

O-01. *KIDscore*TM D5 algorithm as an additional tool to morphologic assessment and PGT-A for embryo selection: a time-lapse study

E Gazzo¹, F Peña¹, F Valdéz², S Sessarego¹, A Chung¹, C Bonomini¹, M Ascenzo¹, M Velit¹, E Escudero¹

¹INMATER Fertility Clinic, Lima, Peru.

²GENOMICS PERÚ, Lima, Peru.

Objective: To evaluate the use of the known implantation data algorithm *KIDscore*TM D5 (Vitrolife®, Canadá) as an additional tool to morphologic assessment and preimplantation genetic testing for aneuploidies (PGT-A) to improve implantation and ongoing pregnancy rates.

Methods: Design: Retrospective Cohort Study. A total of 912 embryos from 270 patients that underwent an IVF treatment at INMATER Fertility Clinic in Lima - Perú, between October 2016 and June 2018, were analyzed. All embryos were cultured for up to 5 or 6 days in the Embryoscope® time-lapse incubator (Vitrolife®, Canada) and evaluated using the *KIDscore*TM D5 algorithm (KS5). 778 (85.31%) of these embryos were also biopsied for PGT-A screening. A total of 184 single embryo transfers (68% of patients), were performed during this period and the embryos transferred were classified into four groups: 1) Euploid embryos transferred without considering their KS5 score in the selection process (n=86), 2) Euploid embryos transferred considering their KS5 score in the selection process (n=48), 3) Embryos transferred without considering their KS5 score in the selection process and that were not evaluated by PGT-A (n=40) and 4) Embryos transferred considering their KS5 score in the selection process and that were not evaluated by PGT-A (n=10). Implantation and ongoing pregnancy rates were compared between the groups and between euploid embryos with the highest/best KS5 score (KS5=6, n=25) and euploid embryos with the lowest/worst KS5 score (KS5=1, n=51). Correlation between KS5 score and embryo euploidy rate was also evaluated.

Results: Implantation rate and ongoing pregnancy rates was found to be significantly higher in euploid embryo transfers when taking into account their KS5 score in the embryo selection process compared to euploid embryo transfers where selection was based on morphology (75.00% vs. 50.00%; $p=0.002$ and 66.66% vs 48.83%; $p=0.037$ respectively). Additionally, implantation rates were significantly higher for blastocysts with highest KS5 score (KS5=6) compared to lowest (KS5=1) (80.00% vs. 49.02%; $p=0.045$), and ongoing pregnancy rates was not found with significantly (72.00% vs 47.06%; $p=0.105$). Euploidy rate was significantly higher in the group of embryos with KS5=6 than in the group of embryos with KS5=1 (61.88% vs. 48.33%; $p=0.006$).

Conclusion: Embryo selection by the use of the KS5 algorithm score improves implantation rates of single euploid blastocysts transfers. Furthermore, embryos with the highest KS5 score have a higher probability of being euploid and implanting.

O-02. Associated factors to pregnancy in intrauterine insemination

LA Vargas Tominaga¹, F Alarcón¹, A Vargas¹, G Bernal¹, A Medina¹, Z Polo¹

¹CFGS - Centro de Fertilidad y Ginecología del Sur - Cusco - Peru.

Objective: To define the factors associated with clinical pregnancy after intrauterine insemination.

Methods: Retrospective study in 633 infertility couples, which made 1053 cycles of intrauterine insemination. We analyze the clinical pregnancy rate associated with different factors through the Chi-square test or Fisher's exact test.

Results: The clinical pregnancy rate was 8.2% per insemination cycle and 13.6% for treated couple. The factors with greater association to clinical pregnancy were: to have more than 2 follicles, to perform the procedure without difficulty, to have 3 years or less of infertility, cervical factor as indication, use of gonadotropins and age less than 38 years.

Conclusion: Intrauterine insemination requires to be accompanied by proper selection and couples' preparation.

O-03. Blastocyst contractions are strongly related with aneuploidy, lower implantation rates and slower embryo cleavage timing: time lapse study

E Gazzo¹, F Peña¹, F Valdéz², A Chung¹, M Velit¹, M Ascenzo¹, E Escudero¹

¹Clínica de Fertilidad INMATER, Lima, Peru.

²Genomics Peru, Lima, Peru.

Objectives: We set out to identify contraction (CT) patterns in human blastocyst and their correlation with their ploidy status (PGT-A analysis), the time they took to reach blastocyst and the pregnancy rate.

Methods: Design: Retrospective study. 912 embryos from 270 patients that went through our center were evaluated. All embryos were cultivated in the Embryoscope incubator. From 912 embryos that started the cohort, 778 were tested for aneuploidy using an NGS platform in a reference laboratory. Blastocyst contractions (CT) were evaluated using the "embryo drawing tool" to obtain the CT percentage. 182 SET were performed, and the mean patient age was 30.44 years, ranging from 24 to 39 years.

Results: Embryos was divided in two groups, those that contracted (CT) and those that did not, we call them "solo expanding" (SE). When this was compared to ploidy status the embryos that SE showed 58.33% to be euploid while 53.58% of embryos that CT where aneuploid. This was statistically significant ($p=0.029$) showing that embryos

that don't contract SE have higher chances of being euploid than embryos that contract CT. When we compared pregnancy rates, we also saw an increase in embryos that SE (63.10%) with embryos that CT (46.67%), this was also statistically significant ($p=0.012$). Finally, we saw that embryos that CT take longer to reach blastocyst stage compared to SE embryos. This also was significant ($p=0.004$). Finally we evaluated if the patients' age impacts on whether the embryo was CT or SE and found no difference, showing that age should not be a factor in embryo contraction.

Conclusion: The results in this study show statistical significance in two analyzed traits. We showed that CT embryos show a higher chance of being aneuploid, and that they have a lower implantation rate. Also, we showed that embryos that CT take longer to reach blastocyst stage. All this was shown to happen regardless of maternal age. This proves that looking for embryo contractions could be helpful for selecting an embryo for transfer.

O-04. Immature oocyte incidence: Contributing factors and effects on mature sibling oocytes in intracytoplasmic sperm injection cycles

DPAF Braga^{1,2}, BF Zanetti^{1,2}, AS Setti^{1,2}, A Iaconelli Jr.^{1,2}, E Borges Jr.^{1,2}

¹Fertility Medical Group, São Paulo, SP - Brazil.

²Instituto Sapientiae - Centro de Estudos e Pesquisa em Reprodução Humana Assistida, São Paulo, SP - Brazil.

RED LARA Award

Best Oral Presentation.

14th RED LARA Taller General, Mérida, Mexico - 2019

Objective: The aim of this study was to investigate which factors contribute to the incidence of immature oocytes (germinal vesicle -GV- and metaphase I -MI-) and how they impact the intracytoplasmic sperm injection (ICSI) outcomes of sibling mature oocytes.

Methods: Data from 3,920 cycles performed from June/2010 to August/2016 in a private university-affiliated IVF center were evaluated for the influence of controlled ovarian stimulation protocol (COS) on immature oocyte incidence and its effects on ICSI outcomes.

Results: MI ($p=0.004$) and GV ($p=0.029$) number were negatively correlated with gonadotropin dose. Patients stimulated by rFSH had increased GV/oocyte rate in both GnRH agonists ($p<0.001$) and antagonist ($p=0.042$) protocols, in comparison to rFSH associated with rLH protocol. MI and GV/oocyte rates were negatively correlated to fertilization ($p<0.001$), high-quality embryo on days two ($p<0.001$) and three ($p<0.001$), blastocyst ($p<0.001$), implantation (MI/oocyte $p<0.001$; GV/oocyte $p=0.033$) and pregnancy (MI/oocyte $p=0.002$; GV/oocyte $p=0.013$) rates. Cycles above a 10.5% MI/oocyte cut-off were correlated to higher response to ovarian stimulation, poor embryo development and almost two times lower pregnancy rate. Immature oocyte incidence is affected by COS and impacts on ICSI outcomes.

Conclusion: Our evidence suggests that oocytes derived from a cohort with high incidence of maturation fail may have detrimental clinical outcomes.

O-05. Serum microRNA profiling for the identification of predictive molecular markers of the response to controlled ovarian stimulation

E Borges Jr.^{1,2}, MGF Mulato³, AS Setti^{1,2}, A Iaconelli Jr.^{1,2}, MV Geraldo³, DPAF Braga^{1,2}

¹Fertility Medical Group, São Paulo, SP - Brazil.

²Instituto Sapientiae - Centro de Estudos e Pesquisa em Reprodução Assistida São Paulo, SP - Brazil.

³Departamento de Biologia Estrutural e Funcional, Instituto de Biologia, Universidade Estadual de Campinas - UNICAMP.

Objective: To identify potential microRNA (miRNA) biomarkers of poor, normal and hyper responses to controlled ovarian stimulation (COS).

Methods: In the present study, 40 serum samples derived from patients undergoing COS were analysed. Ten samples were used to standardise the detection of miRNAs in serum. The remaining 30 samples were split into three groups depending on the patient's response to COS: poor response (PR group, $n=10$), normal response (NR group, $n=10$), and hyper response (HR group, $n=10$). Aberrantly expressed miRNAs were identified by using a large-scale expression analysis platform. Gene set enrichment analysis was performed to assess the biological processes potentially modulated by the identified miRNAs.

Results: Twenty-two miRNAs were exclusively detected in the PR or HR groups when compared with the NR group. From those, 11 presented poor dissociation curves and were excluded from further analysis. A bioinformatic analysis revealed that the selected 11 miRNAs target several genes involved in GnRH, oestrogen and prolactin signalling, oocyte maturation, female pregnancy, and meiosis.

Conclusions: The large-scale analysis of miRNA expression identified distinct miRNA profiles for poor and hyper response to COS, which potentially modulate key processes for human assisted reproduction. All evidence suggests that the serum microRNA profiling may discriminate patients who will respond in an exacerbated manner to those who will respond insufficiently to the COS. Further studies may validate these miRNAs, allowing for the individualisation of treatment and successful outcomes.

O-06. First custom next-generation sequencing infertility panel in Latin America: design and first results

D Lorenzi¹, C Fernández¹, M Bilinski¹, M Fabbro¹, M Galain¹, S Menazzi¹, M Miguens², P Nicotra Perassi¹, MF Fulco², S Kopelman², G Fisz bajn¹, F Nodar^{1,2}, S Papier^{1,2}

¹Novagen. Buenos Aires, Argentina.

²*Centro de Estudios en Genética y Reproducción (CEGYR). Buenos Aires, Argentina.*

Objective: To present the development of the first custom genetic panel for diagnosis of male and female infertility in Latin America.

Methods: We developed a next-generation sequencing (NGS) panel that assesses genes associated with infertility. The panel targeted exons and their flanking regions. Selected intronic regions in *CFTR* gene were also included. The *FMR1* gene and Y chromosome microdeletions were analyzed by other recommended methodologies. An in-house developed bioinformatic pipeline was applied for the interpretation of the results. Samples with known pathogenic variants, a clear infertility phenotype or idiopathic infertility were evaluated.

Results: A total of 75 genes were selected according to female pathologies (primary ovarian insufficiency, risk of ovarian hyperstimulation syndrome, recurrent pregnancy loss, oocyte maturation defects and embryo development arrest) and male pathologies (azoospermia, severe oligospermia, asthenozoospermia and teratozoospermia). 25 DNA samples were evaluated by the designed panel. Two of the variants found were classified as pathogenic, enabling the diagnosis of a woman with secondary amenorrhea and a man with oligoasthenoteratozoospermia. Targeted NGS assay metrics resulted in a mean of 180X coverage, with more than 98% of the bases covered $\geq 20X$.

Conclusion: Our custom gene sequencing panel was designed for the diagnosis of male and female genetic infertility and revealed the underlying genetic cause of some infertile patients. The application of this panel will allow us to achieve more precise approaches in assisted reproduction.

O-07. Obesity and the possibility of conceiving a child during assisted reproduction treatment: An Argentine experience

JC Sánchez Páez¹, V Gómez Arresegor¹, P Zgrablich²

¹*Laboratorio de Embriología Clínica, Centro de Reproducción Asistida GESTAR.*

²*Unidad de Medicina Reproductiva, Centro de Reproducción Asistida GESTAR.*

Objective: The goal of this study was to examine the association between the BMI and the possibility of conceiving a child through an assisted reproduction treatment.

Methods: A study of cases and controls matched by age was done, with 394 patients that underwent treatment at GESTAR (assisted reproduction center), between the 2013-2017. The association between the BMI and the possibility of conceiving a child was analyzed through logistic regression.

Results: Amongst the cases (successful treatments) 14% were obese, while in the control group (patients that did not get pregnant) obesity was 21%. A significant difference ($p < 0,01$) was seen in the BMI, the number of recovered oocytes, normally fertilized oocytes and the number

of transferred embryos. The Odds Ratio (OR) in SPSS was equal to $0.26 \pm (0.14, 0.50)$ IC95%, which indicates that conceiving a child by assisted reproduction is 74 times lower in patients that are obese than in patients not obese ($p < 0.001$). And the Odds Ratio (OR) calculated by logistic regression in Stata 11 was $0.80 \pm (0.76, 0.86)$ IC95% which indicates a 20% decrease in possibility of conceiving for each point on the BMI scale.

Conclusion: Obesity is associated to the diminishment of the possibility of conceiving a child through assisted reproduction technologies.

O-08. Regenerative therapy by endometrial mesenchymal stem cells in thin endometrium with repeated implantation failure. A novel strategy

AE Tersoglio¹, S Tersoglio¹, DR Salatino¹, M Castro¹, A Gonzalez², M Hinojosa¹, O Castellano¹

¹*International Center for Assisted Reproduction, Mendoza, Argentina.*

²*Immunology Laboratory, Central Hospital, Mendoza, Argentina.*

Objective: Our primary objective was to evaluate the endometrial changes before and after transfer of endometrial mesenchymal stem cells (enMSCs) in a population of thinned endometrium with absence or hypo-responsiveness to estrogen and repeated implantation failure (RIF). The secondary objective was to evaluate the clinics results of the intervention in terms of clinical pregnancy (CP), early abortions pregnancy on going and live birth delivery rate (LBR) in in vitro fertilization (IVF) cycle.

Methods: A longitudinal and experimental study. The intervention was defined as "subendometrial inoculation of enMSCs," and the post-intervention changes were evaluated by the variables: endometrial thickness (Eth), endometrial flow cytometry (enFC), endometrial histopathology (enHP) and endometrial immunohistochemistry (IHQ). The variables were analyzed after the intervention (Post-treatment) regarding to previous values (Pretreatment).

Results: The comparison of Eth between pre and post-treatment with enMSCs leads to 5.24 ± 1.24 mm vs 9.93 ± 0.77 ($p = 0.000$) respectively. Endometrial Flow Cytometry show significant differences in favor of Normalized variables in post-treatment, related with pretreatment, LT/Li, Lb/Li, NK/Li, CD8/CD3⁺ and CD4/CD8 ($p = 0.013, 0.002, 0.049, 0.000, 0.000$) respectively. Only two variables Li/PC and CD4/CD3 show NS ($p = 0.167$ and 0.118). Similar analysis is performed on enHP with an increase the normal HP in post-treatment ($p = 0.007$). The CP rate was 79.31% (23/29), with a live birth delivery rate of % 45.45% (10/22) and ongoing pregnancy 7/29 (24.14%).

Conclusion: It was noted a significative increase in endometrial thickness and normalize variables in enHP, enIHQ in post-treatment, previous, with enMSCs subendometrial inoculation. As a result, the IVF after treatment with enMSCs was a higher rate of CP and LBR.