
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

| Confidence in REI | | | |
|---|---|---|---|
| Topics | Pre-Intervention (n=7) | Post Intervention (n=5) | p-value* |
| Knowledge of REI | 0% | 80% | $p < 0.05$ |
| Appropriate exposure to REI | 14.3% | 40% | $p = 0.62$ |
| Workup of Female Infertility | 28.5% | 100% | $p < 0.05$ |
| Interpreting test results of female infertility | 0% | 100% | $p < 0.05$ |
| Best candidates for OI | 0% | 80% | $p < 0.05$ |
| Understanding of oral medications used for OI (instructions, mechanism of action) | 0% | 40% | $p < 0.05$ |
| Which patients are not candidates for OI | 0% | 80% | $p < 0.05$ |
| Understanding hormonal levels at different times in menstrual cycles | 0% | 60% | $p < 0.05$ |
| Oocyte numbers at different times in reproductive lifespan | 14.3% | 100% | $p = 0.05$ |
| Understanding endometrial changes during menstrual cycle | 57.1% | 100% | $p = 0.05$ |
| Understanding follicular stages and recruitment during ovarian life cycle | 28.6% | 80% | $p = 0.18$ |

* p-values calculated using Fisher's Exact Test for Count Data

**P-186** 6:30 AM Monday, October 24, 2022

**RISK FACTORS FOR INCIDENT POLYCYSTIC OVARY SYNDROME (PCOS) DIAGNOSIS.** Jacob Christ, MD,[1] Onchee Yu, MS,[2] Renate Schulze-Rath, MD, MSc,[3] Jennifer Covey, BS,[2] Erika Holden, BA,[2] Jan Hilpert, MD,[3] Elizabeth Micks, MD MPH,[1] Susan D. Reed, MD, MPH, MS[1] [1]University of Washington, Seattle, WA; [2]Kaiser Permanente Washington, Seattle, WA; [3]Bayer AG, Berlin, Germany.

OBJECTIVE: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, yet it is unclear who are at greatest risk of developing this syndrome. Using a large population-based cohort, we sought to identify risk factors for incident PCOS diagnosis.

MATERIALS AND METHODS: A matched case-control analysis was completed utilizing patients enrolled in Kaiser Permanente Washington from 2006 to 2019. Patients were eligible for inclusion if they identified as female, were aged 16-40 years and had at least 3 years of enrollment with at least one healthcare encounter during that time. Individuals were excluded if they had a history of oophorectomy, hysterectomy or a PCOS diagnosis prior to study entry. PCOS cases were identified using International Classification of Diseases (ICD) diagnosis codes (ICD-9 256.4 or ICD-10 E28.2). For each incident case, 5 individuals without a PCOS diagnosis were matched based on birth year and enrollment status. PCOS diagnosis date was the assigned index date for the matched set. Potential risk factors reported in the 3 years prior to index date included: parity, obesity, metabolic syndrome, family history of PCOS, prediabetes, type 1 and 2 diabetes, weight gain, valproate use, premature menarche, and race (included as a marker of social determinants of health). Differences between cases and non-cases in each factor were evaluated using chi-squared and t tests. Multivariable conditional logistic regression was used to identify significant risk factors for incident PCOS diagnosis.

RESULTS: From 2006 to 2019, 2,491 incident PCOS cases were identified and matched to 12,455 non-PCOS females. Median age of PCOS cases was 29 years (standard deviation 6.8). PCOS cases, compared to non-PCOS, were more frequently nulliparous (69.6% vs 62.1%) and more likely to have obesity (53.8% vs 20.7%), metabolic syndrome (14.5% vs 4.3%), a family history of PCOS (8.5% vs 0.5%), prediabetes (7.4% vs 1.6%), and type 2 diabetes (4.1% vs 1.7%) ($p < 0.001$ for all comparisons). In multivariate models, factors associated with higher risk for incident PCOS included: obesity (compared to non-obese) class I-II (BMI 30-40 kg/m$^2$) (odds ratio 3.1, 95% confidence interval 2.0-4.7), class III (BMI $>$ 40 kg/m$^2$) (7.2, 4.3-12.2), weight gain (compared to weight loss or maintenance) of 1-10% (2.0, 1.2-3.2), 10-20% (3.0, 1.8-5.2), and $>$ 20% (3.7, 1.8-7.5), prediabetes (2.7, 2.1-3.4), and metabolic syndrome (1.7, 1.4-2.0). Parity (0.6, 0.4-0.9) and African American race (0.7, 0.5-0.9) were associated with lower risk for PCOS diagnosis.

CONCLUSIONS: Obesity, weight gain and metabolic dysfunction are significant risk factors for incident PCOS diagnosis. The degree of obesity and percentage weight gain in the 3 years preceding diagnosis appear to be directly associated with the likelihood of a new diagnosis of PCOS.

IMPACT STATEMENT: Individuals with significant weight gain and metabolic dysfunction during reproductive years are at high risk for PCOS development. Investigators and healthcare providers should prioritize identifying and implementing novel prevention strategies.

**P-187** 6:30 AM Monday, October 24, 2022

**LONGITUDINAL FOLLOW UP OF PATIENTS DIAGNOSED WITH COVID-19 DEMONSTRATES NO DECREASE IN OVARIAN RESERVE AS DEMONSTRATED BY SERUM ANTI-MÜLLERIAN HORMONE (AMH) AT 3 AND 6 MONTHS: A PILOT STUDY.** Kathryn D. Coyne, MD,[1] Jerry Adam Tribout, Jr., BS,[2] Heather Tribout, BS, CCRP,[1] Rebecca Flyckt, MD,[3] Rachel S. Weinerman, MD[1] [1]University Hospitals Fertility Center/Case Western Reserve University, Beachwood, OH; [2]University Hospitals, Cleveland, OH; [3]Cleveland Clinic Foundation, Cleveland, OH.

OBJECTIVE: To assess the impact of COVID-19 infection on ovarian reserve as measured by serum AMH in reproductive age females at 3 and 6 months post diagnosis of COVID-19 infection.

MATERIALS AND METHODS: An institutional COVID-19 biorepository was used to identify female patients between the age of 18 and 41 years with serum samples collected at time of COVID-19 diagnosis, 3 months post diagnosis, and/or 6 months post diagnosis. After IRB approval, serum samples were analyzed for AMH level at each time point. A power analysis demonstrated a sample size of 22 unique participants provides 80% power to detect a 0.85 ng/mL difference in AMH level, with an alpha of 0.05. The paired Wilcoxon signed rank test was used to determine significant difference in serum AMH levels over two time points and the Friedman test was used to determine significant difference in serum AMH levels over three time points. $P<0.05$ was considered significant.

RESULTS: 22 unique participants had serum samples over at least two separate time points, including either time of diagnosis (0-13 days post diagnosis), 3 months (84-111 days) post diagnosis, and/or 6 months (180-190 days) post diagnosis. Mean age was 32.67±7.0 years and mean BMI was 32.65±9.1 kg/m$^2$. The majority of participants were Caucasian (68.2%) or African American (31.8%). One participant was Hispanic (4.55%) and the remainder were Non-Hispanic (95.45%). 50% of participants had received at least one dose of COVID-19 vaccine by the time of diagnosis, 45.45% were unvaccinated, and vaccination status was unknown for 1 participant. 4 of the participants (18.18%) were on oral contraceptive pills (OCPs) during at least one time point over which serum samples were obtained, and 45.45% had history of prior OCP use.

Overall, there was no difference in paired serum AMH levels between baseline and the follow up values at 3 or 6 months (n=22, median difference -0.41 ng/mL, p=0.08). Median values at baseline and follow up were: 3.04 ng/mL [3.71] and 4.05 ng/mL [3.93]. Similarly, there were no differences in serum AMH when 3 and 6 month follow up was assessed separately: 3 months: n=17, median difference -0.69, p=0.08; 6 months: n=14, median

difference -0.52, p=0.12. When AMH at three time points was assessed for patients with both 3 and 6 month samples (n = 10), no significant differences were noted (p=0.44). In this limited sample, there was a significant difference in baseline median AMH values between patients that were vaccinated compared to unvaccinated (2.0 ng/mL vs. 5.1 ng/mL); however, in a regression analysis controlling for age, race, and BMI, this difference was not significant (p=0.053).

CONCLUSIONS: This study does not demonstrate an association between a COVID-19 diagnosis and a change in ovarian reserve as assessed by serum AMH at 3 and 6 months follow up. The findings are presented as a pilot study as the overall sample size was small, and additional data collection is ongoing.

IMPACT STATEMENT: The long term impact of COVID-19 infection on health are still unknown. This study provides preliminary evidence demonstrating no significant effect of COVID-19 infection on ovarian reserve at 3 and 6 months post infection.

SUPPORT: This study was supported by the University Hospitals R&E Rapid Response COVID Pilot Award.

**P-188** 6:30 AM Monday, October 24, 2022

**USE OF ELECTROCHEMILUMINESCENCE METHODS TO EVALUATE THE RELATIONSHIP BETWEEN OVARIAN RESPONSE AND ANTI-MULLERIAN HORMONE (AMH) LEVELS WHEN THEY ARE LOWER THAN 1 NG/ML.**

Karina Genesio Ceratto, M.SC., Marcela Cullere, PhD, Ivana Capitanelli, M.SC, Cesar Sanchez Sarmiento, PhD NASCENTIS. ESPECIALISTAS EN FERTILIDAD Y GENETICA REPRODUCTIVA, Argentina.

OBJECTIVE: The evolution of biochemical methods to measure AMH allowed to obtain increasingly precise and reliable values of this marker of ovarian reserve. The Elecsys® AMH assay is an ELISA-type immunoassay based on electrochemiluminescence (EQL) technology and represents one of the most robust diagnostic methods for measuring this hormone. Elecsys® AMH assay could allow the analysis of the relationship between the number of oocytes obtained in a follicular puncture after controlled ovarian stimulation (COS) with AMH levels, when they are lower than 1 ng/ml, a value below which the ovarian response could not be predicted with sufficient confidence. We aimed to establish the diagnostic sensitivity of the Elecsys° AMH method when the hormone level is less than 1 ng/ml in relation to the number of oocytes recovered in follicular punctures. Specifically, determine if there are differences in the number of oocytes obtained depending on the concentration of AMH in the sample: less than 0.49 ng/ml and between 0.50 – 0.99 ng/ml

MATERIALS AND METHODS: 1,452 patients who underwent COS for ICSI at Nascentis were studied between 2017 and 2019. All patients with AMH lower than 1 ng/ml were selected. AMH was measured in serum within 6 months prior to COS. In all cases, the diagnostic methodology was by EQL in the ELECSYS ROCHE auto-analyzer. This methodology has a detection limit of 0.010 ng/mL, (0.071 pmol/L) and repeatability 1 - 2.6 % CV (0.33 - 91.1 pmol/L: 0.046 - 20.8 ng/mL). The results of the follicular punctures (Number of oocytes obtained) of two different groups were analyzed based on the concentration of AMH obtained in the samples: A: less than 0.49 ng/ml and B: 0.50 – 0.99 ng/ml.

RESULTS: 351 blood samples were analyzed. Group A had a mean AMH concentration of 0.30 ng/ml, while group B showed a mean of 0.76 ng/ml. When the number of oocytes recovered in the ovarian punctures was analyzed, a significant difference was observed. Specifically, group A obtained a mean of 2.07 oocytes, while group B obtained 3.31 oocytes (W=19,082 p<0.0001).

CONCLUSIONS: The use of the Elecsys°AMH method (ROCHE) allowed us to find significant differences in the number of oocytes obtained post- follicular puncture based on the AMH values, specifically when these were less than 1 ng/mL. The group with the highest concentration of AMH (0.50 – 0.99 ng/ml) presented a significantly higher number of retrieved oocytes. These results lay the groundwork for future studies to assess the predictive value of this technique in poor responder patients (AMH less than 1 ng/mL), with the ultimate goal of improving the EOC prognosis.

IMPACT STATEMENT: It is possible that AMH values less than 1 ng/ml can predict the ovarian response after follicular puncture, if they are analyzed with the appropriate methodology.

**P-189** 6:30 AM Monday, October 24, 2022

**PREVALENCE OF DIGENIC DISEASE IN PATIENTS DIAGNOSED WITH IDIOPATHIC HYPOGONADOTROPIC HYPOGONADISM/KALLMANN SYNDROME.**

Alexandra Poch, M.D.,[1] Michael P. Dougherty, MD,[2] Robert A. Roman, MD,[3] Lynn Chorich, B.S, M.S.,[4] Zoe Hawkins, B.S.,[5] Lawrence C. Layman, M.D.[3] [1]Augusta, GA; [2]Augusta University; [3]Medical College of Georgia at Augusta University, Augusta, GA; [4]Warrenville, SC; [5]Medical College of Georgia at Augusta University.

OBJECTIVE: To determine the prevalence of digenic disease in patients diagnosed with idiopathic hypogonadotropic hypogonadism (IHH)/Kallmann Syndrome (KS).

MATERIALS AND METHODS: Whole exome sequencing (WES) of 158 patients with IHH/KS at Yale underwent bioinformatics analysis and were filtered for 44 known genes associated with IHH/KS. The resulting variants were filtered by pathogenicity determined by ClinVar to identify 33 patients with 18 unique variants in 9 genes. Primers were designed by primer3 to confirm these variants using Sanger Sequencing. The pathogenicity of the candidate digenic variants of these 33 probands was obtained using the Varsome database. Prevalence was then calculated based upon these results.

RESULTS: WES of the 158 patients with IHH/KS resulted in over 370,000 variants. These variants were filtered for the 44 known genes associated with IHH/KS as recognized by OMIM. These variants were further filtered to identify those categorized as pathogenic based upon the ClinVar database. This resulted in 33 patients with 18 unique variants in 9 unique genes (ANOS1, CHD7, DUSPS6, FGFR1, GNRHR, PROKR2, SOX10, SPRY4, TACR3). Gold standard Sanger sequencing confirmed 17 of the 18 variants in 31 of the 33 patients. Of the 33 patients, 27 patients were found to have an additional 36 variants total in genes associated with IHH/KS but not previously identified as pathogenic by ClinVar. Using the Varsome database, only one of the 36 variants was found to be pathogenic (TACR3). Three variants were found to be likely pathogenic (DMXL2, two variants of FGFR1). The remaining variants (32) were benign or variants of uncertain significance. Four patients did not have any additional variants identified. Of note, one patient with a variant in ANOS1 (X linked recessive) was also found to have a heterozygous pathogenic variant in TACR3 (autosomal recessive). Two patients were each found to have two GNRHR variants (autosomal recessive), suggesting possible compound heterozygosity.

CONCLUSIONS: Digenic inheritance occurs when variants in two different genes manifests a phenotype but variants in only one of the genes may or may not manifest the phenotype. The phenotype is often more severe when both genes are affected. Of the 158 patients with IHH/KS sequenced, 33 patients had a pathogenic variant in a gene associated with IHH/KS. Of these 33, 29 patients had at least one additional variant in a gene associated with IHH/KS. Only 4 of those 29 patients (2.5% overall) had the additional variant identified as likely pathogenic or pathogenic by Varsome. Digenicity is difficult to prove and its true prevalence is unknown. However, based upon our results, we suggest a possible prevalence of 2.5% in genes associated with IHH/KS.

IMPACT STATEMENT: The prevalence of digenicity in idiopathic hypogonadotropic hypogonadism/Kallmann Syndrome is unknown and difficult to prove. These results suggest a possible digenic prevalence of 2.5% in genes known to be associated with IHH/KS. Further family studies and mouse models are needed to confirm findings.

REFERENCES

Louden ED, Poch A, Kim HG, Ben-Mahmoud A, Kim SH, Layman LC. Genetics of hypogonadotropic Hypogonadism-Human and mouse genes, inheritance, oligogenicity, and genetic counseling. Mol Cell Endocrinol. 2021 Aug 20;534:111334. https://doi.org/10.1016/j.mce.2021.111334. Epub 2021 May 30. PMID: 34062169.