian cancer). The standard surgical treatment for genital cancers implies the removal of the internal genital organs, with the loss of the reproductive function in younger women. Fertility-sparring surgery (FSS) in young patients with genital cancers is a current issue directly related to quality of life, but not yet solved, due to the lack of large prospective randomized trials and cohort studies. The follow-up of the pregnancy after FSS is challenging, with special accents in cervical and ovarian cancers. **Cases presentation.** We present some cases of follow-up of a pregnancy after cervical and ovarian cancers, which includes aspects of both normal evolution of pregnancy and follow-up of neoplasia during pregnancy. FSS in cervical cancer is associated with a reduction of cervical length, so transvaginal ultrasound is an important tool in pregnancy follow-up. FSS in ovarian cancer is associated with the risk of disease relapse, which is even more difficult to diagnose during pregnancy. In this context, transvaginal evaluation of Douglas pouch could provide data about disease evaluation. **Conclusions.** Transvaginal ultrasound might prove very valuable in post-neoplasia pregnancy follow-up.

Keywords: cervical cancer, ovarian cancer, pregnancy follow-up, trachelectomy

Laparoscopic open versus closed-entry techniques and management of entry complications in gynecologic procedures

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Minimal access surgery now dominates invasive gynecologic pathology approach. Despite years of experience, technological improvements and revised training programs, up to 50% of incidents are related to initial laparoscopic entry into the abdomen. The main two methods used for access are the Hasson (open) technique and the closed-entry with the aid of the Veress needle, each with their benefits and risks. Access complications can be minor (urinary tract lesions, abdominal wall injury, preperitoneal insufflation) or life-threatening, such as injury to viscera (bowel, bladder) or vascular landmarks (major abdominal vessels, anterior abdominal wall vessels). The acknowledgement and timely control of complications is essential. The occurrence of entry incidents will prolong surgery and sometimes the duration of recovery, and it may require the participation of a vascular or general surgeon. Adequate training, respecting the standard protocol of each technique and safety tests, is a reliable tool to prevent and recognize the injury. The best laparoscopic entry technique is still a matter of debate in gynecologic surgery. Most injuries occur before the actual procedure, at installation of peritoneal access. There is no solid evidence proving the superiority of any method of laparoscopic entry in terms of patient safety.

Keywords: laparoscopy, gynecologic surgery

COVID-19 and acute pancreatitis in the obstetric population

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COVID-19 associated infection in pregnancy has been reported to encompass severe outcomes compared to nonpregnant individuals. Even though COVID-19 is essentially a respiratory disease, gastrointestinal symptoms are common, especially in infection with recent viral strains. Exceptionally, acute pancreatitis has been reported to occur in the context of COVID-19, either as a manifestation of direct viral injury to the pancreas, or as an adverse effect of remdesivir treatment through a yet unelucidated mechanism. Case reports of the association between of gestation, severe COVID-19 disease and unexpected acute pancreatitis have been signaled. Suspicions of the possible involvement of remdesivir therapy in the onset of pancreatitis have been raised. While COVID-19 has not yet been specifically identified to cause pancreatitis in humans, it remains a potential cause for acute pancreatitis in pregnant patients.

Keywords: COVID-19, pregnancy, acute pancreatitis

Assessment of congenital diaphragmatic hernia using magnetic resonance imaging: is it better than ultrasound?

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Introduction. In this retrospective study, we investigated the relationship between ultrasound and magnetic resonance imaging (MRI) examinations in cases with congenital diaphragmatic hernia (CDH). This malformation is a rare cause of pulmonary hypoplasia that increases patients' mortality and morbidity. Early diagnosis and the severity assessment are extremely important for adopting the correct medical treatment. We present the new means at our disposal for assessing the severity of the disease. **Methodology.** We analyzed the lung parameters in patients diagnosed with CDH who underwent magnetic resonance imaging examination after the second-trimester morphology ultrasound confirmed the presence of CDH. The inclusion criteria were: patients diagnosed with CDH who underwent MRI examination after the second-trimester morphology ultrasound confirmed the presence of CDH. The patients came from three university hospitals in Bucharest, Romania. We also realized 3D renderings of the diaphragm and lungs to better asses the aberrant morphology. We obtained the informed consent form all the patients and, also, the study was approved by the ethics committee. **Results.** The analysis of the total lung volume (TLV) using MRI and the lung-to-head ratio (LHR) calculated using MRI and ultrasound revealed that LHR can severely underestimate the severity of pulmonary hypoplasia, even showing values close to normal in some cases. This was also proven to be statistically relevant after eliminating certain extreme values. We found significant correlations between the LHR percentage and some herniated organs. MRI also provided additional insights, indicating the presence of pericarditis or pleurisy, and it also allowed the 3D reconstruction of the diaphragmatic defect, aiding the preoperatory planning for the surgery. **Discussion.** The necessity of MRI follow-up in cases of CDH is extremely important, as the accurate measurement of the TLV influences the treatment and the therapeutic strategy, also allowing a much better surgical planning by using multiplanar reconstructions and even 3D modelling.

Keywords: ultrasound, magnetic resonance imaging, congenital diaphragmatic hernia

Vaginal birth versus caesarean section

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The number of women choosing to undergo caesarean section as they primary mode of delivery is increasing in more economically developed countries. It is commonly accepted that the high number of caesarean sections increases the risk of mortality with each delivery. Vaginal birth after caesarean section is an opportunity to reduce the number of caesareans and, therefore, to reduce the risk of mortality. There are, however, many factors that may influence a woman's personal preference for caesarean section: absence of medical indications, patient's education or medical staff recommendation. The relative benefits and risks of birth modes have the potential to influence the preferences toward vaginal birth.

Keywords: vaginal birth, caesarean section

Maternofetal morbidity in pregnancies after *in vitro* fertilization

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Introduction/aim. The health of children born after assisted reproduction is of major interest, since already up to 6% of children born in European countries are the result of assisted reproductive techniques (ARTs). Frozen embryo transfers (FETs) are on a steep rise and comprise 32.6% of all ART treatment cycles in Europe. Although most *in vitro* fertilization (IVF) pregnancies are uncomplicated, there is an association with increased risks of maternal, fetal and perinatal outcomes. **Methodology.** The retrospective, descriptive study included 300 cases of *in vitro* fertilization pregnancies hospitalized in our department between 2016 and 2022. We recommend genetic counseling to all patients who have undergone IVF with or without intracytoplasmic sperm injection (ICSI). **Results and discussion.** The accuracy of first-trimester genetic screening tests for aneuploidies may be affected by IVF, with a potential increased risk of false positive results for aneuploidies in patients who undergo first-trimester combined screening. We did not find associations between IVF (with and without ICSI) and congenital malformations. Several placental implantation disorders are more common with IVF (higher risk for abnormal placental structure: bilobed placenta, accessory placental lobes, *placenta praevia*, *vasa praevia*). We found a higher risk for preterm birth, low birth weight, very low birth weight and preeclampsia. Risks are more than doubled in IVF twin gestations. The assessment of fetal growth should be performed in the third trimester, with weekly antenatal fetal surveillance beginning by 36 weeks. **Conclusions.** IVF is associated with an increased risk of adverse maternal and perinatal outcomes. However, evidence is limited regarding whether specific screening, diagnostic or preventative interventions during pregnancy obviate or reduce such risks. Specific technical characteristics of IVF and the presence of underlying infertility affect the risks of adverse clinical outcomes. Therefore, individualization of care may be ideal for optimizing outcomes.

Keywords: *in vitro* fertilization, infertility, pregnant women

Peripartum hysterectomy following caesarean section: experience from a Romanian tertiary center

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Introduction/aim. Postpartum hemorrhage (PPH) represents one the main causes of maternal death all over the world, among infections, preeclampsia, eclampsia, unsafe abortion and complications of delivery. In cases with severe hemorrhage (≥1500 ml), the blood product transfusion will significantly contribute to maternal morbidity. Thus, only by understanding the complex changes in the coagulation cascade we will be able to intervene optimally, without having harmful side effects. **Materials and method.** The increasing number of caesarean sections (C-section) determined a high incidence of the placenta accreta spectrum disorders, contributing significantly to PPH cases. A retrospective, descriptive study was carried out between 2018 and 2022, which included patients who underwent hysterectomy for severe postpartum hemorrhage after C-section (e.g., accreta, atony, uterine rupture, leiomyomas). Maternal characteristics that include parity, gestational age, number of fetuses, presence of *placenta praevia* and previous C-section were documented. The preoperative coagulation tests were performed in all cases, and a multimodal management regimen was used for the majority of severe PPH cases, before resorting to a hysterectomy, including the administration of tranexamic acid and recombinant activated factor VII. Also, the transfusions of blood products (e.g., packed red blood cells, fresh frozen plasma, thrombocyte concentrate), characteristics of the hysterectomy and intraoperative complications, has been recorded too. **Results and conclusions.** This retrospective, hospital-based study made a considerable share to available knowledge about peripartum hysterectomies. One of the worst scenarios in postpartum hemorrhage represents the coagulopathy. The iatrogenic factors such as hypothermia, massive transfusion, quantity and type of replacement solutions can increase the intraoperative morbidity. The major indication for PPH was abnormal placentation (*placenta accreta*), reason why it should be utilized thromboelastography (TEG) and rotational thromboelastometry (ROTEM) as methods to individualize the treatment for coagulopathy, and to initiate it immediately.

Keywords: coagulopathy, postpartum hemorrhage, thromboelastography

Stillbirth: an eight-year experience and literature comparison

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Introduction/aim. Stillbirth represents a devastating experience for both family and care providers. The proportion of unexplained fetal deaths can be reduced following a rigorous and systematic evaluation and identifying a cause of death helps emotional healing and closure for parents, reducing the recurrence risk for future pregnancies. The objective of this study is to establish the fetal death causes, comparing with other data from the literature, and to propose a protocol for earlier assessment. **Methodology.** The retrospective, descriptive study included 300 cases of stillbirths hospitalized between 2015 and 2022 in the Department of Obstetrics of the "Cuza Vodă" Clinical Hospital of Obstetrics and Gynecology, Iaşi, a Romanian tertiary care maternity. The main inclusion criteria were all stillbirths ≥24 gestational age or ≥500 g weight birth. According to these criteria, the selected cases were subgrouped into four categories: extremely preterm birth (less than 28 weeks), very preterm (28-32 weeks), moderate to late preterm birth (32-36 weeks), and post-term pregnancies. A clinical, laboratory, ultrasonography and histopathological assessment was performed in all cases. **Results and discussion.** Possible causes of fetal death in more than 60% of stillbirth cases were identified, thus obtaining similar results to the scientific international literature. The most common causes of stillbirth were: infectious, hypertensive disorders, preexisting diabetes and gestational diabetes, umbilical cord abnormalities (excluding nuchal loop), and placental insufficiency, fetal structural and genetic abnormalities. Moreover, a checklist was designed in order to evaluate parental and current pregnancy history together with blood test parameters, trying to investigate other possible factors that can contribute to stillbirth. **Conclusions.** A systematic assessment including infectious medical history, placental examination, perinatal autopsy, and chromosomal microarrays represent important tools for determining the cause of stillbirth, and further investigations should be recommended when clinical findings are suggestive for a specific death cause.

Keywords: stillbirth, fetal demise, pregnant women, cause of death

Termination of pregnancy using vaginal misoprostol-only regimen: analysis of number of doses needed for successful termination

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The main objective of this study is to determine the course number of misoprostol to successfully terminate a pregnancy according to gestational age. We retrospectively analyzed the hospital records and the Perinatology Unit registry. The study cohort was divided into three groups, according to the trimesters of the pregnancy. The course number of vaginal misoprostol, hemoglobin levels and indications of pregnancy terminations were compared. We observed that more than half of the medical terminations of pregnancies were due to fetal central nervous system anomalies (51.2%). The course number needed for successful termination of pregnancy was significantly higher in the second trimester of pregnancy, compared to the first-trimester group (p=0.0002). There was no significant difference between first and third trimesters (p=0.652). The increased number of courses of misoprostol was directly associated with drop in hemoglobin levels, regardless of gestational week or parity. Vaginal misoprostol alone is still a safe and effective method for the termination of pregnancy. The number of courses needed for expulsion of the fetus is higher during the second trimester of the pregnancy and as course number increased, the reduction in hemoglobin levels was more pronounced.

Keywords: termination, pregnancy, vaginal, misoprostol

Neuroprotective strategies in neonates with perinatal asphyxia

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For neonates, asphyxia is one of the most dangerous events that could affect vital prognosis or have serious consequences on the long-term development and quality of life. Postasphyxic syndrome may involve all organs and their function, mostly heart and brain, therefore neuroprotection should be a priority goal in limiting the damages for the most important organ of a human being. Several strategies have been proposed for this, from phenobarbital administration, with or without erythropoietin, to the nowadays the gold standard in preventing hypoxic ischemic encephalopathy, the controlled hypothermia, in well-defined limits and for some well-proven categories of severity. Data demonstrated good results for moderate and severe asphyxia, in term and near-term neonates, if controlled hypothermia is applied in the first six hours after neuronal injury, to prevent apoptotic events from reperfusion in the brain. The main benefits from hypothermia are the survival of cells otherwise destined to die through apoptosis, reduced metabolic rate, reduced release of excitatory amino acids (glutamate, dopamine) and lower production of nitric oxide and free radicals. The main beneficial effects consist in significantly reducing death or major sensorineural disability at 2 years of age. However, 46% of cooled infants still die or survive with major disability, mainly in low-income countries. Further strategies are needed: regional guidelines to facilitate earlier induction of cooling, refinement of current hypothermia methods, synergistic neuroprotective therapies. Monitoring for main adverse effects is necessary – thrombocytopenia and hypotension. All treated infants should be followed-up longitudinally. Although there are some attempts to study the potential beneficial effect for premature babies, more studies have to be done for getting a strong recommendation. However, simple strategies like avoiding head healing immediate after birth for asphyxiated infants, together with empiric cooling practices during the transport brought challenges for practitioners, mostly from centers where head-controlled cooling is not immediately available.

Keywords: neuroprotection, controlled hypothermia, neonate

Management in the context of congenital ichthyosis in a newborn with nonbullous ichthyosiform erythroderma in severe form – clinical case

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Introduction. Nonbullous congenital ichthyosiform erythroderma (NBCIE) is a genetic disorder of skin keratinization, with autosomal-recessive transmission, with an incidence of approximately 1 in 300,000 births. Infants with NBCIE can develop infections, dehydration and respiratory problems. **Clinical case presentation.** We present the case of a female newborn, gestations 3, para 3, 40 weeks gestational age, weighing 2900 g, with Apgar score 8/8, born in CP level I. She had a very serious general condition at birth, conditioned by the presence of multiple esthetic changes at the level of the eyes, the ears pavilions, the mouth, the integuments on a pale background, with edema, in the region of the neck and abdomen – massive areas of widespread desquamation with a detachment of the dermis. **Results.** At 16 hours of life, the newborn was transferred to level 3 in the intensive care unit. Clinical diagnosis: congenital ichthyosis. She was placed in an incubator regime with thermal and hygienic comfort, in sterile conditions, with increased humidity (80%). Initiated treatment: analgesic, antibacterial, processing scaly skin areas with emollient preparations, temperature monitoring, correction of fluids and electrolytes. She was consulted by a dermatologist who established the diagnosis of nonbullous congenital ichthyosiform erythroderma. Later, the patient had a good evolution. On the fifth day of life, areas of scarring appeared in the desquamated places, and on the 14th day the child was transferred to the salon with the mother. On the 19th day of life, being in a satisfactory condition, she was discharged home. **Conclusions.** The management of newborns with ichthyosis requires a multidisciplinary approach. They require admission to the intensive care unit, faced with complications related to the impaired barrier function. The main directions of management include ensuring a sterile environment, thermal comfort and increased humidity.

Keywords: newborn, nonbullous congenital ichthyosis

Ninety-six days of learning in intensive therapy – equivalent to positive emotions. Clinical case

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Introduction. Bronchopulmonary dysplasia (PBD) is an important cause of morbidity and mortality in preterm infants. **Materials and method.** Presentation of the clinical case of a premature baby with severe BPD, at the ICU for 96 days. The newborn weighed 690 g, with gestational age 24 +^{6}, with AOC (gestation 2, para 2, IVF, trichorionic-triamniotic triplet). Respiratory distress syndrome (RDS) prophylaxis with complete cure, Apgar score 3/5. Curosurf® 200 mg/kg was administered immediately after birth. At 18 days, a radiography revealed signs of PBD with pulmonary fibrosis. The diagnosis of bronchopulmonary dysplasia in severe form was established as a complication of neonatal sepsis. **Results.** He was in the intensive care unit for 96 days, being O_2 dependent and requiring ventilatory support, mechanical ventilation and CPAP. He followed four courses with dexamethasone on the 14th day, without effect; later, on the 31st, 53rd and 85th days, which allowed him to become ulteriorly independent of O_2. In parallel, he was administered prednisolone and inhalations with Pulmicort®, with a positive impact. He presented hyperglycemia that required insulin correction. During the stay in the preterm ward and up to the age of 1 year old, the weight curve was below the 5th percentile, showing gastroesophageal reflux, but at 1.5 years old, the weight curve was at the 50th percentile. **Conclusions.** Premature babies, especially those with extreme immaturity, are at a major risk of developing severe forms of PBD. The approach is highly variable, with the most pressing needs including medication use, respiratory support, optimal nutrition, and the impact of care on neurodevelopment.

Keywords: newborn, bronchopulmonary dysplasia, 96 days of ITU

Diabetes mellitus during pregnancy – risks and consequences

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Introduction. Diabetes mellitus (DM) is one of the most widespread diseases of the endocrine system in the world. The global incidence of DM is increasing every year. Data presented by IDF Atlas 2016 show that 1 in 7 births is affected by gestational diabetes. In the Republic of Moldova, the registration of DM cases is not unified, this is why we decided to study which group is at risk for the development of gestational diabetes, along with some features of management and its impact on the birth of children with a large mass. **Methodology.** The prospective case-control study was performed within the Scientific Laboratory of Obstetrics of IMSP, Mother and Child Institute (IMC), in the period 2021-2022. The research included 253 births in IMC: 48 births in patients with a diagnosis of DM and 205 births without diagnosed non-transmissible diseases. Twin pregnancy cases were excluded from the study. **Results.** In the group of patients with DM, there was a higher proportion of patients aged above 35 years old – 33.3% (n=15) versus 13.1% (n=41). Such age increases the risk of DM (OR=3.3; 95% CI; 1.58-7.00; p<0.001). Of the patients with DM, 62.5% came from rural areas. The urban environment can be a protective factor against DM (OR=0.52; 95% CI; 0.27-0.988). Among patients with DM, children weighing more than 4000 g were in 48.39% versus 15.63% (p<0.05). The probability of a pregnant woman to give birth to a macrosomic fetus, being diagnosed with DM, is six times higher compared to pregnant women without DM (OR=6.17; 95% CI; 2.89-13.2). **Conclusions.** It is necessary to prevent the DM in the rural population. Multigestational and multiparous women require counseling regarding the possible development of diabetes mellitus. The need of the insulin therapy is underestimated in patients with diabetes mellitus.

Keywords: diabetes mellitus, pregnancy

Peripartum cardiomyopathy: a provocative medical challenge

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Introduction. Peripartum cardiomyopathy (PPCM) is a relatively rare cardiac disease that manifests in the final stage of pregnancy and in the first months after delivery in women with no preexisting heart disease. Many etiological processes have been suggested: viral myocarditis, abnormal immune response to pregnancy, excessive prolactin excretion, prolonged tocolysis and a familiar predisposition to PPCM. Its diagnosis is often delayed because its symptoms, which include fatigue, dyspnea and palpitations, are nonspecific. For this reason, the diagnosis of PPCM is still made by exclusion of other etiologies. **Methodology.** We conducted a multidisciplinary assessment of the case of a 28-year-old patient who presented with suggestive cardiovascular symptoms shortly after caesarean section delivery. Under the guidance of our cardiology department, the patient was diagnosed and treated promptly. Given the complexity of the case, we reviewed multiple literature data and we hereby present a summary of our findings. **Results.** The overall prognosis of PCM is good in the majority of the cases, although some patients may progress to irreversible heart failure. Progression of the condition requiring heart transplantation is described in 4% of cases, and death appears in 9% of cases at a two-year follow-up. Complete recovery of systolic function occurs usually in the first six months after delivery, although the recovery phase need not be limited to the first 12 months. Continuing improvement was observed in the second and third year after diagnosis. Persistence of the disease after six months portends worse survival. **Conclusions.** PCM is a relatively rare disease which can have devasting consequences and should be promptly identified and correctly treated. Early diagnosis is important and, therefore, women who develop symptoms of heart failure during pregnancy or shortly after that should be investigated for this condition. The effective treatment reduces the mortality rates and increases the chance of complete recovery of the ventricular systolic function.

Keywords: peripartum cardiomyopathy, immune response, systolic function, heart failure

Prevalence of heart malformations in a referral center for maternal-fetal medicine

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Background. Prenatal diagnosis of congenital heart disease is associated with improved survival and reduced morbidity for some forms of severe congenital heart malformations. Following a prenatal diagnosis of a cardiac malformation, a team formed by multiple specialists is needed to provide appropriate counseling and parental support. **Materials and method.** We have looked at all the cases seen in our unit over the period of one year, patients who were seen in the first trimester between 11+0-13+6 weeks of gestation, in the second trimester between 18+6-23+6 weeks of gestation, and in the third trimester between 32+0-34+6 weeks of gestation. This was a retrospective observational study looking at 2559 women with singleton pregnancies who had their scans in our fetal-medicine unit. The examinations were performed by two fetal medicine specialists and the patients were referred to a pediatric cardiologist with interest in fetal cardiology if an anomaly was suspected. Our aim was to assess the pick-up rate for heart abnormalities, the false positive rate for referrals, and the overall incidence of heart malformations in our population. **Results.** We have performed 923 first-trimester scans, 1872 second-trimester scans and 817 third-trimester scans. Fourteen women (1.5%) were referred for a suspected heart malformation before 14 weeks, 40 (2.2%) in the second trimester and 15 (1.8%) in the third trimester. The overall prevalence of heart malformations in our population was 29/2559 (1.1%). **Conclusions**. In a low-risk population with well-trained fetal medicine specialists, the pick-up rate for heart malformations can be very high. The most common reason for referral was a ventricular septal defect (VSD). Two patients had a postnatal diagnosis of a congenital heart defect, one with an apical VSD, and the second one with pulmonary stenosis.

Keywords: heart malformations, echocardiography, fetal heart

Varicella-zoster virus infection in pregnancy – fetomaternal and neonatal implications

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Introduction. Considered a highly contagious primary infection, chickenpox, also known as varicella, is one of the biological teratogenic factors in pregnant women. The consequences for the product of conception are correlated with the moment of contact of the infection by the embryo fetus. Thus, the neonatal clinical picture is heterogeneous, consisting of severe congenital abnormalities especially in the nervous system and post-infection sequelae, when the disease is contacted during the first 20 weeks of gestation. Perinatal varicella is based on an epidemiological and clinical diagnosis, the mother presenting with a characteristic rash with vesicular skin lesions before birth, and the newborn's involvement varying according to the time of maternal infection. **Materials and method.** We present our experience with a total of nine cases of perinatal varicella in pregnant women diagnosed over a six-week period (1.01.2023-10.02.2023). As a prophylactic measure, in order to decrease the risk of maternal-fetal transmission of the disease, in all cases it was possible to postpone delivery until the fifth day after the onset of the rash. **Results.** For confirmation or refutation, maternal and neonatal IgM and IgG varicella-zoster virus antibodies were determined. Complete blood count, inflammation markers and cerebral ultrasonography were performed. Newborns were isolated from their mothers and from other newborns. **Conclusions.** Perinatal varicella presents as a condition that can vary depending on the time of maternal involvement; thus, if the infection occurs between six and 21 days before birth, the newborn's involvement will be mild. If birth occurs within the first five days of disease onset or the rash appears within the first two days postpartum, 25-50% of newborns may be affected by a severe form of the disease.

Keywords: perinatal varicella, infection, newborn

Overlapping clinical pattern in a newborn with double fetal infection and typical Noonan syndrome phenotype

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Introduction. A phenocopy is a phenotype that falsely mimics the true phenotype of a genetic disorder. In the case of Noonan syndrome, the phenocopy will express a phenotype that closely resembles this particular syndrome. Phenocopies usually have a different cause and pathogenesis than the disease they mimic. Noonan syndrome, an unusual autosomal dominant disorder, is characterized by facial dysmorphia, pulmonary stenosis, mental retardation, bleeding and cardiac hypertrophy. **Materials and method.** We present the case of a term male neonate diagnosed with fetal pericarditis at 22 weeks of gestational age, using intrauterine ultrasound. Subsequently, the presence of maternal parvovirus infection was revealed. At 32 weeks of gestational age, the pregnant woman became infected with SARS-CoV-2, presenting a mild form of the disease. At birth, a particular phenotype indicating Noonan Syndrome was observed (hypertelorism, Cupid's bow, low inserted ears, microretrognathia, short and wide neck, low posterior hair insertion, systolic murmur grade IV/6). Echocardiography was performed which revealed narrow pulmonary artery stenosis. Genetic testing was performed at birth, using NGS sequencing and deletion/duplication analysis for the 18 genes in the RASopathy Panel. **Results.** No genetic variation (mutation) was identified that is currently recognized as clinically significant for Noonan syndrome. COVID-19 and parvovirus IgGs were present, IgM was negative. **Conclusions.** Although some possible congenital abnormalities caused by parvovirus B19 infection (nervous system, craniofacial, gastrointestinal or musculoskeletal) considered coincidental have been mentioned in the literature, we cannot claim that maternal infection with parvovirus 19 and SARS-CoV-2 were responsible for the infant's clinical picture and pulmonary stenosis. We cannot incline that the cardiac anomaly is an isolated malformation, because the presence of facial dysmorphia is suggestive of a syndrome.

Keywords: newborn, Noonan syndrome, phenotype, pulmonary artery stenosis, COVID-19, parvovirus

The intrapartum ultrasound diagnosis of band-like structures: amniotic band syndrome or uterine malformation?

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Introduction. Ultrasonographic diagnosis of amniotic bands may be difficult due to the similar appearance between uterine malformations and amniotic band syndrome. Band-like structures within the gestational sac are frequently noted on obstetric sonograms during the first and second trimesters of pregnancy. Clinicians should have a high index of suspicion of uterine anomaly to make an early diagnosis of bicornuate uterus and for preventing complications, but when the pregnancy history is unknown, it is difficult to establish a diagnosis in the third trimester. **Materials and method.** A 22-year-old second gravida, with a previous history of caesarean section, with undispensed pregnancy, presented at the "Elena Doamna" Clinical Hospital of Obstetrics and Gynecology, Iași, for routine examination. No uterine abnormality was reported by abdominal ultrasound in the first pregnancy. The ultrasound (US) showed breech presentation of the fetus, with no gross fetal anomalies. The bidimensional US revealed a band of tissue crossing the amniotic cavity, but not sectioning any part of the fetal body. Color Doppler revealed no blood flow through this structure. Due to insufficient data regarding the pregnancy, it was not known any uterine malformation. The patient gave birth, by caesarean section for fetal distress indication, to a female newborn, weighing 3470 g, with an Apgar score at 1 minute and 5 minutes of 4 and 8, respectively, with no structural anomaly observed at the postpartum examination. After the fetal delivery, the uterine cavity was examined and the patient was diagnosed with a bicornuate uterus with a single common cervix. **Discussion and conclusions.** The importance of evaluating the pregnancy in this pathology is essential due to the complications that can appear in the fetus intrapartum development. True amniotic bands are relatively rare. When are detected, the prognosis of amniotic bands is usually very poor. The visualization of a band-like structure should not be confused with amniotic band syndrome, especially when a thorough fetal anatomy survey reveals no structural anomalies.

Keywords: malformation, bicornuate uterus, amniotic bands, fetal anomalies

Congenital diaphragm hernia – the importance of prenatal diagnosis and management

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Introduction. Congenital diaphragmatic hernia (CDH) is based on a defect in the development and formation of the diaphragm, which results in incomplete diaphragmatic muscularization and the protrusion of the abdominal contents into the thoracic cavity. Advances in neonatal management have improved neonatal survival from 50% to nearly 80% over the past three decades. **Materials and method.** By reviewing the latest specialized studies, our aim was to highlight both the progress and results of intrauterine management by fetoscopic endoluminal tracheal occlusion (FETO), as well as the side effects and the alternative genetic therapies. We also present four cases of congenital diaphragmatic hernia managed by FETO in our hospital and their early prognosis. **Results.** For a better prognosis, definite prenatal diagnosis and the exclusion of associated anomalies are essential. The survival rate for severe cases remains low, namely 40%. Thus, studies are directed towards the impact of prematurity on FETO survivors, the impact of early tracheal occlusion, models for early prenatal prediction, techniques to reduce procedural complications and alternative fetal therapies. A prenatal therapy that supplements microRNA deficiency could be a strategy to improve lung development in fetuses diagnosed with CDH. **Conclusions.** A defining attribute of CDH prognosis is the multidisciplinary management integrated into three distinct phases: prenatal, perinatal/postnatal, and childhood/adolescence.

Keywords: congenital diaphragmatic hernia, FETO, prognosis

Intrapartum ultrasound – clinical decision support in modern obstetrics

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Introduction. Clinical palpation and digital pelvic examination for fetal head position and station are subjective and less accurate compared with ultrasound scan. Transabdominal and transperineal ultrasound examinations are increasingly used as adjuncts to clinical assessment during labor. These methods can be used to follow labor progress and to predict a successful vaginal delivery. Ideally, accurate station-based labor progression curves for the second stage of labor can help to determine adequate labor progression and individualized management, based on algorithms and clinical decision support systems. **Materials and method.** We conducted a prospective, longitudinal, observational, monocentric study in the Obstetrics and Gynecology Clinic of the "Sfântul Pantelimon" Emergency Clinical Hospital, Bucharest, during a six-month interval. The main ultrasonographic parameters that we examined were represented by subpubic arch angle, head position, head direction, angle of progression, head-perineum distance, head-symphysis distance, head station, occiput-spine angle, and cervical dilatation. We evaluated the concordance between clinical and ultrasound evaluation and the accuracy of ultrasound examination during labor. **Results.** A total of 162 pregnant women who delivered in our clinic were included in the study. The concordance between the clinical land ultrasound parameters varied between 42% (for head position) and 67% (for cervical dilatation). The highest accuracy in ultrasound examination for determining head station was obtained when various parameters were combined (direct measurement of head station, angle of progression, head-perineum distance), the angle of progression being the most reliable, especially when assessed before uterine contraction and during the uterine contraction apex or maximal pushing effort. **Conclusions.** Sonographic assessment during labor using transabdominal and transperineal planes is feasible and accurate and can be used as a clinical decision support. A more accurate diagnosis improves labor outcome, but this depends on the correct selection of ultrasound parameters and on the existence of a management protocol according to ultrasound findings.

Keywords: intrapartum ultrasound, labor, clinical decision support

Challenges of genetic screening in obese patients

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Obese pregnant patients (BMI>30) raise particular problems to the obstetrician. The existence of uncontrolled diabetes before pregnancy increases the risk of developing congenital anomalies. Ultrasound examination in the first trimester by transabdominal route is possible and the pregnancy can be confirmed, but the use of the transvaginal probe is an opportunity for morphological ultrasound of the first trimester being extremely important, often the examination allowing the confirmation of anatomical details that are difficult to visualize later at the second-trimester morphological ultrasound. Serum screening tests has a low performance in this category of patients. Conducting invasive tests (biopsy of chorionic villi, amniocentesis) raises additional technical problems. In addition, noninvasive NIPT tests are performing worse in this category of patients, with the amount of free DNA being low. In conclusion, despite the technical progress made, obese patients still pose a challenge for the gynecologist.

Keywords: genetic screen, obesity

Intrauterine growth restriction – an algorithm proposal for fetal evaluation

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Intrauterine growth restriction or fetal growth restriction represents a fetal incapacity of achieving its entire growth potential in intrauterine life, as a result of maternal, fetal and/or placental causes, from hypertension, autoimmune diseases, drug consumption, hereditary thrombophilia to genetic syndromes, intrauterine infections, umbilical cord anomalies or placental insufficiency. The ultrasonographic evaluation of the fetus with intrauterine growth restriction identifies an estimated fetal weight or a fetal abdominal circumference below the 10th percentile for gestational age; a severe fetal growth restriction is defined as an estimated fetal weight below the 3rd percentile. The Delphi consensus managed to classify fetal growth restriction as early, being diagnosed under 32 weeks of gestation, respectively late, after 32 weeks of gestation. Up to 10% of pregnancies are complicated by fetal growth restriction, which are then considered high-risk pregnancies for the morbidity and mortality risk carried for the fetus, requiring an accurate diagnosis of the cause, intensifying the fetal monitoring and timing the birth, in order to deliver the fetus in safe conditions. This paper proposes an algorithm for an initial evaluation of fetal growth restriction, with the aim of simplifying the medical approach when encountering a fetus with intrauterine growth restriction, in order to improve morbidity and mortality rates among pregnancies complicated by fetal growth restriction.

Keywords: fetal growth restriction, algorithm, ultrasound, intrauterine infections, placental insufficiency

The prediction of the effects of uterine leiomyoma on pregnancy outcome

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Introduction/aim. The relationship between uterine fibroids and pregnancy is nor fully understood, but the prediction of the fibroids effect on pregnancy outcome may be possible by identifying maternal, fetal and leiomyoma features. **Materials and method.** A retrospective, descriptive study was conducted in a maternal fetal center in Iași, Romania, between 2018 and 2023, which included 147 pregnant women with leiomyomas. Clinical characteristics and ultrasound examinations were conducted to evaluate the features of the leiomyoma, along with fetal and maternal prenatal outcomes to facilitate decision-making and prenatal counseling. In all patients, it was described the type, the number, the size and location of the leiomyoma, trying to establish their influence on obstetric outcomes. Relationships between leiomyoma features and placental localization, risk of *placenta praevia* or placental abruption, fetal malposition and IUGR were made. Maternal characteristics, which included parity, gestational, age, number of fetuses, localization of placenta and previous caesarean sections, were documented. **Results and conclusions.** In the selected cohort, 62 cases with fetal malpresentation were recorded, representing 42.1%. In fifteen cases (10.2%), it was found a lower placental insertion located anteriorly or posteriorly. The number, size and type of leiomyoma vary widely. In 29 of the patients (19.7%), the localization of the fibroids was in the uterine lower segment, but a relationship of their effects and fetal and maternal features was not established. To evaluate the growth pattern of uterine fibroids and their effect on obstetrics outcomes, it is necessary to evaluate patients diagnosed with fibroids prior to pregnancy and enroll them prospectively during the gestation and puerperium period.

Keywords: uterine leiomyoma, pregnancy outcome, fibroids, pregnancy

Assessment of transvaginal ultrasound during pregnancy

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Transvaginal ultrasound remains the gold standard for pelvic examination. Although it is slightly invasive, it can identify such conditions that will affect the normal evolution of pregnancy and provide key information for proper diagnosis. For the purpose of this lecture, I used data from my personal cases selected during everyday work. Thus, early in the first trimester, when ultrasound confirms the location of pregnancy and viability, it searches also for trophoblastic insertion to exclude accreta spectrum disorder and identify predictive signs in pregnancies ending in a spontaneous miscarriage. In the second trimester, a correct measurement of cervical length is very important to predict spontaneous preterm birth and also to identify *vasa praevia* and low-lying placenta. For fetuses in cephalic position, transvaginal approach can examine the fetal brain. Latest ISUOG Practice Guidelines recommend intrapartum ultrasound instead of clinical examination, to aid the management of labor, regarding fetal head position and station, and also the progression of labor towards vaginal or surgical delivery. As a conclusion, transvaginal ultrasound in pregnancy needs to be integrated in local pregnancy guidelines, providing more accurate and reproducible information.

Keywords: assessment, transvaginal ultrasound, pregnancy

Septic incomplete abortion associated with SARS-COV-2 infection – a case report

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The clinical characteristics of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV-2) are still not fully understood, especially related to the interaction with different infections and also comorbidities. We present the case of a 39-year-old pregnant women, in a serious condition, uncooperative, which presented at the Emergency Department of the "Sf. Apostol Andrei" Emergency Clinical County Hospital of Constanţa, Romania. At presentation, the patient had a 80% SaO_2, 110 bpm ventricular rhythm, fever, headache, cough with mucous expectoration, chills pale, sweats, pale skin and mucous membranes, leukocytosis, severe anemia and vaginal blood loss. The examination with valves highlighted the exteriorization of blood with a modified, brick color. The patient was tested with a rapid test for SARS-CoV-2 virus which came out positive, being admitted to the intensive care unit, the admission diagnosis being incomplete septic abortion, severe anemia, and SARS-CoV-2 infection. After approximately 48 hours, when the patient's condition allowed, after an interdisciplinary discussion (i.e., internal medicine physician, intensive care physician and gynecologist), it was decided to remove the septic outbreak by performing an interanexial hysterectomy. The evolution of the patient from a gynecological point of view was favorable; two weeks later the surgical wound was healed. In conclusion, these cases must be managed in multidisciplinary teams, of major importance being the moment of decision on the removal of the septic outbreak.

Keywords: abortion, sepsis, SARS-CoV-2 infection, hysterectomy

Case presentation: gigantic polyfibromatous uterus and pregnancy

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Introduction. Pregnancy and fibroma can occur simultaneously, although depending on the localization of the fibroma, it can pe associated with female infertility. We present a case successfully resolved last year in our clinic: a 44-year-old patient who obtained spontaneously a pregnancy after 10 years of fertility treatments and managed to follow to term the pregnancy simultaneously with a gigantic polyfibromatous uterus. **Case presentation.** The patient D.M. was given small chances to conceive naturally, in her thirties, because of her polyfibromatous uterus (more than 10 uterine fibromas that continued to grow as years followed). She tried *in vitro* fertilization, without success, and in 2021 she managed to conceive naturally. Her doctor was naturally reserved and managed her pregnancy monthly, the patient being diagnosed at 28 weeks of gestation with gestational diabetes. At that moment, we could measure with difficulty the fetus, because there were at least six fibromas of 8 cm each, most of them intramurally. She was programed at 37 weeks of gestation for caesarean section following transverse presentation. A baby boy, weighing 2640 g, with Apgar scores of 5 (at 1 minute) and 7 (at 5 minutes), was born, due to the difficult extraction. **Discussion.** The obstetrics and gynecology team, after the consent of the mother, decided to do simultaneously total interanexial hysterectomy for this patient, because the uterus was globally enlarged up to her diaphragm, even after delivery. We also performed bilateral hypogastric artery ligation. Preoperatively, blood tests were taken, and isogroup and isoRh were prepared. The patient received intravenous ferrum postoperatively and left the hospital after a week of triple antibiotic association and anticoagulant prophylactic therapy, with a hemoglobin level of 9.7 g/dl and a hematocrit level of 27%. **Conclusions.** We successfully present the unique case of a primiparous 44-year-old patient who managed to conceive and to give birth at term to a healthy baby, but also the disciplinary approach to the polyfibromatous uterus, as it further endangered the patient's life.

Keywords: polyfibromatous uterus, pregnancy, fibroma

Malignant arterial hypertension and severe renal artery stenosis and pregnancy

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Introduction. Preexistent maternal hypertension requires usually treatment from the beginning of pregnancy. If the causes remain unknown, they can lead to a poor outcome of the fetus and can have a strong psychological impact on the mother. **Case presentation.** A 27-year-old patient, known for 10 years with severe arterial hypertension, presented for an investigation with angio-MRI following a second-term intrauterine fetal death at 18 weeks of pregnancy. The angio-MRI objectivated a 90% occlusion on the right renal artery. A double-stent was placed, leading to a significative reducing of the occlusion to only 10%. Normal values of the blood pressure were achieved and no medication was further acquired for this pathology. Currently, a second pregnancy was achieved, now the patient being followed-up, at 37 weeks of gestation, with no complications until now, and she will be giving birth the following weeks. **Discussion.** The management of severe arterial hypertension was difficult to achieve for this patient, in her first pregnancy. She was treated with alpha-methyldopa 250 mg per day and nifedipine, without success, unfortunately. The importance and success of this case were given by the resilience of doctors who discovered the stenosis after her fourth MRI. **Conclusions.** Although rare, we can say that there are cases with congenital renal artery stenosis that can be treated in young women, helping them conceive spontaneously healthy babies. The multidisciplinary follow-up was important in this case, as the patient was first refused for angio-MRI because of allergic reaction to intravenous substance.

Keywords: malignant arterial hypertension, pregnancy, renal artery stenosis

Uterine packing with chitosan covered gauze – a new approach to postpartum hemorrhage refractory to usual management

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Introduction/objective. Globally, approximately 529,000 cases of maternal mortality occur annually, or 400 cases per 100,000 live births, which is equivalent to one case of maternal death per minute. Most of these cases can be prevented by ensuring equitable access to health services and by improving maternal health up to birth through appropriate and evidence-based practice. The chitosan-based device is a potent chitin-derived hemostatic agent to treat severe obstetric bleeding induced by uterine atony, multiple vaginal tears, and post-hysterectomy bleeding by hemostasis. **Materials and method.** This scientific paper presents two clinical case presentations in the obstetrics and gynecology section of the Mediaș Municipal Hospital. The study methods used were the research of the specialized literature and the practical application of the innovations offered by it. **Results.** The reported clinical case refers to a 22-year-old female patient who was decided on and performed a caesarean section due to the lack of progression of labor and the onset of fetal distress. At the end of the caesarean section, uterine atony was noted, with massive blood loss refractory to volemic and uterotonic resuscitation therapy. It was decided and applied the uterine packing with Celox PPH, with the achievement of a rapidly installed hemostasis. **Discussion and conclusions.** Uterine packing with chitosan covered gauze is an optimal method of treatment of postpartum uterine hemorrhages refractory to therapy and usual correction maneuvers. This innovative method is of particular interest for reducing maternal mortality and morbidity (avoidance of relaparotomy/laparotomy, vascular ligatures, blood transfusions, prolonged hospital stay).

Keywords: postpartum hemorrhage, chitosan covered gauze (Celox), caesarean section

Prenatal early diagnosis of Turner syndrome

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Turner syndrome (TS) is a genetic disease with a female phenotype and the most frequent 45,XO karyotype. Prenatal diagnosis is based on ultrasound examination, which can suggest structural abnormalities and genetic assessment. Fifty percent of the cases are detected by ultrasound examination with major anomalies. **Case presentation.** A 29-year-old patient, with a caesarean section delivery four years before, referred for routine screening of a first-trimester pregnancy. The ultrasound exam revealed a 12-weeks of gestation singleton pregnancy, with increased nuchal translucency (6 mm), left heart hypoplasia, septal interventricular defect, mitral regurgitation and mitral valve dysplasia, with the reversed aortic flow. After counseling, the couple decided the termination of pregnancy due to its unfavorable prognosis. The suspected ultrasound anomalies were confirmed by autopsy. Also, a new computed fetal heart reconstruction technique was used for confirming fetal heart defects, as for this gestational age is barely impossible to correctly assess the anatomical structures. Turner syndrome (45,XO) karyotype was confirmed. **Conclusions.** The first-trimester structural ultrasound screening is important, as severe structural anomalies can be identified. With an early diagnosis and proper counseling, the couple may decide the termination of pregnancy. The fetal autopsy evaluation confirms the data obtained through the ultrasound examination, and with a proper technique, the microscopic evaluation, with special software reconstruction, can confirm fetal heart disorders, in a proper manner.

Keywords: Turner syndrome, karyotype, prenatal diagnosis, ultrasonography, heart autopsy

Fetal megacystis diagnosed early in the first trimester of pregnancy

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During first-trimester ultrasound examination, the fetal bladder is described as an anechoic structure in the fetal pelvis. It can be observed from 10 weeks of pregnancy when the fetus starts producing urine. Fetal megacystis (FM) is defined, in the first trimester, as longitudinal bladder diameter of more than 7 mm. It can occur in 0.06% of the pregnancies. The management of FM is complex due to the various etiology and uncertain evolution. The leading cause of FM is lower urinary tract obstruction (LUTO). This pathology leads to hydronephrosis, renal dysplasia and severe oligohydramnios, with a poor prognosis. The FM management should search for chromosomal or genetic defects and associated fetal abnormalities. The broad spectrum of etiologies and prognosis makes the counseling challenging. We present the case of a 28-year-old pregnant woman referred for first-trimester investigations. The patient had an obstetrical history of a pregnancy with complex body stalk anomaly (BSA) – with termination of pregnancy at 12 weeks of gestation. Both maternal and paternal karyotype were normal. At 9 weeks of gestation, the ultrasound examination revealed an enlarged bladder, with 5 mm longitudinal diameter. Later on, at 12 weeks of gestation, a cystic appearance at the level of the umbilical cord insertion that communicated widely with the urinary bladder and abnormal aspects of the genitals for the gestational age were detected. These aspects maintained in the second trimester of pregnancy and progressive oligohydramnios was described. At 17 weeks of gestation, after proper counseling, the patient decided to terminate the pregnancy. The fetal necropsy confirmed the presence of FM, bladder exstrophy and the abnormal external genital organs. The genetic testing revealed a normal fetal karyotype. In conclusion, FM and bladder exstrophy occur most frequently due to LUTO. Fetal megacystis can be suspected even from 9 weeks of gestation. Although found in the same patient, BSA and FM syndromes did not seem to have a genetic cause.

Keywords: megacystis, bladder, body stalk anomaly

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

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Abstract Book

Rare severe complications after *in vitro* fertilization

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Introduction. We aim to present some rare complications after *in vitro* fertilization (IVF). There are four types of complications regarding IVF procedures: ovarian hyperstimulation syndrome, complications regarding transvaginal egg collection, ovarian torsion, and complications regarding pregnancy. Ultrasound-guided oocyte retrieval has rare complications. **Methodology.** This is a retrospective study performed in a private medical center. **Results.** Bilateral massive pleurisy as the only sign of ovarian hyperstimulation syndrome, vertebral osteomyelitis, middle cerebral artery thrombosis, rectus sheath hematoma, ovarian torsion, ureteral injury, intraperitoneal bleeding and ovarian abscess are rare but serious complications that we can encounter during *in vitro* fertilization. Ovarian hyperstimulation syndrome complete prevention is not possible, but rapid detection and proper management leading to less severe forms are possible. Patients who bleed after oocytes pick-up are at a high risk for morbidity and mortality. Vaginal lacerations are easy to recognize, and peritoneal hemorrhage secondary to ovary bleeding needs ovarian intervention to stop it. Bleeding is rarely severe. Unstable patients needed intravenous fluid resuscitation and blood product transfusion. Regarding pregnancy, the complication of IVF could be an ectopic pregnancy, heterotopic pregnancy, abnormal placentation, multiple pregnancies, or premature delivery. **Conclusions.** Under good medical and laboratory practice conditions, IVF is a procedure with acceptable risks. Patients should be informed about the possible *in vitro* fertilization complications and sign the informed consent before the process. The complications rarely endanger patients' life, but proper monitorization and measures are necessary.

Keywords: IVF, complications, IVF risks

The social and psychological impact of endometriosis on the Romanian urban population

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Objectives. Our study assesses the social and psychological impact of the symptoms of endometriosis. **Materials and method.** This cross-sectional study was conducted from January 2014 to January 2016. The research involved two groups. The study instrument, the EHP-5 questionnaire, was completed by the respondents on the admission date or on the routine gynecological visit day. **Results.** Endometriosis has a negative social and psychological impact on women's life, the most affected areas being work, fertility and sexual activity. Moreover, pain and the negative perception of self-image are major sources of distress. **Conclusions.** The symptoms and effects of endometriosis – especially chronic pelvic pain, mood changes and infertility – are significant negative factors in women's life. The authors further conclude that the EHP-5 questionnaire can be more widely used to help select women who may need special attention in terms of their quality of life, thus helping gynecologists refer affected women to a healthcare professional.

Keywords: endometriosis, quality of life, psychological impact, EHP-5 questionnaire

Diagnostic challenges and their approach in colposcopic practice

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The content of this session is built upon a preliminary survey which assessed participants' expectations, interests and diverse experience and expertise in colposcopy practice. We also took into account the current widening of colposcopy indications derived from the potential switch to HPV-based primary screening and biomarker triage methods. Richly illustrated presentations will cover essential aspects of cervical pathology linked to difficult diagnostic and management situations, such as the congenital transformation zone, pregnancy, glandular abnormalities or the age-based approach. The entire colposcopic iconography, the complex investigations supporting the treatment plans, the presentation of scientific statements and the comments on case particularity are original. We hope that every colleague from the audience will find and take home interesting points of view, new scientific developments and alternative approaches to absorb into current practice, or even the inspiration to do colposcopy.

Keywords: colposcopy, HPV, biomarkers, congenital and atypical transformation zone

Surgical treatment of intestinal endometriosis

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Introduction. Endometriosis is an estrogen-dependent inflammatory disease of uncertain etiology that affects approximately 10% of women of reproductive age. Intestinal endometriosis affects 3.8-37% of patients diagnosed with endometriosis and may be misdiagnosed as irritable bowel syndrome. Some of the women diagnosed with intestinal endometriosis report catamenial diarrhea, blood in the stool, constipation, bloating, pain on sitting and pain radiating to the perineum, in addition to dysmenorrhea, deep dyspareunia, persistent pain and/or dyschezia. **Materials and method.** We present a one-year study developed in a multidisciplinary endometriosis center involving 321 patients undergoing surgery for deep infiltrating endometriosis (DIE), including 158 patients with intestinal endometriosis. **Results.** Nearly half of the women involved in this study had rectal endometriosis. In 11% of cases, the sigmoid was affected. In 6% of cases, we found endometriosis lesions in the ileum, and in 2.5% of cases, in the appendix. All the intestinal lesions found were removed by various surgical techniques. The most frequently used procedure for the excision of intestinal endometriosis was segmental resection (88.3%), followed by intestinal shaving (10.2%) and only 1.3% had discoid excision. **Conclusions.** Intestinal endometriosis is one of the most severe forms of DIE. The most frequent site of intestinal endometriosis is the rectum. The optimal surgical technique ("shaving", disc excision and/or segmental resection) is still on debate. Dyschezia, persistent abdominal pain and functional bowel symptoms are frequent among patients with intestinal endometriosis, and the surgical treatment may relieve these symptoms.

Keywords: endometriosis, rectal endometriosis, segmental resection, intestinal shaving

Human papillomavirus and immunosuppression

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The increasing prevalence of associated cancers worldwide can be attributed to human papillomavirus (HPV), a commonly transmitted virus that infects stratified epithelia in mucosal or cutaneous regions. While an adequate immune response can clear HPV infection, individuals with compromised immune systems may experience persistent, treatment-resistant and progressive disease. Individuals with compromised immune systems are particularly vulnerable to the occurrence of both cutaneous and mucosal warts, as well as to the development of various types of cancer, including cervical, anogenital and oropharyngeal carcinomas. For example, HIV-positive men who have sex with men are particularly susceptible to anal intraepithelial neoplasia and anal cancer, prompting experts to recommend screening protocols similar to those used for cervical cancer. Organ transplant recipients (OTRs) often experience HPV-induced skin warts, with some cases escalating to a severe manifestation known as generalized verrucosis, especially in individuals with specific primary immunodeficiencies. Genital warts (*condylomata acuminata*) are also prevalent among HIV-positive individuals. This work aims to present the relationship between HPV infection and the different types of immunosuppression (primary, secondary and acquired), emphasizing the importance of developing guidelines dedicated to immunocompromised patients. Some studies evaluated HPV infection in elderly patients. Their observations align with the concept of a natural history model characterized by viral latency and subsequent reactivation, generating a new hypothesis that HPV can persist in a dormant state at low levels and potentially reactivate later in life, leading to the development of diseases. Thus, gaining insights into the origins of newly identified infections in older women holds significant implications for HPV screening and vaccination strategies.

Keywords: human immunodeficiency virus (HIV), human papillomavirus (HPV), cancer, vaccine, screening

Adenomyosis and infertility – in search of an optimal management

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Introduction. A classic histological definition for adenomyosis is the invasion of the myometrium by glands or endometrial stroma, more than 2.5 mm from the level of the junctional zone (JZ), associated with hyperplasia of the adjacent muscle tissue. Adenomyosis is a gynecological pathology frequently encountered in women of reproductive age, being a frequent cause of infertility. The pathogenesis of the disease is correlated with sex steroid hormone abnormalities, inflammation, fibrosis and neuroangiogenesis. The mechanisms are not fully understood. Adenomyosis has been a clinically neglected condition. In the last decade, progress has been made to improve the management of adenomyosis in infertile patients. **Methodology.** We systematically searched the literature for studies that evaluate the main treatments of adenomyosis in infertile patients. **Results.** Various forms of adenomyosis have been described in the literature. External adenomyosis is the adenomyosis of the outer myometrium, and this corresponds to lesions separated from the JZ. Internal adenomyosis (which affects the inner myometrium) is mostly characterized by endometrial implants scattered throughout the myometrium and enlargement of the JZ. Patients with adenomyosis have higher miscarriage rates, lower clinical pregnancy rates, and lower live birth rates following IVF/ICSI. There have been many recently extensive reviews on the management of adenomyosis. Estrogens are considered to determine the progression of ectopic endometrium and, therefore, either hypoestrogenism or estrogen antagonism appear to have therapeutic potential. **Conclusions.** Currently, the main treatments of the disease consist in hormonal drugs. Hysteroscopy might add value in the management of infertile patients with adenomyosis. The diagnostic process and the correct treatment in order to achieve a pregnancy following IVF/ICSI in adenomyosis patients are challenging.

Keywords: adenomyosis, infertility, IVF

Hysteroscopic management of missed abortion and retained products of conception

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Introduction. Missed abortion is defined by early pregnancy loss or spontaneous loss of gestation up to 12 weeks. The prevalence of missed abortion is up to 31% of clinical recognized pregnancies. The management of missed abortion can be expectant, medical or surgical. The main benefits of surgical management are shorter completion of treatment, lower risk of unplanned hospital admission, and higher patient's satisfaction. The main potential complications of blind intrauterine procedure (curettage) are represented by incomplete procedure (retained products of conception; RPOC), uterine perforation, cervical trauma, infections, intrauterine adhesions formation etc. Recently, an emerging and promising technique has been introduced in the infertility management: hysteroscopy. **Methodology.** We systematically searched the literature for studies that evaluate the benefits of hysteroscopy in missed abortion and retained products of conception. **Results.** The main benefits of hysteroscopic approach for RPOC are: reducing intrauterine trauma, avoiding intrauterine adhesions, avoiding blind dilation and curettage, lowering infection risk, and increasing pregnancy rates. The main benefits of hysteroscopic management for missed abortion are: anatomy survey of the embryo, cord accidents detection, selective tissue biopsy, minimal endometrial trauma, and low RPOC incidence. Other benefits of hysteroscopy are represented by the diagnosis of intrauterine anomalies and higher pregnancy rate at six months post-procedure. **Conclusions.** Embryoscopy allows the visualization and the selective biopsy of the embryo. It also allows a better understanding of human embryonic malformations. Selective hysteroscopy for residual trophoblastic tissue or missed abortion significantly reduces the incidence of intrauterine adhesions and increases pregnancy rates.

Keywords: hysteroscopy, missed abortion, retained product of conception, RPOC, embryoscopy

Episiotomy scar endometriosis – case presentation

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Endometriosis is a frequent gynecological disease among women of reproductive age, a benign condition with an uncertain etiology, but with multiple theories being proposed as main mechanisms of development. Perineal endometriosis is an uncommon condition, with various theories about its pathogenesis, including the contiguous propagation of endometrial tissue over the episiotomy perineal scar. A 36-year-old woman, G2, P2, presented with cyclic inflammation and pain in the episiotomy area, with significant impairment of her daily quality of life. The clinical examination revealed a palpable mass in the episiotomy area, and a probable clinical diagnosis of perineal scar endometriosis was considered, with further investigation being recommended. The patient was surgically treated by local excision of the perineal mass and the histopathologic examination of the mass confirmed the diagnosis of perineal endometriosis in the episiotomy scar. Although perineal endometriosis remains a rare condition, it should be considered in all patients with an anterior vaginal delivery and a painful perineal mass during menstrual cycle, a wide excision of the affected tissue remaining the best option for a permanent cure.

Keywords: endometriosis, perineal endometriosis, scar endometriosis

Ultrasound and hysteroscopic diagnosis of adenomyosis

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Introduction. Adenomyosis is a benign uterine pathology defined by the presence of endometrial tissue inside the myometrium. Although it was first described at the end of the 19th century, Bird was the first to establish a more elaborate definition, in 1972. Despite the fact that it affects a large female population, adenomyosis received little attention through the years and is yet to be fully investigated and understood. Despite the wide abundance of imaging and other methods for diagnosing adenomyosis, there are currently no standard verified diagnostic criteria for pathologists. The gold standard for the diagnosis of adenomyosis remains the histological exam, but with the development of new imagistic tools such as ultrasound and the direct visualization of the uterine cavity via hysteroscopy, a new set of diagnostic parameters can help classify the disease and dictate further therapeutic conduct. **Methodology.** In order to dictate a reliable classification of the disease, a sum of pathognomonic characteristics were searched using MUSA ultrasound criteria for the diagnosis of adenomyosis, alongside the hysteroscopic imaging of the uterine cavity. **Results.** Ultrasound and hysteroscopic-based characteristics were noticed to be frequently found in adenomyosis. Parameters such as location, dimension, type and differentiation of myometrial invasion (focal/diffuse or the presence of cysts) can be observed through ultrasound. Although hysteroscopy is not suitable to allow a pathognomonic sign for adenomyosis, some authors have reported the hysteroscopic uterine framework of women with adenomyosis; findings such as irregular endometrium with endometrial defects, hypervascularization, strawberry pattern or cystic hemorrhagic lesions are possibly associated with adenomyosis. **Conclusions.** The need for a comprehensive, user friendly and clear categorization of adenomyosis seems to be an urgent need. Along with histological diagnosis, a combination of hysteroscopic and ultrasound findings while diagnosing adenomyosis can be adopted in creating a classification system using patterns for each subtype, and decide a personalized treatment.

Keywords: adenomyosis, ultrasound, hysteroscopy, classification

HPV urinary screening for cervical cancer: a noninvasive approach to early detection

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Cervical cancer continues to be a significant global health burden, necessitating novel approaches for early detection and prevention. Human papillomavirus (HPV) infection is the primary etiological factor in the development of cervical cancer, highlighting the importance of effective HPV screening methods. Traditional screening strategies involve cervical sampling, which may be invasive and inconvenient for some individuals. In recent years, the emergence of noninvasive HPV urinary screening techniques has shown promising potential as a feasible and reliable alternative for the early detection of cervical cancer. This presentation aims to critically review the existing literature on HPV urinary screening in cervical cancer and to highlight its potential as a paradigm shift in the early detection. The presentation critically evaluates the diagnostic accuracy, sensitivity and specificity of HPV urinary screening methods compared to traditional cervical sampling, highlighting their potential as an effective tool for the early detection of cervical cancer. The advantages of urinary screening – such as its non-invasiveness, ease of collection and potential for self-sampling – are also discussed. In conclusion, HPV urinary screening represents a promising alternative to traditional cervical sampling methods, offering a noninvasive and convenient approach for the early detection of cervical cancer. Embracing the shift to the urinary screening of HPV has the potential to revolutionize cervical cancer screening programs, leading to earlier detection, improved patient outcomes and, ultimately, to a reduction in cervical cancer-related morbidity and mortality rates.

Keywords: urinary detection of HPV, cervical cancer, screening of HPV

Does HPV infection increase the risk of preterm birth? What should we know

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Human papillomavirus (HPV) infection is known to be sexually transmitted and can range from benign lesions (genital warts) to anogenital and oropharyngeal cancer. Women carrying HPV have an increased risk of preterm birth. A connection can thus be seen between the virus itself and the risk for preterm birth that previously has been observed in pregnant women who have undergone treatment for abnormal cell changes due to HPV. The risk of preterm birth was specific to HPV 16 and 18, being the greatest when the infection persisted between the first and the third trimesters. The detection of any type of vaginal HPV DNA in the first trimester alone wasn't associated with an increased risk of preterm birth. Also, the treatment of cervical intraepithelial neoplasia (CIN) is associated with an increased risk of preterm delivery, preterm prelabor rupture of the membranes and neonatal mortality, even though the exact pathomechanism is not yet understood. Although the ascending bacterial infection is an established leading cause of preterm delivery, there is limited knowledge concerning whether preterm delivery after excisional treatment for CIN is associated with infectious complications. All these studies results support the idea that strategies to mitigate HPV infection, such as vaccination programs, may be beneficial for maternal and neonatal pregnancy outcomes.

Keywords: preterm delivery, treatment of CIN, neonatal mortality

Endocrine disruptors and infertility

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Introduction. Endocrine-disrupting chemicals (EDCs) are defined as any exogenous chemical that is capable of interfering with any aspect of hormone action, while representing a worldwide health problem. EDCs interfere with synthesis, action and metabolism of sex steroid hormones that can cause developmental and fertility problems, infertility and hormone-sensitive cancers in women and men. Studies also suggest that EDCs could play a potential role in the etiopathogenesis of endometriosis *via* multiple mechanisms. There is new evidence which suggests that EDCs may be etiologically involved in the development and severity of the disease. **Objective.** The objectives of this review are to analyze and summarize the impact of EDCs on fertility and the role of EDCs in the etiology of infertility. **Methodology.** We have primarily focused on the role of EDCs in this presentation. This was performed by searching relevant articles in order to ensure a comprehensive review on EDCs exposure and reproductive function on PubMed up to 2022. The search terms used were: androgens, endocrine-disrupting chemicals, estrogens, female, infertility, ovary. **Conclusions.** Estrogens and androgens are major players in the normal growth and reproductive functioning in organisms. Any disruption in the pathways can lead to malfunctioning in both male and female reproductive systems. Almost all major classes of EDCs have the ability to target the androgen or estrogen pathways or both. EDCs can affect both pathways at both genetic and epigenetic levels. There is consensus that EDCs exposure has a deleterious effect on ovarian function. Most epidemiologic evidence demonstrated that EDCs exposure could increase the overall risk of ovarian aging, leading to fertility or fecundity decline.

Keywords: endocrine disrupting chemicals, estrogens, female, infertility, reproduction

High-grade cervical intraepithelial neoplasia and HPV infection – one-year follow-up after electric therapeutic conization

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Introduction. Today, high-risk HPV infection is a causal factor for the emergence of cervical cancer, and effective strategies for preventing cancer of the uterine cervix are based on detecting cervical intraepithelial neoplasia (CIN). Conization is one of the recognized treatments of CIN, since it makes it possible to exclude invasive neoplasia, evaluate resection margins and preserve fertility. The aim of this study was to evaluate if electric conization is sufficient to eliminate cervical intraepithelial neoplasia and the associated high-risk HPV infection. **Methodology.** This is a one-year retrospective study that included 94 women. The inclusion criteria were an abnormal Papanicolaou test (Pap test) or a high-risk HPV positive test and an abnormal colposcopy. All patients benefited from an electric therapeutic conization with clinical-pathological analysis. The follow-up included co-testing (Pap test and HPV test) at six months and at 12 months post-conization. **Results and discussion.** Twenty-three patients were confirmed with high-grade CIN after electric conization, and all had a previous high-risk HPV positive test. Negative resection cone margins were confirmed in 19 cases. The six-month and the 12-month follow-up in all these 19 cases showed normal Pap tests results and negative HPV testing. In four cases with positive cone margins, the six-month and the 12-month follow-up showed the persistence of the HPV infection. **Conclusions.** The data of the present study demonstrated that a high-risk HPV infection is successfully eliminated by conization in most cases. The persistence of high-risk HPV infection was observed in patients who had positive resection cone margins. The presence of CIN in the cone margin gives strong indication of potential treatment failure and for an increased rate of disease recurrence. Electric conization is highly effective in the treatment of cervical intraepithelial neoplasia, and HPV testing proved to be a valuable tool to monitor the therapeutic results of conization.

Keywords: cervical intraepithelial neoplasia, HPV infection, conization

Diagnosis of uterine adenomyosis in patients of reproductive age

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Uterine adenomyosis is a gynecologic condition characterized by the presence of islands of ectopic endometrial tissue inside the myometrium. This disease affects 20% of women of reproductive age, causing pelvic pain, abnormal uterine bleeding and infertility. This paper is a review based on information found in literature. The analysis was limited to articles in the English language published between 1 January 2000 and 13 November 2019 on PubMed. In this review, we discuss the current trends in the management of uterine adenomyosis, especially ultrasound and MRI diagnosis. Adenomyosis remains an underdiagnosed condition. Through a careful description of the sonographic aspects of adenomyosis and using a standardized classification, we can improve the diagnosis rates in women of reproductive age.

Keywords: adenomyosis, transvaginal ultrasonography, magnetic resonance

HPV and premature delivery risk

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Preterm delivery represents the leading cause of perinatal morbidity and mortality. Among possible etiologies of premature birth, there are the infectious ones, human papillomavirus (HPV) infection being less documented than others. The available data on the role of HPV infection in premature delivery pathogenesis is limited and controversial. This review article attempts to make an assessment of current information on the risk of premature delivery in women with HPV infection during pregnancy. A systematic literature electronic search for journal articles and guidelines regarding HPV infection during pregnancy was undertaken. The relationship between HPV infection and pregnancy is bidirectional, as physiological changes that occur during pregnancy modulate the mechanisms of HPV infection, and HPV infection determines adverse maternal, obstetrical and fetal outcomes.

Keywords: human papillomavirus, preterm delivery, adverse pregnancy outcomes

Impact of lifestyle and diet on endometriosis: a holistic approach?

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Introduction. Endometriosis is a chronic inflammatory condition, estimated to affect approximately 1 in 10 women worldwide, defined by the presence of endometrium stroma and glands outside of the uterus, associated with disturbances in inflammatory regulation, cellular attachment and invasion mechanisms, angiogenesis, as well as estrogen activity and clearance. Because of the lack of an effective and consistent means of treatment, in addition to the chronic character of endometriosis, many women use additional management strategies to control this disease. These include changes in lifestyle, diet habits and implementing physical activities with a soothing role on central nervous system. The aim of this review is to highlight the beneficial effects of lifestyle changes on endometriosis, with a focus on diet, physical activity, benefic habits and mental health. **Methodology.** A systematic review was conducted by searching Medline, PubMed and Embase to identify randomized controlled trials and observational studies. **Results.** Multiple active compounds offering various therapeutic properties, such as antiproliferative, anti-inflammatory, antioxidant and analgesic properties, are considered highly effective in endometriosis. Soothing activities, such as walking, meditation, yoga or pilates, have a positive effect on the central nervous system, activating the parasympathetic pathways and enhancing the quality of life of the patient. In addition, optimizing the intestinal microbiome by correcting the gut dysbiosis through a high intake of pre- and probiotics aids in the modulation of the estrobolome, with the normalization of an otherwise hyperestrogenic environment, characteristic of endometriosis. **Conclusions.** The management of endometriosis should also include a holistic approach, with an important effect on reducing the overall pain, as well as other important symptoms that may otherwise impact the quality of life of the patients, mainly achieved by adopting healthy habits, with an emphasis on anti-inflammatory diets, physical exercise and stress-lowering activities.

Keywords: endometriosis, nutrition, lifestyle, diet, estrobolome, physical exercises

Hysteroscopic diagnosis of adenomyosis

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Introduction. Adenomyosis is a medical condition characterized by the presence of ectopic endometrial tissue inside the myometrium. This accumulation of endometrial glands and stroma in the myometrium causes hypertrophy. This condition is becoming increasingly common in teenage girls and affect women throughout their reproductive lives. Hysteroscopy is today a diagnostic method for adenomyosis. Although the invasion is at the myometrial level, and not endometrial, there are some suggestive images for the diagnosis: irregular endometrium, pronounced hypervascularization, with surface defect, with visible cystic lesions and areas of fibrosis. The definitive diagnosis is established by biopsy which can easily be obtained by hysteroscopy. **Methodology.** A systematic review was conducted by searching PubMed and *Hysteroscopy Newsletter* to identify randomized controlled trials and observational studies. We have selected the most suggestive and impressive hysteroscopic images of adenomyosis from our clinic. **Results.** The incidence of adenomyosis in patients with dysmenorrhea, menorrhagia and infertility has been reported to be about 60% of these cases. Although it is not the gold standard method for diagnosis, the hysteroscopy is a quick and direct method of visualizing the lesions and the local changes in adenomyosis. The pre-treatment with GnRH agonists may help reduce vascularization and bleeding during the surgical procedure and has been demonstrated to inhibit the development of this pathology. **Conclusions.** It is believed that adenomyosis may contribute to infertility by altering the normal architecture and function of the myometrium. Ultrasound diagnosis of adenomyosis was subsequently confirmed by performing a hysteroscopy. Multiple endometrial lesions with particular pattern were recognized as being specific in adenomyosis.

Keywords: adenomyosis, hysteroscopic, treatment, diagnosis

Management and counseling in extragenital endometriosis

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Extragenital endometriosis is a condition characterized by the presence of endometrial tissue outside of the pelvic region. This condition can lead to a range of symptoms and complications, requiring timely diagnosis and appropriate management. Extragenital endometriosis can manifest in various sites, including the gastrointestinal tract, the urinary system, the respiratory system, and even distant locations like the skin or central nervous system. The exact cause of extragenital endometriosis remains unclear, although several theories have been proposed, such as retrograde menstruation, genetic predisposition, and immune system dysfunction. The symptoms of extragenital endometriosis often depend on the affected site. The management of extragenital endometriosis focuses on relieving symptoms and on improving the quality of life. Extragenital endometriosis poses a significant challenge due to its variable and often nonspecific symptoms. Furthermore, it may be overlooked or misdiagnosed, leading to delayed treatment. Increased awareness among healthcare providers and the general public is crucial to ensure the early recognition and the appropriate management of this condition. Our aim is to present the challenges in extragenital endometriosis with an emphasis on timely diagnosis and proper management, in order to alleviate symptoms, improve the quality of life and prevent complications. Ongoing research is necessary to further understand the causes and develop more effective treatments for extragenital endometriosis, but the proper approach to this rare pathology is more important.

Keywords: extragenital endometriosis, thoracic endometriosis, umbilical endometriosis, rare endometriosis

Endometriosis-induced infertility – what do we know so far?

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Introduction. Known as a complex, multifactorial, poorly understood and systemic disease, endometriosis negatively influences fertility. Although there has been extensive research throughout the literature, a precise cause and effect relationship between endometriosis and infertility, as well as an accurate treatment are still under debate. **Materials and method.** Research of the literature has been conducted to select the latest information available regarding pathophysiology, the underlying mechanisms and the abnormal processes related to endometriosis, as well as the heterogeneous alterations associated to decreased fertility or infertility. Not least, there have been under attention the conditions in which abnormal mechanisms may additionally impact one another to further decrease fertility, but also the impact of endometriosis treatment upon patient's reproductive status. **Results.** Endometriosis is a heterogeneous, chronic, estrogen dependent, progesterone resistant, inflammatory condition, with an incidence up to 50% in women addressing for infertility. The highly complex nature of the disease reflects in the variety of symptoms and sigs, making difficult to both completely characterize, classify and predict disease's evolution and complications. Patient's reproductive status and endometriosis-associated infertility are most probably the result of heterogenous and self-influencing anomalies associated to the disease, namely inflammatory syndrome, including pain, anomalies of the peritoneal cavity and adherences, altered pelvic anatomy, compromised endometrial function and impaired ovarian function/oocyte quality. Despite the general concern related to fertility status, the treatment options are limited and should highly be individualized, analyzing the role of surgery and of assisted reproductive technologies, and focused towards fertility sparing and increasing pregnancy outcome. **Conclusions.** The mechanisms involved in both endometriosis and infertility or decreased fertility associated to the disease are highly complex. The multifactorial condition induces profound alterations, making fertility preservation and infertility treatment a major concern for the medical personnel, with limited treatment options and a highly tailored approach for each patient.

Keywords: endometriosis, inflammatory syndrome, pregnancy, infertility

Hysteroscopy for treating subfertility associated with suspected endometrial polyps

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Introduction. Endometrial polyps (EPs) are a common benign gynecologic condition associated with abnormal uterine bleeding (AUB), infertility and recurrent pregnancy loss. Transvaginal ultrasound (TVU) provides an excellent diagnostic technique to diagnose the size and the anatomic location of endometrial polyps (EPs). Its accuracy increases when color Doppler, 3D investigation and saline infused sonohysterography are used. However, hysteroscopy showed the highest diagnostic accuracy in infertile patients with suspected endometrial polyps and provides safe and feasible opportunity for EPs removal. This study aims to demonstrate the effectiveness of hysteroscopic polyps' removal in infertile young female patients. **Methodology.** This is a one-year retrospective study that included 75 women, aged 20-35 years old. The inclusion criteria were infertility with or without abnormal uterine bleeding. All the patients benefited from a complete transvaginal ultrasound examination and only 20 patients from a hysterosonography. Diagnostic and therapeutic hysteroscopy was performed in all cases. The study noted the incidence of pregnancy in the first 12 months following the hysteroscopic polyp removal. **Results and discussion.** Endometrial polyps were confirmed in 73 cases by the clinico-histological analysis, while in two cases a submucous fibroid was found. Ten patients were lost to follow-up. Forty-five women out of 63 had a confirmed intrauterine pregnancy in the first 12 months after hysteroscopy. Three patients presented a relapse of the EPs in the first year after hysteroscopy. **Conclusions.** Endometrial polyps are safely and effectively diagnosed and treated with the hysteroscopic treatment modality. Dilation and curettage should be avoided for the diagnosis and treatment of EPs. The hysteroscopic removal of endometrial polyps suspected on ultrasound in women led to a higher pregnancy rate in the first 12 months in young female patients.

Keywords: endometrial polyps, infertility, hysteroscopy

Hormonal therapy versus surgical approach – a double-edged sword

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Introduction. Endometriosis, the disease for which the etiology and mechanism of pain are far from being fully understood, benefits from a limited number of therapeutic solutions. The treatment methods can be grouped into two categories: surgical and medical. **Method.** The medical treatment is often the first line of treatment, while surgical intervention is addressed to patients who have not responded favorably to hormonal therapy, who have a suspicious ultrasound appearance and require histopathological diagnosis, or for those cases with deep endometriosis that affects the function of the pelvic organs and life quality. Patients with infertility must benefit from surgical treatment which can restore the normal anatomy of the pelvis and restore the reproductive capacity with maximum chances in the first six months post-intervention. **Results.** Important information from recent guidelines and relevant literature is highlighted. Ovarian and deep endometriosis case series from personal experience will be commented on. The patients benefited from personalized therapeutic management and follow-up in terms of symptoms, quality of life and infertility. **Conclusions.** The main thought that must guide the medical act is how to improve the quality of life of patients with endometriosis. The treatment must be established considering multiple factors: national and international guidelines, symptoms, age, ovarian reserve, the patient's desire, compliance to treatment and, last but not least, the balance of advantages versus disadvantages of the proposed therapy. As long as there is no miracle treatment for endometriosis, the holistic management must be considered. Alternative therapies such as diets and physical relaxation exercises (yoga, pilates) can make a major contribution to increasing the quality of life.

Keywords: management, endometriosis, quality of life

Cervical cancer in pregnancy

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Introduction

What are the situations? Modified Pap test, known HR HPV infection, pregnancy occurring shortly after the treatment for CIN, the need for histopathological confirmation to rule out invasion, vulvar condylomatosis.

Materials and method

Woman, HPV HR +, 18-24 years old.

- in 90% of cases they eliminate the infection (transitorial infection) within 6-14 months
- in 10% of cases viral persistence (latent infection).

What does p16/Ki67 actually do?

If it is negative:

- the transforming infection is absent
- that now the patient does not present the risk of developing high-grade injuries
- HPV-HR absent
- No indication for colposcopy.

If is positive:

- the transforming infection is present
- HPV-HR present
- the patient is now in a high risk group
- colposcopy is indicated.

Childbirth in pregnant women with HPV infection:

- cervical cancer is a contraindication to natural childbirth.

Depending on the histopathological result, the following actions are adopted:

- CIN I – postpartum reassessment.
- CIN II/III – cyto-colposcopic re-evaluation at 12-week intervals during pregnancy, with repeat biopsy if necessary.

Microinvasive carcinoma (IA1) in the first trimester:

- Conization (if the margins are negative, colposcopy is performed at 8 weeks during pregnancy and cyto-colposcopic re-evaluation at 6-8 weeks postpartum);
- if the diagnosis takes shape after 24 weeks of gestation, it is preferable not to perform conization during the pregnancy.

Invasive cancer: therapy is guided by staging and gestational age, but is modulated by ethical principles and the patient's personal desire.

Results

- Postpartum re-evaluation: optimal interval 8-12 weeks. Before 6-8 weeks there is a greater risk of bleeding and thus missed diagnosis.
- it is preferable to do co-testing as well.

Conclusions

- Treatment must be optimal for the mother and safe for the fetus.
- Treatment must be optimal for the mother and able to preserve the mother's fertility.

Keywords: cervical cancer, pregnancy, HPV, cervical dysplasia

HPV infection in genital and head and neck cancers – from pathogenesis to gender-neutral vaccination

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HPV infection is a very common sexually transmitted infection that causes almost 5% of all cancers in women and men worldwide. These include cervical, anal, penile, vaginal, vulvar and oropharyngeal cancers. HPV also causes genital warts and recurrent respiratory papillomatosis (RRP). Almost all of these HPV inflicted pathologies can be prevented through vaccination. Ideally, this should be done in adolescence, before exposure to the virus and provided to both sexes. However, most countries in Europe do not currently vaccinate boys, and HPV vaccination uptake remains low in some countries. Although the utility of HPV screening in the management of cervical dysplasia and cancer has been demonstrated and cervical cancer screening programs are available in most European countries, only a minority of programs can be described as adequate. Moreover, most countries do not yet offer HPV testing, now recognized to be a more effective screening method. Our presentation will tackle HPV infection, presenting aspects of epidemiology, pathogenesis, genotypes, the relation with vaginal dysbiosis, its involvement in cancers such as cervical cancer, other genital cancers and head and neck cancers. The last part of the presentation will include management options, from general measures to vaccination and management of cervical HPV-related lesions, insisting on arguments for gender-neutral vaccination and public awareness.

Keywords: HPV infection, cervical cancer, HPV head and neck related cancers, gender-neutral vaccination

The role of biological markers in predicting infertility associated with non-obstructive endometriosis

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Objectives. Our study evaluates if the use of biological markers can predict the infertility in women with non-obstructive endometriosis. **Materials and method.** Two prospective, non-randomized studies were conducted to identify if CA-125, IL-6 and IL-8 can be used as predictive markers for infertility in women with non-obstructive endometriosis. Peripheral levels of CA-125, IL-6 and IL-8 were measured before laparoscopy in all patients. **Results.** We found a total number of 152 patients with non-obstructive endometriosis, and we divided them into two groups: fertile and infertile women. There was a statistically significant difference of the mean of CA-125 values between the two groups (p=0.00). The patients with infertility had a significantly higher IL-6 serum values than the fertile patients (p=0.00). Regarding the IL-8 serum values, there was no statistically significant difference between the two groups, fertile versus infertile women (p=0.06). **Conclusions.** The elevated serum levels of CA-125 and IL-6 were associated with an increased probability of being diagnosed with infertility. The IL-8 serum level had no value in predicting infertility associated with non-obstructive endometriosis.

Keywords: CA-125, IL-6, IL-8, biological marker, non-obstructive endometriosis, prediction of infertility

Psychosocial implications of cervical cancer screening

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Introduction. Highlighting some correlations between psychosocial factors and certain biomarkers incriminated in the diagnostic management of cervical cancer can represent an essential element in establishing the therapeutic protocol. **Materials and method.** In the analysis of the reluctance towards screening programs, five main themes were identified: lack of knowledge of the issue of cervical cancer, of the role of screening and health awareness, fears related to the procedure itself and the results of the screening, emotional and cultural barriers, practical barriers and cognitive barriers. **Results.** The multidisciplinary approach and the involvement of the partner must take into account the seriousness of the medical situation and the psycho-socio-familial aspects, because factors such as age, marital status, the existence of children in the family or the desire to have children, along with cultural or religious factors can increase the stress associated with the diagnosis. **Conclusions.** The information campaigns in the mass media and the programs of the public health departments, through the informational strategies used, unfortunately fail to address the psychosocial side of the screening.

Keywords: cervical cancer, screening, psychosocial factors

Medical treatment in endometriosis

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Introduction. Women with endometriosis are confronted with one or both of two major problems: endometriosis-associated pain and infertility. Currently, guidelines and specialty literature are focusing on medical treatment in endometriosis because of the need to raise the quality of life, to reduce pain, but there are many individual symptoms (endometriosis-associated pain includes painful ovulation and menstruation, pain during or after intercourse, heavy bleeding, chronic pelvic pain, fatigue and infertility, as well as detrimental effects on the patient's general physical, mental and social well-being) that we need to control with medical therapy, personalized for each patient. **Materials and method.** Studies of the literature and guidelines. **Results.** Hormone therapy is based on the evidence that endometriosis is a "steroid-dependent" disease. The most prescribed treatments for endometriosis include drugs that modify the hormonal environment (hyperestrogenism) either by suppressing ovarian activity or by acting directly on steroid receptors or on enzymes found in the lesions (aromatase inhibitors). These include progestogens, antiprogestogens, oral contraceptives, gonadotrophin releasing hormone (GnRH) agonists, GnRH antagonists, the levonorgestrel intrauterine system (LNG-IUS), danazol and aromatase inhibitors. **Conclusions.** There is no known cure for endometriosis so far, that's why researchers are studying the molecular mechanisms behind endometriosis in the hope of finding new treatment options for the millions of women around the world who suffer from this chronic inflammatory disease. Those women who cannot attempt to or decide not to conceive immediately after surgery may be offered hormone therapy, as it does not negatively impact their fertility and improves the immediate outcome of surgery for pain.

Keywords: endometriosis, pain management, hormone therapy

Can endometriosis be regarded as a preneoplastic lesion? Particular clinico-imaging and morphopathological aspects

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Introduction. Endometriosis is a benign pathology with features resembling malignancy. It is represented by the ectopic presence of endometrial glands in the structure of certain organs such as the ovaries, the peritoneum, the abdominal wall and, less frequently, in the lung and even the brain. Ectopic endometrial epithelium can undergo hyperplastic and even malignant transformations, affecting the cell structure and the proliferation rate. **Materials and method.** We present a retrospective study, analyzing the clinical, imaging and morphopathological aspects involved in the hyperplastic transformation of ectopic endometrial tissue, by applying classical histological and specific immunohistochemical techniques. Vascular, inflammatory and oncoprotein morphopathological changes can lead to hyperplastic changes of ectopic endometrial tissue and, subsequently, to malignant lesions. **Results.** CK7+/CK20- expression was present in the ectopic epithelium and differentiated it from digestive metastases. We found more dense vascularization (CD34+) in areas of hyperplastic transformation than in normal endometrium. CD3+ T lymphocytes, CD20+ B lymphocytes, CD68+ macrophages and tryptase+ mast cells were abundant near the endometriosis sites, thus marking the proinflammatory microenvironment. In addition, we found significantly higher division index (Ki67+), inactivation of tumor suppressor genes p53+ and PTEN and oncoprotein BCL2 in the structure of hyperplastic and neoplastic endometriosis sites. **Conclusions.** The inflammatory, vascular, hormonal and oncoprotein mechanisms trigger endometriosis progression and neoplastic changes that can be detected by imaging techniques and may represent future therapeutic targets. High-resolution imaging, associated with immunohistochemistry techniques, are essential tools for improving the positive and differential diagnosis in deep endometriosis.

Keywords: endometriosis, adenomyosis, cell proliferation

Endometriosis-associated infertility: a systematic review

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Introduction. Endometriosis affects 10-15% of all women of reproductive age and 70% of women with chronic pelvic pain, being responsible for infertility among couples. **Materials and method.** A recent literature search was conducted, based on PubMed, using as keywords "endometriosis" and "infertility". Based on the articles by Anastasiu et al., 2020, Bonavina and Taylor, 2022, Bulletti et al., 2010, Chapron et al., 2019, Falcone and Flyckt, 2018, Ferrero et al., 2018, Hirsch et al., 2018, and Parasar et al., 2017, we attempted to examine the association between endometriosis and infertility. **Results.** The relationship between endometriosis and infertility has been debated for many years. The frequency of infertility in women with endometriosis can reach 50%, while 25% to 50% of women with infertility are finally diagnosed with endometriosis. In normal couples, fertility is in the range of 15% to 20% per month and declines with age. Women who have endometriosis tend to have a lower monthly fertility of about 2-10% per month. The association between endometriosis and infertility and vice versa is therefore obvious. The pathogenesis of infertility in endometriosis patients is multifactorial and difficult to explain. Although it is easy to understand that advanced and severe endometriosis can cause pelvic disorders, resulting in mechanical infertility, it is not well understood how the mild form of the disease can affect a woman's ability to conceive and reach childbirth. In women with severe endometriosis, extensive tubal-ovarian adhesions or large endometriomas have been reported to prevent ovulation or fallopian tube transport (mechanical factor). However, in cases with minimal or slight endometriosis, the mechanical factor is not present, thus other mechanisms are involved in the pathogenesis of infertility, such as endocrine changes, the luteinized ruptured follicle syndrome (LUF), increased macrophages, increased prostaglandin levels, the change in the motility of the fallopian tube and its cilia, disorders of egg maturation, and immunological disorders, such as the increased ratio of T-helper to T-suppressor cells, decreased activity of natural killer cells and increased levels of cytokines. The peritoneal fluid in women with endometriosis contains many macrophages. These macrophages are probably responsible for the production of high levels of proinflammatory cytokines (TNF-α, IL-1, IL-6, IL-8) and angiogenic growth factors. In addition, there is a reduction in the activity of natural killer cells in the peritoneal fluid of women with endometriosis. It has been suggested that activated macrophages may be involved in endometriosis-induced infertility through the production of free radicals such as nitric oxide. Interleukin 6 is significantly involved in the development of endometriosis. Interleukin 6 is reported to be elevated in women with endometriosis, and increased IL 6 concentrations suppress NK activity. **Conclusions.** There is a correlation between endometriosis and infertility. Women with endometriosis tend to have lower monthly fertility. Women with endometriosis have adhesions, increased volume of peritoneal fluid, high concentration of activated macrophages, prostaglandins, proinflammatory cytokines, angiogenic growth factors, and reduced activity of natural killer cells. These alterations may have adverse effects on the function of the egg, sperm or fallopian tube.

Keywords: endometriosis, infertility

Origin theories of endometriosis: a systematic review

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Introduction. Endometriosis is defined as the presence of endometrial glands and layers outside the uterus. Although there is no definitive etiology of endometriosis, there are several hypotheses about how endometriotic lesions develop. **Materials and method.** A recent literature research was conducted, based on PubMed, using the keywords "endometriosis" and "theories". Based on the articles by Anastasiu et al., 2020, Chapron et al., 2019, Falcone and Flyckt, 2018, Ferrero et al., 2018, Hirsch et al., 2018, and Parasar et al., 2017, we attempted to study the origin theories of endometriosis. **Results.** The histopathogenesis of endometriosis has not been fully elucidated. Various theories have been formulated that try to explain this disease. Today, three theories mainly prevail, Sampson's theory, Meyer's theory and Halban's theory. According to the implantation theory developed by Sampson in 1922, endometriotic foci are caused by the retrograde dispersion of endometrial cells during menstruation into the peritoneal cavity or to distant sites. But some facts cannot be explained, such as that retrograde menstruation is not always accompanied by endometriosis and that sometimes endometriosis occurs in different organs, as in non-reproductive people – e.g., with Turner syndrome or uterine agenesis or even in some men. Another theory of pathogenesis is the "theory of visceral epithelial metaplasia", or Meyer's theory. According to this theory, due to certain factors, metaplasia occurs in mesothelial cells of the peritoneum, so that eventually glands and the endometrial layer are formed. This explains why endometriosis can occur even in people without menstruation. Also, the appearance of endometrium in distant parts of the body can be explained by the Halban's theory, or "the theory of the transfer of endometrial cells through the lymphatic and blood vessels". In this theory, it is argued that distant lesions are established by the hematogenous or lymphogenic spread of viable endometriotic cells. Thus, metastases to the brain and lungs are explained. **Conclusions.** Consequently, a better understanding of the pathophysiologic mechanisms of endometriosis will provide us with more insight to better identify noninvasive diagnostic approaches and novel therapeutic targets to prevent the surgical morbidity and the diminished ovarian reserve.

Keywords: endometriosis, theories

Rat models of experimental endometriosis: a systematic review

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Introduction. Among the various types of animal models used for the study of endometriosis, rat models have many advantages. The main advantages are the low cost and the easy handling. In comparison to some non-human primates, they don't develop spontaneous endometriosis, therefore a surgical procedure in rats is required. According to literature, the most common way of inducing endometriosis in rats is intraperitoneal endometriosis. **Materials and method.** A recent literature research was conducted, based on PubMed, using the keywords "endometriosis", "rat model" and "rats". Based on the articles by D'Hooghe et al., 1995, D'Hooghe and Debrock, 2002, Edwards et al., 2013, Grummer et al., 2006, Hastings and Fazleabas, 2006, Hirata et al., 2005, Lagana et al., 2018, Sharpe-Timms, 2002, Stilley et al., 2009, Te linde et al.,1950, and Tirando-Gonzalez et al.,2010, we attempted to study rat models of experimental endometriosis. **Results.** In contrast to humans and non-human primates, other animal models do not develop spontaneous endometriosis. Endometriosis, however, can be induced in these organisms by transplanting endometrial tissue to ectopic sites. According to the origin of the tissue used for the induction of endometriosis, these mouse models can be separated into two main types: 1) the homologous models and 2) the heterologous models. In homologous models, endometrium is received from the uterus of a related animal and it is either inserted or dispersed into the peritoneal cavity of a second animal. The reproductive system of the homologous models of rodents remains intact and provides an opportunity to study cross-communication between the immune system and the endometrial cells through the peritoneal microenvironment, which appears to play a major role in the human body. In heterologous models, human endometrial parts are received and injected into immunodeficient mice. The heterologous model of xenograft uses immunodeficient mice to prevent graft-versus-host reaction, which would create a biological state that does not match a chronic inflammatory environment present in human endometriosis. Xenotransplantation of human endometrium tissue into immunodeficient mice is usually carried out by injecting a vaccine in the peritoneal cavity, given either subcutaneously or by microlaparotomy. According to literature, the most common way of inducing intraperitoneal endometriosis is by injecting fragments of the endometrium into the peritoneal cavity or by suturing a part of the endometrium to the peritoneal wall of the same animal. Interestingly, according to literature, rats with induced endometriosis demonstrated reduced fertility, reduced implantation rate, and reduced neonate height and fetal weight. **Conclusions.** Rat models may be used to expand the effect of endometriosis on fertility. Their easy handling and the lower cost in comparison to other *in vivo* models contribute to their wide use in the study of endometriosis. It demonstrate the utility of the baboon as an animal model for the study of endometriosis, however it should be noted that the use of baboons in experiments has a high cost.

Keywords: endometriosis, rat model, rats

Clinical factors influencing discordant colpo-cyto-histological results in the diagnosis of cervical lesions

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Objectives. Identifying the factors that influence the occurrence of discordant results between cytology/colposcopic impression/initial histology and the histopathological result after an excisional procedure. **Methodology.** Different clinical scenarios characterized by discordant results between cytology, colposcopy and histopathology were analyzed on a group of 89 patients investigated colposcopically in the period 2019-2022, with cytological abnormalities and a positive HR-HPV test. **Results.** The concordance between colposcopy and histopathological examination was 69.6%, with a sensitivity of colposcopy in identifying CIN3+ lesions of 79.7%. Factors associated with colposcopic underestimation were: absence of vaginal births, type 3 TZ, HPV genotype, HSIL cytology, age above 50 years old. **Conclusions.** Colposcopic impression, type of transformation zone, initial histology, cytological changes, age, HPV genotype and molecular markers are to be considered at the time of diagnosis and management of cervical lesions. The use of molecular markers or the increase in the number of colposcopic targeted biopsies were useful in identifying patients with HSIL lesions, but with LSIL/ASCUS cytology. Age above 50 years old and the presence of type 3 TZ were frequently associated with the underdiagnosis of HSIL lesions. The association of ASC-H/HSIL cytology and HPV 16/18 infection requires conization.

Keywords: cervical intraepithelial neoplasia, colposcopy

Extragenital endometriosis – a diagnostic challenge

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Introduction and objective. Thoracic endometriosis is an extremely rare condition that can lead to a variety of clinical manifestations, characterized by the presence of endometriotic deposits on the diaphragm, lungs or pleural space. It is a complex condition that often proves challenging to diagnose, leading to underdiagnosis, delays in treatment and significant morbidity in women of reproductive age. **Methodology.** We report a case of endometriosis in a 38-year-old woman with both genital (ovarian) and extragenital (rectal + diaphragmatic) localization that started with significant dysmenorrhea and a painful abdominal syndrome accompanied by episodes of vomiting at the time of menstruation. We mention that the patient had two previous natal births. **Results.** The diagnosis of ovarian endometriosis was established by endovaginal ultrasound. The patient underwent six months of Zafrilla® treatment, with no improvement in symptoms. Abdominal pain syndrome was accompanied by vomiting at the time of menstruation, at which time it was decided to perform a pelvic MRI with endometriosis protocol. The result was nodular lesion (7-8 mm) in the right diaphragm, pelvic endometriosis lesions – stage 4 rASF, Enzian O0/2, T3/3, B1/1, C3 (rectosigmoid junction and sigma), FA (uterine torus), FO (uterine round ligaments), diffuse uterine adenomyosis changes. The patient was successfully managed with surgical treatment, which consisted in the cure of stage 4 endometriosis with subtotal hysterectomy and bilateral salpingectomy. **Discussion and conclusions.** The meticulous investigation of patients suspected of endometriosis helps us to confirm the diagnosis and therefore accelerates the proper patient's management. This also prevents the chances of malignant transformation of the condition, although the possibilities are extremely rare.

Keywords: MRI, imaging, diaphragmatic endometriosis, endometriosis cure

Bidirectional relationship between HPV infection and pregnancy

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Human papillomavirus (HPV) infection is the most common sexually transmitted infection, putting young women at a high risk of contracting it. Although in most cases spontaneous resolution of the infection is observed within 1-2 years, persistent infection can represent a serious problem, as it has been associated with dysplasia and neoplasia in the anogenital and oropharyngeal regions. The incriminated risk factors include alcohol or nicotine consumption during pregnancy, short duration of pre-conceptional relationship with the child's father, single motherhood, and a low level of maternal education. In addition, studies suggest a negative effect of HPV infection on pregnancy, and this effect is attributed to hormonal changes and significant adaptations of the maternal immune system which favor the persistence of the virus. The high prevalence of HPV during pregnancy may also be the result of the reactivation of latent HPV infection during pregnancy. Various studies have reported an increased risk for adverse pregnancy outcomes among HPV-infected women, including preterm birth, spontaneous abortion, pregnancy-induced hypertensive disorders, intrauterine growth restriction and low birth weight, premature rupture of membranes and intrauterine fetal demise. Therefore, understanding the mechanisms that cause the negative effects of HPV on pregnancy and evaluating potential approaches to counteract them could improve pregnancy outcomes and the health of babies.

Keywords: HPV, pregnancy, immunity

Operative hysteroscopy in infertility – clinical cases

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Introduction. Hysteroscopy is a minimally invasive diagnostic and treatment method that offers, in just a few minutes, a various range of information and therapeutic options. Many international assisted human reproduction societies recommend routine hysteroscopy as a standard part of the infertility investigation plan. In this presentation, we will discuss the pathologies that can be diagnosed and treated hysteroscopically in order to improve the pregnancy rate: endometritis, Asherman's syndrome, polyp, fibroid, septum, T-shaped uterus, isthmocele, extraction of placental remnants etc. **Materials and method.** Clinical cases – video presentation of 12 different pathologies treated hysteroscopically. **Results.** Using correct techniques and protocols, with a personalized intrauterine pressure and with a good hysteroscopic visualization, the patients obtained post-procedurally an anatomically and functionally normal uterine cavity. Many have achieved full-term pregnancies, others have ongoing pregnancies at this moment, and some patients have received the consent to start the assisted human reproduction (AHR) procedures after the hysteroscopic resolution of the uterine pathologies. **Conclusions.** Hysteroscopy should be included in the list of standard investigations in patients with infertility.

Keywords: infertility, hysteroscopy, metroplasty, T-shape, polyp, fibroma

Autologous hematopoietic bone marrow stem cells for improving fertility

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Objectives. Autologous hematopoietic stem cells have the potential to multiply and differentiate into various mature cell types. They are obtained by harvesting from the bone marrow at the level of the iliac crest, for example, from the same patient, in the same intervention as the treatment. The goal is to improve the quality of oocytes, develop new ovarian follicles and improve the quality and receptivity of the endometrium. **Materials and method.** We performed an analysis of studies in the literature regarding the results of treatment with autologous hematopoietic stem cells in improving fertility. **Results.** Laparoscopic injection of stem cells proved superior to transvaginal injection. The use of autologous stem cells from bone marrow has proven superior to the use of stem cells from adipose tissue, being a minimally invasive technique with low associated risks. After the procedure, studies show follicular growth, improved vascularity, increased follicular and stromal cell proliferation and, at the same time, reduced apoptosis and cellular atresia. In refractory cases of Asherman's syndrome or endometrial atrophy for various reasons, studies have shown that instillation of autologous hematopoietic stem cells has had favorable results in endometrial regeneration and for the return of menstruation and fertility. **Conclusions.** Stem cell therapy offers solutions for dozens of women suffering from ovarian failure, reduced oocyte quality, premature menopause, infertility or endometrial pathology, such as Asherman's syndrome

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

Updates on head and neck cancers related to HPV infections

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We present a short update on head and neck cancers related to HPV infections. It is well known that there is a causal relationship between high-risk HPV strains and cervical cancer, but, in recent years, the role of HPV in oropharyngeal cancers has also been explored. To be able to identify an HPV infection, there are several methods: virological examination from the operative piece, p16 testing by immunohistochemistry, and HPV-DNA detection. A new method of detection is related to magnetic resonance imaging and suggests a correlation between the apparent diffusion coefficient (ADC) values on diffusion-weighted imaging (DWI) of primary tumor lesion and the HPV status in head and neck cancers. There are some studies about new methods of screening – HPV16 E6 seropositivity was present more than 10 years before the diagnosis of oropharyngeal cancers. Regarding the differences between HPV-positive and HPV-negative oropharyngeal cancers, we know that HPV-positive ones have a better prognosis and better treatment response rates. The HPV-negative cases are more frequently associated with smoking, alcohol consumption and genomic complexity. That's the reason why, in the 8th Edition of AJCC Cancer Staging Manual, the staging of HPV-associated cancer of the oropharynx was modified and gave a much more accurate and reasonable prediction of the survival for newly diagnosed patients. Related to the principles of treatment, the treatment of HPV-positive HNSCC includes surgical intervention, radiotherapy and chemotherapy, with very high success rates in early-stage disease. From our clinical experience, we made a study in which we enrolled 20 patients (10 HPV-positive cases and 10 HPV-negative cases) as a control group. The conclusions were: head and neck cancers were frequent in males no matter the HPV status; the HPV-positive group had a lower age incidence (50-60 years old) than the HPV-negative group; the association with smoking was less frequent in the HPV-positive group and, although the initial staging was almost the same between the both groups, the rate of survival was higher in the HPV-positive group.

Keywords: oropharyngeal cancer, human papillomavirus, p16 status, E6 protein, human papillomavirus screening, squamous cell carcinoma

HSIL at screening cytology. What to do?

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Cervical cancer is one of the most common malignant tumors affecting the female genital tract worldwide. Human papillomavirus (HPV) is the major etiological agent involved in the pathogenesis of cervical dysplasia and cervical cancer. Babeş-Papanicolaou cytology is an exfoliative cytology by which cells from the superficial layers of the epithelium are detached, displayed on a glass slide and stained. The current American Congress of Obstetricians and Gynecologists (ACOG) recommendations for cervical carcinoma screening in women depend on age, on HIV infection/immunodeficiency and on pregnancy status. Screening should be initiated at the age of 21 years old. Women between the ages of 21 and 29 should be screened by cytology every three years. Women between the ages of 30 and 65 should be screened with cytology and HPV co-testing every five years or cytology alone every three years. The risk of high-grade squamous intraepithelial lesion (HSIL) in a patient with a positive HPV test and an abnormal Pap smear is approximately 20% and increases to 33% if she is HPV positive at more than one visit. **Conclusions.** Educating patients about the risk factors for HPV exposure, as well as safe sex practices can reduce the risk of HPV infection. Vaccines have been developed against high-risk HPV types 16 and 18, as well as low-risk HPV types 6 and 11. Because most high-grade lesions are associated with HPV16, vaccination is predicted to reduce the incidence of HSIL/CIN2/CIN3 by up to 87%.

Keywords: HSIL, screening cytology, HPV

Bowel endometriosis – Bucharest Endometriosis Center experience

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Introduction. Endometriosis is a chronic, inflammatory, estrogen-dependent condition which affects approximately 10-15% of reproductive-aged women. Affecting up to 37% of women with endometriosis, bowel endometriosis is the most common site for extragenital endometriosis. We present our five-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 technique) specialists. In five years, we managed 1444 endometriosis cases in women with ages between 14 and 55 years old. All surgeries were done laparoscopically. **Results.** Among all our cases, 960 patients proved to have deep infiltrating endometriosis and 494 patients had bowel endometriosis. We emphasize the chosen types of excision, their location and the 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 to the bowel endometriosis split into three categories: shaving, disc resection and segmental resection. 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, who is able to diagnose and treat it accordingly, in a minimally invasive fashion.

Keywords: bowel endometriosis, resection, laparoscopy

Pudendal neuralgia – a common cause of pelvic pain

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Introduction. Pudendal neuralgia is a frequent condition which is often misdiagnosed. This delay in diagnosis happens because there is still no well-established specialty for this pathology. The main symptoms of pudendal neuralgia are long-term pelvic and perineal pain, radiating to the pelvic limb. Like endometriosis/adenomyosis (with which it is often associated), it manifests with pelvic and perineal pain. In contrast to (most of the time) the pain caused by endometriosis/adenomyosis, pudendal neuralgia causes a continuous, excruciating pain, that radically affects the patient's quality of life. **Method.** The treatment of this pathology can be conservative (drug treatment – neurological or antipsychotic medication), invasive (anesthetic block of the nerve) or surgical – laparoscopic decompression of the external pubic nerve. **Results.** The surgical approach – decompression of the pudendal nerve (right/left) – represents a laborious, meticulous intervention and requires a very good knowledge of the pelvic anatomy (vessels, muscles, nerves), as well as a correct surgical technique, based on an extensive experience. **Discussion and conclusions.** The surgical approach carries the highest chance of providing the appropriate treatment. As it worsens, this pathology is even more difficult to treat. Therefore, the surgery should not be postponed very much in these cases.

Keywords: pudendal nerve, pelvic pain, decompression

HPV latency – a new challenge

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Clinical and epidemiological studies suggest that after HPV infection the virus still persist in basal epithelial cells, although current diagnostic tests fail to detect it. Extensive work is performed to understand the mechanism by which HPV becomes detectable, after a period of undetectability. Current explanations include long-term persistence, a new acquired infection, autoinoculation and reactivation from a latent infection. Molecular evidence from animal models suggest that a latent HPV infection could be located in a limited number of cells from a distinct subset of basal epithelial cells. Extensive sampling of otherwise normal human cervices in patients with a history of cervical dysplasia also reveals small focal areas of HPV latent infection, randomly distributed. The existence of HPV latency provides a challenge for diagnosis, screening policies and therapeutic attitudes.

Keywords: HPV latency, latent infection, cervical dysplasia

Is fertility preservation a necessity before endometriosis surgical treatment?

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Endometriosis is a common cause of infertility. Personalized counseling regarding fertility preservation should be offered particularly to young women with a high risk of recurrence of endometriosis or to those with bilateral endometriomas. The surgical treatment of ovarian endometriosis consists in cystectomy. The methods used for preserving fertility in women with endometriosis are represented by oocyte or embryo cryopreservation. In this study, we reviewed the literature in order to investigate if fertility preservation is necessary before the surgical treatment of endometriomas. We concluded that more clinical data and economic analyses are needed in order to recommend fertility preservation as a routine procedure for all women before undergoing surgical treatment for endometriosis.

Keywords: fertility preservation, endometriosis, oocyte, cryopreservation, embryo cryopreservation

Variations of histological features of the microenvironment in HPV lesions of the genital tract

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This retrospective study involved the analysis of 5059 Pap smears recorded in our department. Of these, 11.3% exhibited a range of cytological abnormalities, including ASCUS to HSIL, as well as AGC. We collected clinicopathological data, including age, tobacco smoking history, abnormal vaginal secretion, paraclinical results, and details of surgical interventions, from the medical records. Among these cases, 23.7% underwent surgical interventions in our unit, which ranged from LOOP procedures to hysterectomies. For these cases, we conducted a reevaluation of histological slides to explore the inflammatory response in both the epithelial and stromal components. Our evaluation criteria remained consistent regardless of whether the lesions were squamous or glandular in origin. Some patients were lost to follow-up, while others adopted a "wait and see" approach. Our study revealed variations in the microenvironmental response, which were influenced by the histological subtype of the lesions and the specific HPV types involved. These variations encompassed the extent and intensity of the inflammatory infiltrate, the cellular subtype, the presence of angiogenic responses, and associated epithelial alterations in the surrounding areas. Given the well-established connection between the tumor microenvironment and the responses to immunotherapies, our findings underscore the need for further investigation into the variables associated with squamous and glandular lesions of the cervix. Such research may hold significant implications for the development of targeted therapies and treatment strategies in cervical pathology.

Keywords: HPV, microenvironment, inflammatory cells, CD4, CD8

PD-L1 expression in p16-positive oral squamous cell carcinomas

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Oral squamous cell carcinoma (OSCC) is a highly malignant disease, traditionally associated with risk factors such as alcohol and tobacco use. An increasing number of cases are now linked to human papillomavirus (HPV) infection. This study explores the expression of programmed death-ligand 1 (PD-L1) in HPV-positive OSCC cases and its association with clinicopathological features. A total of 11 cases of p16-positive OSCC were included in the study. PD-L1 expression was assessed using immunohistochemical techniques. Immunohistochemical scores were determined by the combined positive score (CPS) method. Histopathological features – including tumor subtype, grade and tumor-infiltrating lymphocytes (TIL) – were reviewed for all cases. PD-L1 expression was identified in four out of the 11 cases of OSCC, considering PD-L1 positive cases as those with a CPS score ≥1. Patients with both PD-L1-positive and p16-positive SCC exhibited higher tumor grades. Tumor-infiltrating lymphocytes were also more abundant in PD-L1 positive cases, compared to negative ones. The presence of PD-L1 expression in a subset of HPV-positive OSCC cases highlights the potential for immunotherapeutic interventions in these patients. The correlation between PD-L1 positivity, higher tumor grade and increased TIL suggests a complex interplay between the tumor microenvironment and the immune responses. Further research is needed to elucidate the clinical implications of these findings and to explore the role of immune checkpoint inhibitors in the treatment of HPV-positive OSCC. This study sheds light on the practical aspects of interpreting PD-L1 expression in HPV-positive OSCC. Understanding the relationship between PD-L1 expression and clinicopathological features can contribute to the development of more targeted and effective treatment strategies for this subset of OSCC patients.

Keywords: oral squamous cell carcinoma, PD-L1, p16, HPV

Adenomyosis and *in vitro* fertilization – controversies

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Adenomyosis has been reported to adversely impact fertility *via* abnormal uterine contractility, including altered endometrial function and receptivity, and impaired implantation. The sonographic features of adenomyosis, including the differential diagnosis between diffuse and focal adenomyosis and a uterine fibroid, are reviewed. We discuss the impact of uterine adenomyosis on *in vitro* fertilization (IVF)/intracytoplasmic sperm injection (ICSI) clinical outcomes and we also evaluate the impact of gonadotropin-releasing hormone agonist (GnRHa) and surgical treatments. The administration of GnRHa increased the implantation rate, the clinical pregnancy rate and the ongoing pregnancy rate of patients with adenomyosis in FET cycles. The adenomyosis tissue, which contained estrogen, progesterone and androgen receptors, develops in an estrogen-dependent manner. The administration of GnRHa can suppress the hypothalamic-pituitary axis, resulting in a hypoestrogenic status, and then suppress the proliferation of cells derived from the endometrium, reducing the size of pathologic lesions in patients with adenomyosis. With the increasing use of embryo freezing/thawing, the pre-treatment with GnRHa is recommended for adenomyosis patients in FET cycles. A novel oral GnRH antagonist, elagolix, has also been increasingly used to manage endometriosis and adenomyosis. Elagolix with add-back therapy significantly reduced heavy menstrual bleeding in women with uterine fibroids and coexisting adenomyosis, suggesting that elagolix's efficacy was not adversely affected by the presence of adenomyosis. The major part of the studies has not divided focal and diffuse adenomyosis, and this represents a relevant source of bias: studies conducted with standardized diagnostic criteria for adenomyosis are still needed to determine if the different clinical presentations of such condition could compromise IVF outcomes. We suggest screening for adenomyosis before embarking in medically assisted reproductive procedures. After an IVF failure, 3D ultrasound and MRI are recommended to rule out adenomyosis.

Keywords: adenomyosis, IVF, gonadotropin-releasing hormone agonist

New research directions in the therapy of endometriosis

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Introduction. Endometriosis is a chronic benign inflammatory disease, hormone-dependent, characterized by the presence of endometrial tissue in extrauterine areas, which affects one in ten women of reproductive age. **Method.** The current treatment is multimodal and addressed to the symptomatology, the goals being represented by the relief of pain, the prevention of infertility, but also the prevention of post-surgical disease recurrence. Different factors are involved in the pathogenesis of endometriotic implants, including: angiogenesis, inflammation, oxidative stress, estrogen production and decreased apoptosis. New drugs in the treatment of endometriosis are based on these factors and include: hormonal therapies, antiangiogenic drugs, inflammation inhibitors, immunomodulators, antioxidant agents and epigenetic inhibitors. The available treatments do not address endometriosis itself, but aim at alleviating the symptoms of the cause. The limitations of the current treatments (surgical and hormonal) involve a suppressive rather than curative approach, contraceptive rather than pro-fertility, limited therapies for deeply infiltrative cases or for disease with extrapelvic localization. **Conclusions.** Endometriosis is a multimodal disease which has a variety of treatments aimed at different ways of action, and it is important to identify a personalized management, precise in the functioning of the case. New research directions are looking for nonsurgical, nonhormonal and minimally invasive methods for the long-term disease control. The current approach involves improving the quality of life with minimal adverse effects and good long-term disease control.

Keywords: endometriosis, hormonal therapies, antiangiogenic drugs

Prevalence of vaginal HPV infection in adult girls from Durres in correlation with the dysplasia of column uteri

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Introduction. It is well known that there is a strong correlation between some HPV genotypes and dysplasia of column uteri. There are more than 100 types of human papillomavirus which can infect humans. This study was triggered by the start of HPV vaccination in 12-13-year-old girls, in September 2022, in Albania. Since 2017, there have been no figures on the spread or the existence of this infection, while the cases of cervical cell dysplasia have increased, and the mortality from cervical cancer ranks second in the female population of our country. **Objective.** To study the current situation of this pathology in young girls from our country, associated with the possibility of complications from HPV high-risk genotypes in the column and vagina. **Methodology.** Following the primary processing of patients' data, individuals at risk were separated and categorized according to age, clinical signs, and results of genotype. **Results.** The study, carried out between February 2022 and February 2023, included a random female population who presented for various gynecological complaints at the "Nena" Gynecological Clinic or referred for HPV testing. This resulted in 743 gynecological visits for various problems, with 84 patients with genital AF test, 90 cases with PAP tests, and 37 cases with HPV tests. The results indicated that in 30% of the presented cases we had a positive HPV test, and only 9% presented ASCUS cellular dysplasia at the PAP test. Of these 37 cases, there were nine low-risk cases and 28 high-risk cases. In the last group, the highest percentage was recorded for HPV 18 and 39, while the other cases presented mixed low- and high-risk strains. The age of the women presented for the HPV test was between 21 and 37 years old, 79% being under 27 years old.

Keywords: low-risk HPV, high-risk HPV, dysplasia, column uteri, young women

Impact of human papillomavirus infection on reproductive health

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Introduction. Infertility can be considered a condition with a multifactorial etiology, caused in approximately equal proportions by female and male factors or by unidentified factors. Worldwide, the primary cause of infertility is represented by sexually transmitted diseases. One of these viral infections is human papillomavirus (HPV). Contrary to the clinical importance of HPV in the development of genital tract carcinoma, little attention has been paid to the impact of HPV on fertility. **Methodology.** We studied the publications related to the implications and association of human papillomavirus on reproductive health. Literature analysis was performed on the electronic databases PubMed/Medline, Embase and ScienceDirect, considering the time interval from January 2000 to May 2023. The key terms included: "HPV semen infection", "HPV male infection", "HPV and infertility", "HPV-infected spermatozoa and fertilization", "HPV and fertility outcome". We considered randomized trials, observational and retrospective studies, original articles having as topic the relationship between HPV infection and the following items: reproductive health, infertility, and altered sperm parameters. **Results.** The literature search, based on previously mentioned key terms, identified a total of 85 papers eligible for this review. **Discussion and conclusions.** At this moment, it is well known that infertility men have a higher prevalence of seminal HPV infection, compared to the general population. Many original studies reported that HPV semen infection is related to reduced fertility both in natural and assisted reproduction. The impact of HPV genital tract infection in females on reproductive health is not very clear; however, the presence of the virus in embryos has been related to reduced pregnancy rate and can increase the abortion rate.

Keywords: HPV, semen, infertility, male, spermatozoa

Laparoscopic management of adenocarcinoma arising from rectovaginal endometriosis

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The reported incidence of malignant transformation of endometriosis is between 0.7% and 1% of patients. Eighty percent of endometriosis-associated malignancies occur in the ovaries, with only 20% occurring in extraovarian sites. Extragonadal malignancies arising from endometriosis are extremely rare. We report the case of a 42-year-old patient with clear cell carcinoma of the rectovaginal septum secondary to endometriosis, managed by primary radical laparoscopic surgery. Due to the rarity of such cases and the lack of adequate data, standard management guidelines are not available.

Keywords: rectovaginal endometriosis, adenocarcinoma, laparoscopic management

Implication of neuropeptides in endometriosis – clinical study and literature review

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Introduction. Endometriosis represents the presence of endometrial glands and stroma outside the uterus. The most encountered lesions can be identified on the ovaries (cysts), peritoneal lesions and superficial implants, or deep infiltrating endometriosis. It affects 10-15% of all women during their reproductive age and 70% of women with chronic pelvic pain, and it can have different etiologies. The latest studies have identified higher levels of serum kisspeptin in patients diagnosed with endometriosis. Kisspeptin was first described as a tumor metastasis suppressor of the melanoma cells. Later on, its function was linked to its receptor GPR54 and has been discovered to have effects on various cancers. **Materials and method.** We performed a prospective case-control study, between January 2021 and March 2023, in the "Elena Doamna" Clinical Hospital of Obstetrics and Gynecology, Iași. We selected patients with ages between 18 and 45 years old, with a Body Mass Index between 18.5 and 39 kg/m^2, and we divided them into two groups. The study group consisted in patients with endometriosis and primary/secondary infertility, and the control group was comprised patients with a normal reproductive life, without suspicions or diagnosis of endometriosis and at least with one child. All patients agreed to take part in this study and signed the consent form. During the follicular phase of their menstrual cycle, all patients accepted to have a sample of blood withdrawn. We tested the serum levels for LH, FSH, kisspeptin, estradiol, prolactin, testosterone, insulin and glycemia. All patients went through a clinical examination and pelvic ultrasound. **Results.** We enrolled 10 patients in each group and managed to identify significant differences between serum kisspeptin levels, but not statistically significant differences between other hormonal dosages. Patients in the study group had medical evidence (ultrasounds, MRI) for the presence of ovarian endometriomas, but none had a laparoscopic diagnosis performed. **Conclusions.** Although the hypothesis of kisspeptin playing its role as a suppressor in endometriosis has been highlighted, further research must be performed.

Keywords: endometriosis, kisspeptin, infertility

Immunology and genetics in endometriosis

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Endometriosis is a hormonal-dependent chronic disease, now being considered an inflammatory condition characterized by endometrium-like tissue at sites outside the uterus. Many etiopathogenic theories have been postulated, but we lack the complete understanding regarding its mechanisms. Multiple investigators have suggested that there is an association between the presence of endometriosis and an altered immune system, which allows the immune evasion of the ectopic endometrial tissue. This theory suggests that changes in cell-mediated immunity and humoral immunity may contribute to the development of the disease. In addition to alterations in cell-mediated immunity, considerable evidence has been gathered indicating that there are alterations in B-cell activity and an increased incidence of autoantibodies in women with endometriosis. Moreover, recent studies have suggested that there is a genetic predisposition towards the development and the evolution of endometriosis. Genome-wide association studies have revealed 23 genome-wide significant loci that are associated with the risk of endometriosis. The loci were either intergenic or in/near genes with known functions of biological relevance to endometriosis, varying from roles in developmental pathways to cellular growth/carcinogenesis. It seems that some loci have a stronger correlation with stage III/IV cases, implying that they are likely to be implicated in the development of moderate to severe or ovarian disease. For the moment, the recommendation of the European Society of Human Reproduction and Embryology (ESHRE) is for clinicians not to use biomarkers in plasma, urine or serum to diagnose endometriosis, but blood, tissue/endometrial and urine biomarkers could, in the near future, serve as markers for the diagnosis and stratification of patients, for assessing the therapeutic efficacy, for establishing the best treatment option, the drug design, or recurrence markers for endometriosis.

Keywords: endometriosis, adenomyosis, inflammation, immune response, immune disorders, immune evasion, genetic predisposition, genetic markers

Changes in the vaginal microbiota caused by HPV infection in women from the region of Moldova

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Introduction. The heterogeneity of the vaginal microbiota can be assessed in both pathological and non-pathological conditions and may vary according to various factors, such as biological and environmental ones. Vaginal microbiota could play a considerable role in HPV (human papillomavirus) infection and in the genesis of HPV-induced cervical tumors. We aim to investigate whether the composition of the vaginal microbiota differs according to HPV status. **Materials and method.** A total of 110 women from the region of Moldova were enrolled in this study. Vaginal swabs were collected. Viral testing was performed using the Roche Linear Array HPV Genotyping Test. The V3-V4-V6 region of the 16S rDNA gene was amplified by polymerase chain reaction (PCR) followed by Illumina MiSeq sequencing. **Results.** The phylum *Gardnerella*, *Prevotella*, *Atopobium vaginae*, and *Atopobium* was more represented in HPV-positive patients. *Lactobacilli* represented the dominant genus, with a high percentage of *Lactobacilli iners*, being more abundant in HPV-negative patients. Patients with normal cytology and HPV positive have a lower number of *Lactobacillus vaginae*, *Lactobacillus iners*, *Ureaplasma* and *Prevotella*, but with a higher number of cases with *Gardnerella* infection compared to patients with normal cytology and HPV negative. **Conclusions.** An altered vaginal microbiota could play an important role in cervical HPV infection, in persistence or clearance. A better understanding of the vaginal microbiota could be a key element in achieving complete viral clearance in highly affected populations.

Keywords: HPV, vaginal microbiota, cervical cancer

Cervical cancer screening – how can we raise compliance?

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Cervical cancer represents one of the biggest health issues in Romania – as we still remain the second European country in both incidence and mortality rates, mainly due to poor results regarding both screening and vaccination. The main reasons for low screening coverage are: the patient's belief that screening procedures are invasive and produce physical discomfort, low medical education, religious and cultural factors, lack of time, inconvenient clinic hours, and lack of transportations. We need to either change the women's views on cervical testing, or to find alternate methods of screening. Urinary HPV testing seems to be a good enough method of screening, with higher chances of patients' compliance.

Keywords: HPV, cervical screening, cervical cancer, urinary testing

A systematic literature review on the efficacy and safety of HPV vaccination and national immunization programs in Europe

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Introduction. Since the introduction of human papillomavirus (HPV) vaccines, several studies have been conducted in different countries to assess HPV knowledge and vaccine acceptance. Europe is increasingly described as the region in the world with the least confidence in vaccination, and particularly in the safety of vaccines. The aim of this systematic literature review was to gather and summarize all peer-reviewed and grey literature published about human papillomavirus vaccine immunization programs in Europe and describe some studies regarding the safety and efficacy of HPV vaccine. **Methodology.** A systematic literature review was conducted for studies published between 2005 and 2022. **Results.** A total of 117 articles were included in the review. By 2019, most European countries had introduced HPV vaccination in their national immunization programs. Fifty percent of countries introduced HPV vaccination within the first three years after the European Commission granted a license for human use of the first HPV vaccines, in 2006-2007, and the remaining countries have progressively introduced vaccination in the last five years. Virtually all countries in Europe currently have an HPV vaccination program targeting pre-adolescent girls. A growing number of the member states are considering or have already adopted gender-neutral HPV vaccination. The extension of HPV vaccination to pre-adolescent males can further improve the indirect protection of unvaccinated girls and women through herd immunity and can directly prevent HPV-related conditions in men, including men who have sex with other men. **Conclusions.** HPV vaccine coverage should be monitored and included in national immunization data reporting systems, registries and periodic surveys. All countries should consider developing population-based cancer registries or specific cervical cancer registries and improve links between immunization and screening services and cancer registries in order to measure the impact of vaccination and of the cervical cancer prevention programs.

Keywords: HPV, HPV vaccination in Europe, cervical cancer, HPV vaccine

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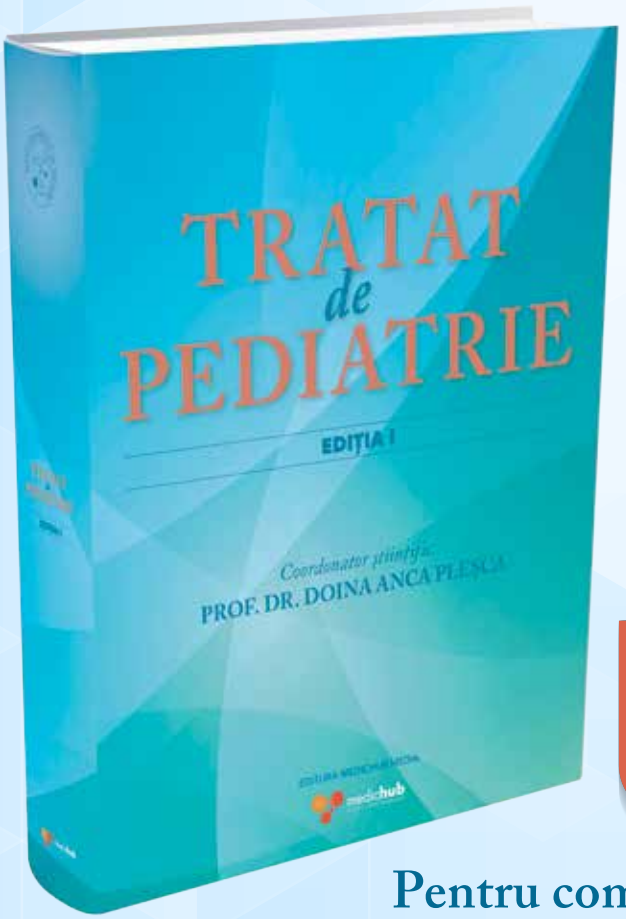

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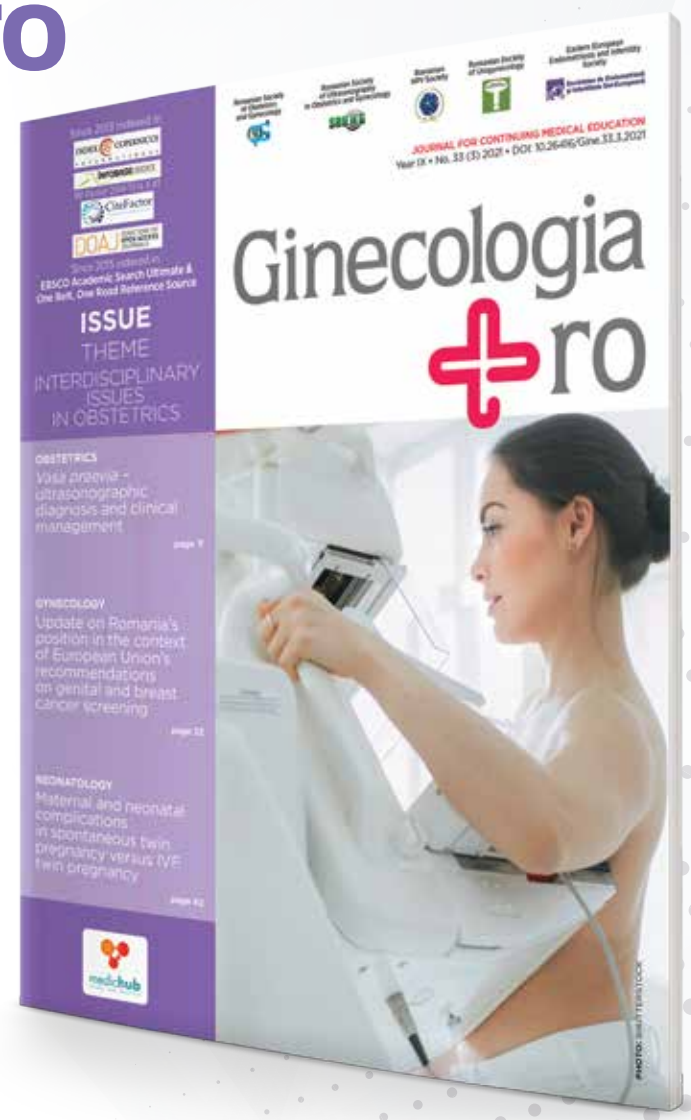

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