

Abstract Book

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## Controversies in Human Reproduction

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# Oral Presentations





## Oral Presentations I

### OP1

#### AGEING REGULATES RECEPTIVITY OF THE HUMAN ENDOMETRIUM

**Panagiota Meramveliotaki<sup>1</sup>**, Fanourios Makrygiannakis<sup>1,2</sup>, Maria Marmara<sup>1,2</sup>, Thomas Vrekoussis<sup>2</sup>, Dragana Nikitovic<sup>1</sup>, Antonios Makrigiannakis<sup>2</sup> and Aikaterini Berdiaki<sup>1</sup>

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**Background and aims:** Our previous published work proved a negative association of increasing women's age and endometrial proliferation and decidualization. Decidualization, endometrial preparation for successful embryo implantation involves the change in expression of receptivity factors. The effect of female ageing on the expression of receptivity factors in the endometrium, remains unclear. The aim of this study was to correlate increasing age with protein expression of receptivity factors osteopontin (OPN), CD44, and HOXA10.

**Methods:** Endometrial biopsies were collected from women aged 25–46 years, stroma cells were isolated at the proliferative phase of the menstrual cycle. OPN, CD44 and HOXA10 mRNA and protein expression were analysed using quantitative PCR (qRT-PCR) and Western blot, respectively.

**Results:** Results reported a statistically significant decrease in mRNA expression of OPN and HOXA10 ( $p = 0.03158$  and  $p = 0.02578$ , respectively) with increasing age. In addition, significant decrease of the same proteins was detected (OPN:  $p < 0.01$ ; HOXA10:  $p < 0.05$ , respectively). CD44 levels did not change with age.

**Conclusions:** In summary, decreased expression of receptivity factors with age, in human endometrial stromal cells, was evident. Further investigation on expression of different endometrial receptivity factors' changes with increasing age could aid the identification of targets for diagnosis and therapy of human infertility.





## OP2

### MANAGEMENT OF A RARE CASE OF C3 GLOMERULOPATHY DURING PREGNANCY: A CASE-BASED REVIEW

**K. Kalligianni Sofikiti<sup>1</sup>**, F. Makrygiannakis<sup>1</sup>, I. Tzanaki<sup>1</sup>, M. Rasidaki<sup>1</sup>, S. Koustas<sup>1</sup>, G. Andreadakis<sup>1</sup>, A. Makrigiannakis<sup>1</sup>

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**BACKGROUND:** C3 glomerulopathy (C3G) is a rare complement-mediated renal disease characterized by abnormal activation of the alternative complement pathway. Its presence in pregnancy poses significant diagnostic and therapeutic challenges and is associated with increased risk for preeclampsia, fetal growth restriction, and progression to end-stage renal disease.

**CASE PRESENTATION:** We present the case of a 40-year-old woman with biopsy-proven C3 glomerulonephritis, positive anti-Ro/La antibodies, and isolated antiphospholipid antibody positivity. The patient achieved pregnancy via IVF and was closely monitored throughout gestation. Baseline renal function was impaired. Antihypertensive and immunomodulatory therapy included methyldopa, hydroxychloroquine, aspirin, and low molecular weight heparin.

**METHODS AND RESULTS:** At 37+3 weeks, she underwent an emergency cesarean section due to a non-reassuring NST. Intraoperative findings included a five-times wrapped umbilical cord and a true knot of the umbilical cord. Postoperatively, she developed acute kidney injury, requiring careful fluid balance, antihypertensive titration, and nephroprotective measures. No dialysis was required. A flare or relapse of C3G was suspected postpartum, and initiation of targeted therapy with iptacopan was planned.

**CONCLUSION:** Optimal management of C3G requires a multidisciplinary approach, strict blood pressure control, avoidance of nephrotoxins, and personalized therapy based on complement pathway dysregulation. This case underscores the complexity of C3G in pregnancy and highlights the need for early recognition, tailored treatment, and postpartum follow-up to mitigate maternal and fetal risks. Emerging treatments like iptacopan offer targeted modulation of the complement system with potential benefits in high-risk cases.





### OP3

#### **Placenta Previa cases management: Cases report and literature review**

**M. Charitou,** G. Iakovidou, I. Tzanaki, K. Kalligianni, F. Makrygiannakis, G. Andreadakis, T. Vrekoussis, A. Makrigiannakis

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**Background and Aims:** Placenta previa describes a placental coverage of the internal cervical os, occurring in approximately 0.3% to 2% of third-trimester pregnancies. It is closely associated with the placenta accreta spectrum, abnormal placental invasion into the uterine wall or adjacent organs, which significantly increases maternal morbidity and mortality. The aim is to present the management of placenta previa cases at the Obstetrics and Gynaecology clinic of the University General Hospital of Crete.

**Methods:** Following diagnosis and if asymptomatic admission occurs during the 28th week of gestation, otherwise on symptom onset. The inpatient management includes ultrasound and MRI imaging, for placental invasion status determination. Symptomatic treatment involves potential intravenous analgesics, antibiotics, tocolytics, corticosteroids for fetal lung maturation, blood transfusions etc. Persistent symptoms may necessitate an emergency Caesarean section, although most cases are electively delivered between 32 and 36 gestational weeks. Due to the diverse severity level, preparation for operation requires a team effort and cooperation with other medical specialties such as Radiologists, Urologists and General Surgeons. The most skilled Obstetrics and Gynaecology physician carries out the operation with a trained team. Many operation techniques are described in literature, thus the procedure is carried out usually by preoperative placement of bilateral ureteral stents, a pfannenstiel incision, careful and extensive detachment of the vesicouterine pouch with the bladder from the uterus, transverse uterine incision, careful placental removal, curettage and uterine suturing.

**Results:** Hospital admission, imaging, intravenous medication, peri-operative care and Caesarean section operation are the clinic's standard of care. Newborns can be admitted in NICU, if deemed necessary.

**Conclusion:** In conclusion, placenta previa is a condition that requires multidisciplinary management because it can lead to premature birth, fetal and/or maternal morbidity and mortality.





#### OP4

### RECOGNITION AND MANAGEMENT OF HELLP SYNDROME IN THE SECOND TRIMESTER: A RARE CLINICAL CASE REPORT

**E. Kouloulia**, K. Kalligianni, A. Kouvalakis, V. Mytaras, M. Rasidaki, A. Makrigiannakis  
*Obstetrics And Gynaecology Department Of University Hospital Of Crete*

#### BACKGROUND AND AIMS:

HELLP syndrome, defined by Hemolysis, Elevated Liver enzymes, and Low Platelet count, is a life-threatening complication usually linked to severe preeclampsia. Though commonly developing in the third trimester, it may rarely present before 20 weeks of gestation.

**METHODS:** A 32-year-old primigravida at 19 weeks presented with headache, dyspnea, vomiting, chest pain, and subsequent seizures. Initial investigations excluded cardiopulmonary pathology, but alarming laboratory findings suggested HELLP syndrome. She was stabilized with magnesium sulfate, crystalloids, and antihypertensives before transfer to a tertiary center. On admission, she showed severe thrombocytopenia, hemolysis, liver dysfunction, proteinuria, and renal impairment. Fetal evaluation confirmed a live intrauterine pregnancy.

**RESULTS:** An emergency cesarean section for termination of pregnancy was performed, followed by ICU admission. Postoperatively, the patient required transfusions, intubation, and further evaluation to exclude thrombotic thrombocytopenic purpura (TTP). Plasmapheresis and corticosteroids were initiated. Complications included failed extubation attempts due to seizures and respiratory compromise. Imaging revealed Posterior Reversible Encephalopathy Syndrome (PRES). After four days, successful extubation was achieved, and the patient stabilized on oral antihypertensives. TTP was later excluded. She was transferred to the obstetrics department for continued care and subsequently repatriated for ongoing hospitalization.

#### CONCLUSION:

HELLP syndrome during the second trimester is exceptionally rare and carries high maternal and fetal risks. Prompt recognition, multidisciplinary intervention, and aggressive management are critical for improving outcomes.





### OP5

#### **A plot twist in late pregnancy: Incomplete ovarian torsion presenting as acute abdomen.**

##### **Case report and literature review**

**Alexandros Kouvalakis<sup>1</sup>**, Eleni Kouloulia, Ismini Tzanaki, Georgios Lamprakis, Georgios Andreadakis, Antonios Makrigiannakis

<sup>1</sup>University Hospital of Heraklion, Crete, Greece

**Background:** Ovarian torsion is a rare but urgent gynecological condition that requires prompt diagnosis and surgical intervention to prevent ischemic damage to the adnexa. In the third trimester of pregnancy, diagnosis becomes particularly challenging due to overlapping symptoms with other causes of acute abdomen and the limited utility of imaging. This case highlights the diagnostic complexity and underscores the need for clinical vigilance in pregnant patients with known adnexal pathology.

**Case presentation** A 26-year-old primigravida at 32 weeks of gestation presented with sudden-onset right lower quadrant abdominal pain and vomiting. Her medical history was unremarkable except for a previously identified right paratubal cyst under annual surveillance.

**Methods:** Initial transabdominal ultrasound revealed no significant abnormalities. Due to persistent symptoms, a contrast-enhanced MRI was performed, which showed minimal free fluid in the pelvis but no definitive signs of torsion. Despite inconclusive imaging findings, clinical suspicion for adnexal torsion remained high, and exploratory surgery was undertaken.

**Results:** Intraoperative findings confirmed torsion of a right paratubal cyst. A right salpingo-oophorectomy and partial salpingectomy were performed. The appendix appeared normal and was not removed. Postoperative recovery was uneventful, and the patient was discharged with scheduled obstetric follow-up. The pregnancy progressed without complications.

**Conclusion:** This case underscores the importance of considering ovarian torsion in the differential diagnosis of acute pelvic pain during pregnancy, particularly in patients with known adnexal masses. Imaging may be inconclusive, and surgical exploration should not be delayed to prevent complications and preserve reproductive potential.





### OP6

#### **Bacal Cell Cancer of the Vulva: Case report and literature review –**

**Iakovidou G.,** Lamprakis G., Charitou M., Volonaki Z., Vrekousis T., Makrigiannakis A.

Affiliation

**Background and aims:** BCC is the most common form of skin cancer and highly curable when detected early, however BCC of the vulva accounts for less than 1% of all BCCs. Vulvar cancer is associated with i) Lichen sclerosus, ii) VIN and CIN, iii) HPV infection, iv) smoking and v) immunosuppression. The aim of this report is to present a case of Vulvar BCC and its management in our department and to review the literature on similar cases.

**Methods:** A 82 y/o ( G3P3) woman was presented at the Colposcopy outpatient clinic due to vaginal pruritus and a vulvar lump on the left labia majora and in the periclitoral area. Routine blood work and skin-punch biopsy of the lesion were held in combination with MRI scan.

**Results:** An extensive evaluation was performed by the Gynaecology, Radiology, Pathology and Oncology department. After this multidisciplinary approach, the patient underwent radical vulvectomy with negative margins after surgery and no other forms of treatment such as chemotherapy or radiotherapy were offered.

**Conclusions:** Vulvar BCC is a rare, slow-growing malignancy, that rarely metastasises and has an excellent prognosis if managed appropriately.





### OP7

#### OVARIAN REJUVENATION: CLINICAL PROFILE

**Khaled Salech**<sup>2</sup>, Spyridon Topis<sup>1</sup>, Ioannis Arkoulis<sup>1</sup>, Petros-Pavlos Nikolopoulos<sup>2</sup>, Argyro Papadopoulou<sup>2</sup>, Anastasios Potiris<sup>1</sup>, Peter Drakakis<sup>1</sup>, Ekaterini Domali<sup>2</sup>, Sofia Anysiadou, Sofoklis Stavros<sup>1</sup>

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**Background and Aim:** Infertility challenges couples worldwide. Ovarian dysfunction, a key cause, appears as anovulatory cycles, high follicle-stimulating hormone, and low ovarian reserve markers like AMH and AFC. Blood therapies like PRP are used in women with low ovarian reserve or premature ovarian insufficiency. This study evaluates the impact of intraovarian PRP on ovarian function in women with anovulatory cycles.

**Methods:** The initial results of this prospective cohort study involve the first 60 patients. Their average age was 42.6 years, with a range of 33 to 49 years. Monitoring included hormonal profile assessments and AFC calculations, both before and after PRP treatment. Venous blood samples were obtained to prepare autologous platelet-rich plasma (PRP). Each patient received two intraovarian PRP injections, administered under transvaginal ultrasound guidance. Serum reproductive hormone levels were measured before and after treatment.

**Results:** A noticeable enhancement in ovarian function was seen after transvaginal ultrasound-guided PRP infusion. There was a 68% (mean  $\pm$  SD) rise in Antral Follicle Count (AFC), which was statistically significant. Additionally, significant decreases in follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin levels were observed. Serum Vitamin D 1–25 levels also increased markedly following the injection.

**Conclusions:** These findings highlight the potential positive effects of intraovarian PRP injections on improving ovarian function and associated metabolic parameters. Nonetheless, the existing research on this topic is limited, and additional clinical studies are needed to validate the effectiveness of intraovarian PRP in fertility treatments.

**Topic:** fertility preservation





### OP8

#### **VAGINAL STRENGTHENING (PRP): AN ALTERNATIVE METHOD FOR TREATING VAGINITIS?**

**Petros-Pavlos Nikolopoulos<sup>2</sup>**, Spyridon Topis<sup>1</sup>, Ioannis Arkoulis<sup>1</sup>, Petros-Pavlos Nikolopoulos<sup>2</sup>, Argyro Papadopoulou<sup>2</sup>, Anastasios Potiris<sup>1</sup>, Khaled Salech<sup>2</sup>, Peter Drakakis<sup>1</sup>, Sofia Anysiadou, Sofoklis Stavros<sup>1</sup>, Ekaterini Domali<sup>2</sup>

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**Background:** Vaginitis, a common gynecological condition caused by infection, inflammation, or recurrent irritation, leads to burning, itching, discharge, and pain during sex. Traditional treatments like antimicrobials and topical agents may only offer temporary relief and tend to recur. Platelet-rich plasma (PRP), containing a patient's own platelets and growth factors, is being studied as a regenerative therapy to restore mucosal health and boost local immunity.

**Aim:** Evaluate PRP's potential in alleviating vaginitis symptoms and its effectiveness as an adjunct or alternative to standard therapy.

**Methods:** The initial findings from this prospective cohort study include the first 24 patients, with an average age of 34 years. Monitoring covered recording of personal sensations such as itching, foul odour, rushing, heavy liquids, and dyspareunia, as well as vaginal cultures before and after PRP injections.

**Results:** Mostly vaginal cultures showed a sustained fungal infection, which cannot be cured via traditional methodology up to now known. There was a 97% (mean  $\pm$  SD) improvement regarding the personal feelings, and in 85% of the women showed negative vaginal cultures. PRP was well tolerated, with no serious adverse events reported.

**Conclusions:** PRP appears to be a promising, safe, and biologically plausible therapy for vaginitis, offering symptom improvement through mucosal regeneration and enhancement of the local microenvironment.

**Topic:** Fertility Preservation





### OP9

#### THE CONTROVERSIAL ROLE OF ENDOMETRIAL MICROBIOME IN FERTILITY

**Argyro Papadopoulou<sup>2</sup>**, Ioannis Arkoulis<sup>1</sup>, Spyridon Topis<sup>1</sup>, Petros-Pavlos Nikolopoulos<sup>2</sup>, Petros-Pavlos Nikolopoulos<sup>2</sup>, Anastasios Potiris<sup>1</sup>, Khaled Salech<sup>2</sup>, Peter Drakakis<sup>1</sup>, Sofia Anysiadou, Sofoklis Stavros<sup>1</sup>, Ekaterini Domali<sup>2</sup>

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**Background and aims:** In 2011, a groundbreaking article proposed classifying the vaginal microbiome of reproductive-age women into five groups based on the type of Lactobacillus species dominance or absence. In 2017, it was proven that there is a difference in the composition of vaginal, cervical, and endometrial microbiomes. Today, although there is evidence of lower implantation rates in women with endometrial dysbiosis, the role of the endometrial microbiome in fertility remains uncertain.

**Methods:** Endometrial microbiome profiling in women with unexplained infertility after a comprehensive diagnostic work-up according to ESHRE guidelines. The sample is collected in the mid-luteal phase of the menstrual cycle using a sterile Pipelle catheter. Genomic DNA is extracted, further amplified by PCR, and sequenced targeting the 16S rRNA gene using the ThermoFisher NGS Platform.

#### Results:

To date, fifty women have undergone testing. All participants were of White ethnicity, with a mean age of 37.7 years; only two had a previous live birth. In terms of detected bacterial phyla, the Firmicutes phylum was the most common, followed by Actinobacteria, Proteobacteria, and Bacteroidetes. Cyanobacteria and Tenericutes were relatively rare. In our cohort, Firmicutes dominance was primarily driven by the dominance of Enterococcus in about half of the samples. Notably, Lactobacillus iners was the most frequently identified species of the genus. The calculated Shannon index ranged from 0.05 to 2.26, though no universally accepted cut-off value indicative of pathology has been established.

#### Conclusions:

Our preliminary results suggest considerable diversity without substantiated pathology.

TOPIC: endometrium





### OP10

#### **Mir-99a and Mir-143 expression levels in follicular and seminal fluids in infertile couples: Preliminary findings of a prospective study**

**Anastasios Potiris<sup>1</sup>**, Eleni Nazou<sup>1</sup>, Ekaterini Domali<sup>2</sup>, Peter Drakakis<sup>1</sup>, Sofoklis Stavros<sup>1</sup>

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**Background/Objectives:** The identification of microRNAs (miRNAs) in follicular fluid (FF) and semen has provided new insights into their roles in reproductive disorders like polycystic ovarian syndrome (PCOS), endometriosis, premature ovarian failure (POF), and male infertility. Studying miRNAs in FF may lead to reliable biomarkers for assessing embryo quality and diagnosing reproductive disorders. This study aims to compare the expression levels of miR-99a and miR-143 in FF and semen from infertile couples, to understand their role in human reproductive health and fertility.

**Methods:** 15 follicular fluid and 17 semen samples were collected from couples undergoing assisted reproductive techniques. Quantitative real-time PCR was conducted to calculate the relative miRNA expression levels of miR-99a and miR-143.

**Results:** MiR-99a expression in sperm was significantly different ( $p < 0.001$ ) compared to its expression in FF, while no significant variations were observed in miR-143 expression. No associations were found between these miRNAs and other parameters, including hormone levels, BMI in women, sperm motility, and oocyte retrieval.

**Conclusions:** Emerging miRNA profiling techniques may improve the precision of reproductive health diagnostics and personalized treatment options. Further research is needed to understand the interactions between miRNAs and ovarian hormones, which could enhance infertility treatments and contraceptive strategies





## Oral Presentations II

### OP11

#### Dehydroepiandrosterone (DHEA) EFFECTS IN THE EXPRESSION OF RECEPTIVITY AND DECIDUALIZATION FACTORS OF THE human endometrium

**Maria Marmara**<sup>1,2</sup>, Fanourios Makrygiannakis<sup>1,2</sup>, Thomas Vrekoussis<sup>2</sup>, Dragana Nikitovic<sup>1</sup>, Antonis Makrigiannakis<sup>2</sup> and Aikaterini Berdiaki<sup>1,2</sup>.

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**Background and aims:** Increasing maternal age has been shown to negatively affect endometrial function, especially proliferation and decidualization. Our unpublished data has additionally showed decreased expression of receptivity factors with increasing women's age, in human stromal endometrial cells. Dehydroepiandrosterone (DHEA) is an adrenal androgen precursor, abundant in the circulation. It's well known that androgen levels in the female reproductive system are downregulated with age. Thus, we investigated if DHEA addition could modulate endometrial stromal cell decidualization and receptivity potential.

**Methods:** Endometrial biopsies from women of different ages (23y-50y) were obtained, with informed consent. Stromal cells were isolated, cultured and treated with DHEA in different concentrations, with and without 8-bromo-cAMP addition. After treatment, cells were further analyzed depending on the cellular process of interest. Expression of mRNA levels of receptivity modulators (OPN, CD44, HOXA10) and decidualization factors (IGFBP, PRL, STAT3, BMP2) was performed by Real-time PCR. Protein expression of the same factors was investigated using immunofluorescence experiments.

**Results:** Our data showed a statistically significant increase in the mRNA levels of IGFBP ( $p < 0.0001$ ), PRL ( $p \leq 0.05$ ), OPN ( $p < 0.0001$ ) and STAT-3 ( $p < 0.01$ ). Contrariwise, BMP-2 ( $p < 0.0001$ ) and HOXA-10 ( $p \leq 0.05$ ) demonstrate a significant downregulation. Our protein levels' preliminary data displayed an upregulation of IGFBP1 ( $p < 0.05$ ), OPN ( $p < 0.0001$ ) and HOXA ( $p < 0.05$ ) after DHEA addition.

**Conclusions:** Overall, our results showed that DHEA can regulate receptivity and decidualization markers of the endometrium, suggesting possible mechanisms to overcome age related endometrial dysfunctions.





### OP12

#### ENDOMETRIAL AND SEMINAL MICROBIOTA IN INFERTILE COUPLES: IS THERE A LINK?

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**Background and Aims:** The female reproductive tract microbiota plays a crucial role in implantation and pregnancy outcomes. Less is known about the male reproductive tract microbiota. Next Generation Sequencing (NGS) microbiota analysis allows the identification, characterization and quantification of microbial communities in both the endometrium and seminal environment. The aim of the study was to evaluate endometrial and seminal NGS findings in couples with infertility.

**Methods:** Sixteen paired endometrial and seminal samples were analyzed using NGS. Study population included couples experiencing infertility. Frequencies of microbial taxa were calculated and comparative analysis was performed. Endometrial NGS findings were compared with hysteroscopic and histopathologic results.

**Results:** Abnormal endometrial NGS samples were identified in 56%. Among these, 89% showed hysteroscopic endometritis and 56% had concordant hysteroscopic and histopathologic evidence. Abnormal seminal NGS samples were found in 81%. Half of the couples presented with both abnormal endometrial and seminal NGS.

**Conclusions:** These NGS preliminary findings suggest a possible correlation between abnormal endometrial and seminal microbiota. Approximately, half of women with abnormal NGS had concordant hysteroscopic and histopathologic endometritis. Moreover, endometrial and seminal microbiota showed partial overlap with common pathogens that may negatively impact fertility. There is a need for a carefully designed study in order to evaluate the role of endometrial and seminal microbiota in infertility.





### OP13

## NUTRITIONAL PREDICTORS OF HYPOTHALAMIC INFLAMMATION: AN MRS STUDY IN WOMEN WITH AND WITHOUT PCOS

**Bompoula Maria Sotiria**<sup>1</sup>, Valsamakis Georgios<sup>2</sup>, Zouganeli Sofia<sup>3</sup>, Koussis Panagiotis<sup>4</sup>, Toulas Panagiotis<sup>4</sup>, Bompoulas Dimitrios<sup>1</sup>, Drakakis Peter<sup>5</sup>, Mastorakos George<sup>6</sup>, Kalantaridou N. Sophia<sup>5</sup>

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**Background and Aims:** Polycystic ovary syndrome (PCOS) is a common endocrine disorder associated with systemic inflammation, obesity, and metabolic dysfunction. Hypothalamic inflammation (HI), a chronic low-grade inflammation is characterized by gliosis. It can be assessed by magnetic resonance spectroscopy (MRS). The role of obesity and diet in HI remains uncertain. The aim of the study was to investigate whether dietary macronutrients and/or obesity influence radiological hypothalamic metabolites, as measured by MRS, in women with and without PCOS.

**Methods:** Thirty-nine women, aged 18–40 years, were recruited at a tertiary University Hospital and underwent anthropometric, dietary, hormonal, and MRS assessment. Eighteen women fulfilled Rotterdam Criteria. MRS measurements included hypothalamic N-acetylaspartate (NAA), myoinositol (MI), choline (Cho), creatine (Cr), and their ratios.

**Results:** In all subjects, dietary carbohydrate intake was the best negative predictor of hypothalamic NAA/Cr ( $\beta = -0.26$ ,  $p=0.03$ ), suggesting an important role of carbohydrate-rich diets in neuronal integrity. Protein intake correlated positively with NAA/Cr and Cho/Cr, indicating a potential protective effect. PCOS status was not associated with NAA/Cr. No statistically significant differences were recorded by comparing MRS metabolites between BMI and aged-matched groups.

**Conclusions:** Across the total study population, macronutrient composition—particularly high carbohydrate intake—was significantly associated with hypothalamic metabolites linked to neuroinflammation. These findings highlight the role of diet, beyond PCOS status and shows that lifestyle intervention and a balanced diet are essential and may be the potential targets for manipulating HI in women with PCOS.





### OP14

#### **Network interrogation of the progesterone-receptor-galectin-3 axis with STRING/STITCH**

**Ioannis Boutas<sup>1</sup>**, Adamantia Kontogeorgi, Fanourios Makrygiannakis, Pantelis Messaropoulos, Sophia Kalantaridou, Antonios Makrigiannakis

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**Background:** Galectin-3 (LGALS3) modulates cell adhesion, migration and receptor signaling, while progesterone signaling shapes endometrial biology and tumor behavior. We sought in silico evidence for functional connectivity between the progesterone receptor (PGR) and galectin-3, to guide downstream wet-lab work.

**Methods:** We built protein-protein and drug-protein interaction networks using STRING and STITCH (Homo sapiens). Seed nodes were PGR and LGALS3. Networks were expanded with first-shell interactors under high-confidence edges, integrating experimental, database and text-mining channels. We summarized topology (degree/betweenness), identified bridging nodes, and performed functional enrichment for GO Biological Process and KEGG terms related to epithelial dynamics and angiogenesis. Selective progesterone receptor modulators (SPRMs; mifepristone, ulipristal acetate) were added in STITCH to visualize putative pharmacologic perturbations around PGR and LGALS3.

**Results:** STRING linked PGR and LGALS3 indirectly through hubs involved in growth-factor signaling and cytoskeletal control, prominently EGFR/ERBB family members, MAPK nodes, and angiogenic mediators (VEGFA/VEGFR2). Enrichment analyses emphasized pathways for cell migration, epithelial remodeling, and angiogenesis, consistent with a model where galectin-3 lattices modulate growth-factor receptor retention and downstream signaling while progesterone signaling intersects the same axes. STITCH positioned mifepristone and ulipristal in close proximity to PGR with projected network spill-over toward EGFR/VEGF pathways, supporting the hypothesis that SPRMs could secondarily influence galectin-3-dependent signaling phenotypes in endometrial cells. These bioinformatic signals motivated our experimental plan to quantify galectin-3 expression and morphology-linked readouts after hormonal and SPRM exposures.

**Conclusions:** Network analysis supports a biologically plausible PGR↔LGALS3 linkage mediated by growth-factor and angiogenic nodes, generating testable predictions that SPRMs may modulate galectin-3-associated pathways in endometrium. These in silico findings provide a focused framework for mechanistic validation via immunohistochemistry and Western blot in endometrial models.





## Oral Presentations III

### OP15

#### **Integrative Profiling of Endometrial Effects During Breast-Cancer Endocrine Therapy: Galectin-3 as a Translational Biomarker**

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**Introduction:** Hormone-dependent breast cancer is primarily treated with endocrine therapy, but there are frequently adverse endometrial effects associated with this treatment, particularly for patients receiving tamoxifen. Prior studies have suggested potential alternatives, including antiprogestins such as mifepristone (RU38486) and ulipristal acetate (CDB-2914), although little has been done to assess the endometrial safety of these agents either alone or in combination with other drugs. This study sought to assess the direct and comparative effects of tamoxifen, mifepristone, and ulipristal acetate at doses with both potential therapeutic and toxic endometrial effects, focusing on endometrial morphology and galectin-3 expression.

**Materials & Methods:** Galectin-3, a lectin involved in cell adhesion, apoptosis, and tumorigenesis, was used as a biomarker. In an in vivo mammary carcinogenesis animal model and in vitro using Ishikawa endometrial epithelial cells, changes were examined in histology, immunohistochemistry, and galectin-3 protein modulation.

**Results:** Tamoxifen resulted in the highest frequency of complex hyperplasia, while mifepristone and ulipristal acetate produced simple hyperplasia with variable preservation of normal architecture. Immunohistochemistry revealed that normal endometrium displayed low basal galectin-3 levels, which were absent in hyperplastic lesions. In Ishikawa cells, tamoxifen and mifepristone caused dose-dependent inhibition of galectin-3, whereas ulipristal showed a biphasic, bell-shaped response with induction of galectin-3 followed by a normalizing effect at higher doses.

**Conclusions:** Downregulation of galectin-3 was consistent with hyperplastic transition, supporting its potential role as a biomarker for alterations in endometrial remodeling during treatment with endocrine therapy agents. These findings delineate galectin-3 as a possible translational marker for monitoring and managing endometrial risks in breast cancer patients receiving hormonal modulators.





### OP16

#### END STAGE RENAL FAILURE AND PREGNANCY MANAGEMENT AND OUTCOMES

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**BACKGROUND AND AIMS:** Present a case of successful management of G1 P0, with personal history of hemodialysis due to chronic kidney failure.

**MATERIALS AND METHODS:** A 30 y.o patient G1 P0 with personal history of end stage renal failure due to vasculitis under hemodialysis and in the list for kidney transplant, was referred to our department for further management, at 28 weeks of pregnancy. After reviewing the literature and consulting the Neuphrologists of our hospital, we admitted the patient in our high risk pregnancy department and performed a new immune check up. The patient was already under antihypertensive medication. The fetal scan was normal and the cervical length was 3cm. After the check, she was discharged and was referred for outpatient management once to twice a week. Also, the gravida was being submitted to hemodialysis 6 days per week during inpatient and outpatient management. At 33w GA, she was readmitted in our department because of myometrial contractions. She was administered corticosteroids for lung maturation and delivered a healthy newborn through caesarean section.

**RESULTS:**The pregnancy was successfully terminated. The patient was then admitted to the Intensive Care Unit and the newborn to the NICU. The post operative course of out patient was fine with continuation of the hemodialysis less frequently.

**CONCLUSIONS:**Significantly impaired renal function is accompanied by subfertility that may be corrected with chronic renal replacement therapy—either hemodialysis or peritoneal dialysis. Not unexpectedly, maternal complications are common and include severe hypertension, placental abruption, heart failure, and sepsis. The high incidences of hypertension, low birthweight, and preterm delivery result in a high perinatal mortality rate. Such cases would be best managed at tertiary referral centers where there are available High Risk Pregnancy Assessment Units and multidisciplinary treatment can be provided.





### OP17

## PREGNANCY COMPLICATIONS IN WOMEN WITH POLYCYSTIC OVARIAN SYNDROME AND GESTATIONAL DIABETES MELLITUS\_

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**Background and aims:** Gestational diabetes mellitus (GDM) affects about 8-18% of pregnancies and is associated with fetal and maternal complications. A prior diagnosis of polycystic ovarian syndrome (PCOS) is associated with increased GDM risk. This report aims to document and investigate complications in pregnancies with GDM and PCOS.

**Patients and Methods:** Our population consisted of 95 women with spontaneous singleton pregnancy and a history of PCOS, according to Rotterdam criteria. We documented maternal history, demographics, ultrasound and biochemical data of all gynae and obstetrics' visits and the outcome of the pregnancy. All women had a glucose-tolerance test (75 g) at 24 -26 weeks. The rate of complications was compared in between pregnancies with and without GDM and in between pregnancies with and without PCOS.

**Results:** There were 115 pregnancies, 20 of which developed GDM (17,4%). The median age was 35,63 years and the median body mass index was 23,8. PCOS' phenotype A was associated with GDM. Women with GDM had a higher BMI and lower PlGF MoMs at the first trimester. History of GDM was associated with recurrence of the disease. Pregnancies with GDM had a similar rate of complications to normal pregnancies.

**Conclusions:** Increased BMI and history of PCOS phenotype A or GDM are associated with GDM.

Although GDM increases the risk for various pregnancy complications, this effect disappears in pregnancies with good glycemic control starting early in pregnancy.





### OP18

#### Combination of Continuous Use of Oral Clomiphene Citrate with Injectable Gonadotropins for Ovarian Stimulation: A Single-Center Study

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**Introduction:** This single-center, retrospective observational study evaluates the safety and efficacy of a novel ovarian stimulation protocol for embryo banking that combines continuous administration of clomiphene citrate (CC) with gonadotropins, without the use of GnRH antagonists.

**Methodology:** A total of 250 women aged 25–45 undergoing IVF at Serum IVF Clinic in Athens were included. Participants received daily CC (150 mg) from cycle day 2 until the day before hCG trigger, along with 150 IU/day of Meriofert. Outcomes assessed included oocyte yield, fertilization rates, and incidence of ovarian hyperstimulation syndrome (OHSS).

**Results:** The protocol demonstrated an excellent safety profile, with no OHSS reported, and achieved a mean of 10.25 oocytes per patient. Women under 40 yielded more oocytes, whereas fertilization rates were higher in women over 40. Regression analyses identified basal FSH as a key predictor, inversely associated with oocyte yield but positively correlated with fertilization rates. Continuous CC effectively suppressed premature LH surges, allowing for flexible, cost-effective stimulation with reduced monitoring requirements.

**Conclusion(s):** These findings suggest that continuous CC administration combined with gonadotropins offers a promising, antagonist-free approach to embryo banking, particularly beneficial for women of advanced reproductive age. Further prospective studies are warranted to confirm efficacy and optimize clinical application.



