

OBSTETRICS AND GYNECOLOGY

ORAL PRESENTATIONS

MATERNAL SERUM SCREENING IN PLEVEN REGION – A REVIEW OF CLINICAL LABORATORY EXPERIENCE FOR EIGHT YEAR PERIOD

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Summary

The most reliable approaches for prevention of congenital anomalies are antenatal screening programs and prenatal diagnosis. Nowadays, maternal serum screening (MSS) is the most widely used method for early detection of common chromosomal aneuploidies, such as Down syndrome (DS). This study aimed to present the experience of our laboratory for eight years (2011-2018), after initiating MSS. The method is a fluorimetric dual assay, and the risk is calculated by specialized software. A total of 7829 women were tested (14% of them were above the age of 36 years) and physicians from the Pleven region referred most of the women (95%). For the study period, 2729 women underwent MSS only in the second trimester, 3386 women - MSS only in the first trimester, and 1714 women had both MSS. A high risk

for DS was calculated in 2.3% (78/3386) of the women who had only early MSS, and 8.8% (241/2729) of the women who had only a late MSS. Among the women who underwent Sequential Screening, a high integrated risk was calculated in 5% (34/1714) of the cases. In the high-risk cases, a prenatal genetic test was recommended. The detection rate for DS in the risk group of women above 36 years was 6% on the average and higher (to 10%), particularly for women with an early MSS. MSS is still the most accessible and inexpensive approach for mass prevention of DS. Sequential Screening decreases positive screening rate of the test and unnecessary invasive procedures.

Key words: maternal serum screening (MSS), Down syndrome (DS)

HYSTEROSCOPIC MORCELLATION – A CONTEMPORARY ALTERNATIVE IN THE TREATMENT OF SUBMUCOUS MYOMAS

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Summary

The study aimed to analyze the intraoperative parameters of hysteroscopic morcellation (HM) and conventional resectoscopy in the treatment of submucous myomas. A prospective study from February 2015 to February 2017 included 66 patients with ultrasound imaging of submucous

myomas. Of them, 26 (39.4%) underwent HM and 40 (60.6%) – hysteroscopic resection (HR). For the study, myomas were divided into two groups - according to their size and type. We analyzed the following intraoperative parameters: total duration of the procedure, total operative time, time for dilation, operative time for HM/HR (actual operative time), the total amount of fluid distension media, and fluid deficit. The mean operative time, measured as “total duration of the procedure”, “total operative time” and “actual operative time”, was significantly shorter in the HM group, as compared to HR – 25.12 and 51.13 min ($p<0.001$), 21.69 and 45.20 min ($p<0.001$), 17.12 and 38.85 min (0.001) respectively. The total amount of fluid distension media was trustworthy lower in the HM group compared to HR, 2690.00 ml and 7743.50 ml ($p<0.001$), respectively, as well as for the parameter “fluid deficit” 238.08 ml and 832.75 ml ($p<0.001$) respectively. In conclusion, HM is a possible alternative to conventional resectoscopy for removal of submucous myomas with the favourable perioperative outcome, but further research is needed regarding some preoperative approaches that increase its effectiveness.

Key words: hysteroscopic morcellation, hysteroscopic resection, submucous myomas

COLD LOOP MYOMECTOMY AS A SAFE AND FEASIBLE SINGLE-STEP HYSTEROSCOPIC TECHNIQUE FOR REMOVAL OF G1 AND G2 SUBMUCOUS MYOMAS: OUR CASES

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Summary

The biggest challenge in hysteroscopic surgery have been and still are the submucous myomas. Submucous myomas, which account for approximately 5% to 16% of all uterine fibroids, are a common structural cause of abnormal uterine bleeding and infertility. Hysteroscopic myomectomy currently represents the best minimally invasive surgical procedure for their removal. We present cold loop myomectomy as a safe and feasible hysteroscopic technique for one-step removing of G1 and G2 submucous myomas. Complete removal of G1 and G2 submucous fibroids using a monopolar (electrical) resectoscope and a cold loop is presented. Hysteroscopic treatment of submucous fibroids G1 and G2 has always been a challenge for surgeons because of the possibility to complete the myomectomy as a single-step procedure. The mechanical approach by using a cold loop to enucleate the intramural portion of fibroids avoids the unnecessary extensive electrical cut, thermal injury of the adjacent myometrium, and fibrosis in the area of surgical intervention. At the same time, the combination of electrical (slicing) and non-electrical (cold) loops provides a single-step complete resection of G1 and G2 submucous fibroids. In conclusion, cold loop hysteroscopic myomectomy seems to be a feasible, safe and effective method of choice for complete removal of G1 and G2 myomas in a one-step procedure, at the same time sparing the surrounding healthy myometrium and the myoma’s pseudocapsule.

Key words: submucous myoma, cold loop myomectomy, hysteroscopic resection

DIAGNOSIS AND TREATMENT OF PRECANCEROUS CONDITIONS OF THE CERVIX

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Summary

Cervical cancer is the most common type of carcinoma of the female reproductive system. The yearly incidence in Bulgaria is 10:100000. It affects women in the age range of 30 - 50 years, and it is becoming more common in females below that age. Worldwide screening for cervical cancer leads to a reduction of the cases of invasive carcinoma as opposed to Bulgaria, where the tendency shows an increase of newly diagnosed patients.

Cervical precancerous lesions include CINI, CIN II, CINIII, and Ca colli uteri in situ. The main reasons for the development of these changes are chronic infections with oncogenic viruses HPV and HSV type II. The principle diagnostic methods are cytologic examination, also known as PAP test by Papanicolau, colposcopy and targeted biopsy. LLETZ (large loop excision of transformation zone) is considered a method for treatment of premalignant lesions up to CIN II, cervical conization is performed as a diagnostic or treatment procedure for CIN III and Ca in situ. A retrospective study was conducted in HinKoMed Medical centre – Pleven and Saint Marina University Hospital for two years. It included 128 women, aged 16 to 73 years. The results of the diagnostic procedures and pathohistological analysis performed were compared and analyzed. In 23 (31%) of all 74 patients with PAP I and II, atypical colposcopic

findings in the transformation zone were detected, and cervical precancerous lesions were proved pathohistologically. Combined application of the established diagnostic procedures allows performing of organ-preserving interventions in women with precancerous lesions of the cervix.

Key words: cervical precancerous lesion, colposcopy, cytology screening, LLETZ, conization

**SURGICAL METHODS FOR
TREATMENT OF UTERINE MYOMAS**

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Summary

Myomas are the most common benign tumours of the female reproductive system and occur in over 30% of women. In recent years, with the birth postponement of the modern woman, the need for conservative treatment of myomas and the application of organ-preserving surgery is necessary. Therapeutic procedures include the use of classical abdominal approach and minimally invasive surgical techniques - standard endoscopic approach and robot-assisted laparoscopy. From June 2016 to May 2019, 814 myomectomies were included in a retrospective study conducted at Saint Marina University Hospital – Pleven, Bulgaria. Of these, 483 were performed laparoscopically. In

331 cases, an abdominal approach was used. We analyzed the following parameters: total duration of the operative procedure, actual operative time, clinical and histological characteristics of the myomas, paraclinical parameters, and postoperative hospital stay. Laparoscopic myomectomy is an acceptable surgical method due to its short duration, low blood loss, shorter length of hospital stay, and patient comfort.

Key words: uterine myomas, laparoscopic myomectomy, abdominal myomectomy

COMPARISON OF MEDICO-SOCIAL AND OBSTETRIC CHARACTERISTICS OF WOMEN IN CHILDBIRTH IN 3 AGE GROUPS: UNDER 19, 20-35 AND OVER 35 YEARS OF AGE

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Summary

We aimed to compare the medico-social and obstetric characteristics of women in childbirth in three age groups: under 19, 20-35 and over 35 years of age. A case-control study was carried out in 2017 at the University Hospital – Pleven. The study included 1212 women in childbirth and 1212 live-born babies after

single pregnancies. The women were divided into three age groups: under 19 (n=193), 20-35 (n=862), and over 35 years (n=157). The live-born infants were divided into two groups: cases (preterm low-birth-weight babies) and controls (full-term newborns with normal birth weight). The role of 34 risk factors on pregnancy, birth and newborn was studied. The proportions of unemployed (86.46%), unmarried (97.93%), low-educated (92.75%), anaemia (24.34%) and maternal pelvic size abnormalities (9.84%) were significantly higher in women in childbirth under 19. The average birth weight (3020±546 g) and birth length (49 cm, 39÷56) were lower in the youngest women. The proportions of family history (19.87%), previous surgical operations (32.88%) and previous abortions (37.6%), preeclampsia (9.55%), Cesarean births (54.78%), breech presentation (8.00%) were significantly higher in women in childbirth over 35. The women in childbirth under 19 and over 35 are risk groups for pregnancy, childbirth and health status of the newborn.

Key words: medico-social characteristics, obstetric characteristics, women in childbirth, age groups

A CASE-CONTROL STUDY OF OBSTETRIC RISK FACTORS FOR LOW BIRTH WEIGHTS AND PRETERM BIRTHS

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Summary

We aimed to study the role of obstetric risk factors for low birth weight and preterm birth. The case-control study was carried out in 2017 at the University Hospital – Pleven, with 1212 women in childbirth and 1212 live-born babies after single pregnancies included. The live-born infants were divided into two groups. The cases involved the preterm low-birth-weight (PLBW) newborns weighing less than 2500 grams (g). The controls were full-term newborns with normal birth weight (FTNBW). We did not include 37 full-term low-birth-weight (FTLBW) newborns and 100 preterm births with normal birth weight (PNBW) newborns in the study to control confounding effects. The role of 8 obstetric risk factors (RFs) on PLBW was studied (maternal age, type of birth, amniotic fluid deficiency and congenital abnormalities, maternal pelvic size abnormalities, placental abnormalities, abnormalities of fetal membranes, umbilical cord abnormalities, and presentation of the fetus). The obstetric RFs (except abnormalities of fetal membranes and umbilical cord abnormalities) were significantly associated with PLBW ($p < 0.05$). The risks of PLBW were significantly higher ($p = 0.001$) in breech presentation ($\exp(\beta) = 6.622$), placental abnormalities ($\exp(\beta) = 5.556$), maternal pelvic size abnormalities ($\exp(\beta) = 4.426$) and amniotic fluid deficiency and congenital abnormalities ($\exp(\beta) = 2.903$). The results of that study can be useful for effecting prevention programming of pregnancy and prematurity. Thus, the risk of preterm births would be minimized, as well as adverse health outcomes, economic and social consequences for premature children and their families, health system and society.

Key words: obstetric risk factors, women in childbirth, preterm low-birth-weight newborns

CLINICAL DECISION MAKING BASED ON THE SFLT-1/PLGF RATIO TEST FOR PRE-ECLAMPSIA IN SCREEN-POSITIVE WOMEN - A CASE REPORT

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Summary

Pre-eclampsia is characterized by hypertension and proteinuria after the 20th gestational week, and it is a major cause of maternal, perinatal morbidity and mortality during pregnancy. The incidence on a global scale is a subject of discussions, but it is accepted in the last years that it has affected between 2% and 8% of all pregnancies. The pre-eclampsia is divided into early (before 34th gestational week), and late (after 34th gestational week), and 42% of all pre-term deliveries are correlated to pre-eclampsia. Despite intense research efforts, the pathogenesis

of pre-eclampsia is still a mystery, and it is mostly multifactorial. It is known that the beginning of the condition is in the placenta, while its target is the maternal endothelium. Several markers were studied to determine their role in calculating the risk for development of pre-eclampsia, for the introduction of combined screening and improvement of its predictive value. We present a case of 30-year-old tertiparous woman with high-risk for developing severe pre-eclampsia, in which we used sFlt-1/PIGF ratio for optimal management of the pregnancy. The presented case demonstrated the benefit of evaluation of the sFlt-1/PIGF ratio that may allow optimal management in women at high risk of pre-eclampsia. Further studies are necessary for assessment of the reliability of the sFlt-1/PIGF ratio test for prediction, diagnosis, and prognosis of pre-eclampsia.

Key words: pre-eclampsia, sFlt-1/PIGF ratio, adverse pregnancy outcome

POSTERS

GESTATIONAL HYPERTENSION: CURRENT IMMUNOLOGICAL MARKERS AND FUTURE TRENDS

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Summary

Gestational hypertension (GH) is the development of new hypertension in a pregnant

woman after 20 weeks' gestation without the presence of protein in the urine or other signs of pre-eclampsia. GH is defined as having blood pressure higher than 140/90 on two separate occasions at least 6 hours apart. Despite the current intensive search of tools for early detection and prognosis of GH, no routine tests have been established yet.

Immunological markers were used to indicate an abnormal immune response. In GH, they were grouped into the following categories: anti-cardiolipin autoantibodies, trophoblast-induced cell-mediated immunity, C3 and C4 complement components, serum immunoglobulins IgA, IgG, IgM, interleukin (IL)-6, IL4, IL5, IL12, IL10, IL8, IL1-beta, interferon (IFN)-gamma, tumor necrosis factor (TNF)-alpha and beta, and transforming growth factor (TGF)-beta. These molecules showed low predictive values as individual markers. Moreover, the sensitivity of a single molecule tended to be very low. When a combined model was used, the predictive value was higher. Therefore, there is an urgent need for high quality, novel research in immunological markers for GH, so that the best predictive strategy can be identified to improve the management of women in high risk for development GH. A single immunological marker predicting GH has not been discovered yet. However, a combined model, using immunological markers and uterine artery Doppler assessment would eventually be more sensitive and specific. More extensive studies are needed to clarify the possible use of immunological markers as GH predictive markers, possibly in combination with an echographic examination.

Key words: gestational hypertension; immunological markers

GLUTATHIONE PEROXIDASE ACTIVITY AND GLUTATHIONE CONTENT OF SPERM IN MALES WITH UNEXPLAINED INFERTILITY

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Summary

Our study aimed to investigate glutathione peroxidase (GPx) activity and glutathione (GSH) levels in the sperm of patients with unexplained infertility. Sperm samples were collected from male subjects with normal semen parameters divided into two groups: fertile males (n=23), mean age 34.6±6.2 years; infertile males (n=24), mean age 35.1±5.9 years. Sperm analysis was performed according to the 2010 WHO criteria and Kruger's strict criteria. Measurement of the GPx activity and GSH were performed by standard enzymatic assay kits. We found significantly higher GSH levels in the seminal plasma in the fertile group, as compared to the infertile (p=0.045). For intracellular GSH, the difference was close to significant (p=0.057). We found a positive correlation between the GSH levels in the seminal plasma and intracellular GSH. No significant differences were detected in the activity of GPx. An interesting deviation from the conventional was the higher enzyme activity recorded in spermatozoa and seminal plasma in the infertile group, with the significance very close to statistical (p=0.054 for seminal plasma and p=0.086 for the spermatozoa). One other cause of unexplained infertility is oxidative stress. In normospermic patients with unexplained fertility, the level of glutathione was reduced, and the activity of one of the significant enzyme antioxidants - GPx, was not significantly changed, and even showed a tendency to rise. We need a more significant number of samples to confirm this finding in further studies.

Key words: oxidative stress, glutathione (GSH), glutathione peroxidase (GPx), unexplained male infertility.

LEVELS OF MMP₂, TIMP₁ AND TIMP₂ IN FOLLICULAR FLUIDS IN WOMEN UNDERGOING IN VITRO FERTILIZATION AND THEIR RELATIONSHIP TO OOCYTE QUALITY

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Summary

Finding an accurate marker to determine the quality of the oocytes and embryos is essential for the success of assisted reproduction. Recently, the critical role of matrix metalloproteinases (MMPs) has been identified in follicular development and subsequent ovulation. Currently, a limited number of studies have examined intrafollicular, and serum MMP levels and the conclusions of these studies are quite controversial. Although the role of MMP in ovarian tissue remodelling during folliculogenesis has been well studied, the relationship between matrix protease activity and its inhibitors and ageing of the oocytes is still unclear. The present study aimed to establish the probable relationship between the expression levels of MMP-2 and TIMP-1 and TIMP-2 in follicular fluid with the degree of oocyte maturity and quality. Follicular fluids from 20 women, collected on the day of follicular puncture, were tested for the presence of MMP-2, TIMP-1 and TIMP-2 using Enzyme-Linked Immunosorbent Assay (ELISA). The oocytes obtained were described in terms of maturity, morphology and fertilization, as well as the embryo's quality and rate of development. Based on our results, we can conclude that MMP-2 concentration in follicular fluids during the IVF / ICSI procedure has a significant relationship with oocyte maturation

levels. The concentration is significantly higher in the case of immature oocytes. On the other hand, oocytes with normal morphology are associated with a significantly higher MMP-2 concentration in follicular fluids. Regarding the concentration level of TIMP 1 and TIMP 2, no significant differences were found for any of the studied groups.

Key words: MMP2, TIMP1, TIMP2, quality of the oocytes and embryos, follicular fluid

PREVALENCE OF RUBELLA IGG ANTIBODIES AMONG PREGNANT WOMEN - APPROACH FOR MONITORING OF PREGNANCY

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Summary

The teratogenic effect of Rubella virus determines the importance of rubella infection as a public healthcare problem during pregnancy. The study aimed to evaluate the prevalence of IgG antibodies against Rubella virus in a population of pregnant women, hospitalized in the Clinic of Obstetrics and Gynecology, of the University Hospital in Pleven, Bulgaria. A prospective cross-sectional study was carried out on pregnant women admitted to the Clinic. Demographic data of participants (age, education, occupation, location of residence) was collected via interview. Health status details were obtained from medical documentation. Quantitative determination of specific immunoglobulin G (IgG) antibodies against the rubella virus was performed by enzyme-like immunosorbent assay (ELISA), and UVmax kinetic microplate

reader was used. This study was carried out on a scientific research Project № 1/2018 funded by the Medical University, Pleven, Bulgaria. Between January 2018 and December 2018, we collected and tested 242 serum samples for Rubella virus IgG antibodies. The age of the women was between 14 and 45 years, average 27, $sd \pm 6.429$. The overall seroprevalence of rubella was 84.3% (n=204), the negative samples were 11.98% (n=29) and 3.72% (n=9) samples were equivocal. High seropositivity was reported in the age group between 21-30 years – 107 (89.92%). The seroprevalence of rubella virus was found to be high. About 12% of the pregnant women were not immune and represented the susceptible group. Elimination of rubella and congenital rubella syndrome requires improvement of surveillance of the disease at all levels of the healthcare system.

Key words: prevalence, Rubella IgG antibodies, pregnant women

A RARE CASE OF MITOTICALLY ACTIVE CELLULAR FIBROMA OF THE OVARY

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Summary

Ovarian fibromas are the most frequent benign stromal tumours, composed of spindle/ovoid fibroblastic cells producing collagen. They account for 4% of all ovarian neoplasms. Approximately 10% of fibromas exhibit

increased cellularity with a small amount of collagen. In cases with mild nuclear atypia, they are referred to as cellular fibromas. However, a cellular fibroma may show significant mitotic rate and should be named as mitotically active cellular fibroma (MACF) and is categorized as a benign ovarian tumour, representing a relatively new disease entity. The natural history of MACF is still somewhat unknown and appropriate guidelines for diagnosing, and treatment remains undetermined due to the limited number of case reports. The distinction of MACF from fibrosarcoma and granulosa cell tumour is crucial because of the difference in treatment strategies and prognosis. We report the clinical and pathological characteristics of a rare case of ovarian MACF in a 68-year-old patient, initially diagnosed as a granulosa cell tumour. We believe that it is essential to report and describe such rare tumours in detail because this would help to determine the clinical and morphological features of these tumours. The extended follow-up of patients with MACF is also of great importance because it could provide information about the predictive value of the morphological features.

Key words: mitotically active cellular fibroma, cellular, fibrosarcoma

PREMATURITY – INCIDENCE, MORBIDITY, OUTCOMES

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Summary

The aim of the study was to analyze the incidences, complications and outcomes of prematurity in the University Hospital of Pleven. A retrospective analysis of all preterm babies, born from 01/01/2018 to 31/12/2018 was performed. Patients were divided into two groups: 1 (≤ 33 gestational weeks – GWs) and 2 (34-36 GWs). The criteria studied were: mechanism of conception, ante- and intrapartum history, gestational age (GA), sex, anthropometric data at birth, morbidity, hospital stay, and outcome. During the studied period, 1154 neonates were born. One hundred thirty-nine of them (12%) were premature – 71 in Group 1 and 68 in Group 2. Factors compromising the fetal condition were established in 64.8% of the newborns. Two-thirds of all babies were delivered via Caesarean Section, and one-third was twins. At discharge, 68.4% were healthy, 20.1% - with residual problems, and 11.5% died. Group 1 differed significantly from Group 2 concerning the rate of corticosteroid prophylaxis (42.3 vs. 5.9%), premature rupture of amniotic membranes – PRAM (33.8 vs. 13.2%), need of intubation in the delivery room (33.8 vs. 1.5%), hospital stay (20 \pm 17 vs. 8 \pm 4) and outcome (Group 1 included all the deceased). Despite the higher incidence of PRAM in Group 1, the rate of congenital infections in the both groups was similar. The incidence of prematurity in our hospital was higher than the country average (10.8%). Multiple pregnancies and insufficient outpatient monitoring were the main risk factors. Mortality and morbidity were inversely proportional to the GA and the neonates in the highest risk were those born before 34th GW.

Key words: newborn, preterm, follow-up