AE-PCOS

ANDROGEN EXCESS & PCOS SOCIETY

21st ANNUAL MEETING OF THE ANDROGEN EXCESS & PCOS SOCIETY

5 - 7 OCTOBER 2023

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DAY 1: THURSDAY, 5 OCTOBER 2023		
Time	**Event**	
2:00 - 3:30 pm	**Registration**	
3:30 - 3:40 pm	**Welcome**	**Prof. Joop Laven** Erasmus MC, The Netherlands President of the AEPCOS Society **Dr. Anju Joham** Monash University, Australia Program Chair of the Annual Meeting Committee
SESSION 1: MEET THE PROFESSORS **REFLECTIONS – 20 YEARS ON FROM THE 2003 ROTTERDAM DIAGNOSTIC CRITERIA** Moderators: Dr. Anju Joham and Prof. Joop Laven		
3:40 - 4:05 pm	The 2003 Rotterdam Meeting	**Prof. Bart Fauser** University of Utrecht, The Netherlands
4:05 - 4:30 pm	The 2008 Thessaloniki Meeting	**Prof. Basil Tarlatzis** Aristotle University of Thessaloniki, Greece
4:30 - 4:55 pm	The 2010 Amsterdam Meeting	**Prof. Adam Balen** Leeds Teaching Hospitals NHS Trust, U.K.
4:55 - 5:20 pm	The 2013 Washington Meeting	**Prof. Rick Legro** Penn State University College of Medicine, U.S.A.
5:20 - 5:45 pm	The 2018 Barcelona Meeting	**Prof. Helena Teede** Monash University, Australia
5:45 - 6:30 pm	**PANEL DISCUSSION**	
6:30 - 8:00 pm	**Welcome reception**	

DAY 2, FRIDAY OCTOBER 2023		
Time	**Event**	
SESSION 2: THE 2023 PCOS EVIDENCE-BASED GUIDELINE – DIAGNOSIS WHAT'S NEW IN THE GUIDELINE? Chairs: Prof. Aled Rees and Dr. Alexia Pena		
09:00 - 09:20 am	PCOS diagnosis – hyperandrogenism	**Prof. Ricardo Azziz** University of Alabama at Birmingham, U.S.A.
09:20 - 09:40 am	PCOS diagnosis – what is the most effective ultrasound criteria to diagose PCOS?	**A/Prof. Marla Lujan** Cornell University, U.S.A.
09:40 - 10:00 am	PCOS diagnosis – is AMH effective for diagnosis of PCOM or PCOS?	**Dr. Yvonne Louwers** Erasmus MC, The Netherlands
10:00 - 10:20 am	Are women with PCOS at increased risk of cardiovascular disease?	**Dr. Anju Joham** Monash University, Australia
10:20 - 10:40 am	**PANEL DISCUSSION**	
10:40 - 11:00 am	**COFFEE BREAK**	
SESSION 3: AWARD LECTURE AND EARLY CAREER AWARD WINNERS Chairs: Prof. Ricardo Azziz and Dr. Noel Ng		
11:00 - 11:40 am	**Ricardo Azziz Distinguished Researcher Award** (including 10 minute question time)	**Prof. Daniel Dumesic** University of California, U.S.A.
11:40 - 11:55 pm	**Azziz-Baumgartner Family Early Career Investigator Travel Award** *Overactivation of GnRH Neurons is Sufficient to Promote PCOS-like Cardinal Traits in Female Mice*	**Dr. Mauro Silva** Harvard Medical School, U.S.A.
11:55 - 12:10 pm	**Azziz-Baumgartner Family Early Career Investigator Travel Award** *Unsupervised Steroid Metabolome Cluster Anaylsis to Dissect Androgen Excess and Metabolic Dysfunction in 488 Women with PCOS – Results from the Prospective DAISy-PCOS Study*	**Dr. Thaís P. Rocha** University of Birmingham, U.K.
12:10 - 1:30 pm	**LUNCH**	

12:10 - 1:30 pm	**ECR NETWORKING SESSION**	
SESSION 4: THE 2023 PCOS EVIDENCE-BASED GUIDELINE **WHAT'S NEW IN THE GUIDELINE?** Chairs: Prof. Selma Witchel and A/Prof. Heidi Vanden Brink		
1:30 - 1:45 pm	Pregnancy outcomes in PCOS	**Prof. Ezster Vanky** University of Trondheim, Norway
1:45 - 1:55 pm	Metformin in PCOS	**Dr. Johanna Melin** University of Helsinki, Finland
1:55 - 2:05 pm	Combined oral contraceptive pills in PCOS	**Dr. Maria Forslund** University of Gothenburg, Sweden
2:05 - 2:15 pm	Light therapy for hair reduction	**Dr. Daniela Romualdi** Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Italy
2:15 - 2:25 pm	Lifestyle management	**Prof. Kathy Hoeger** University of Rochester Medical Center, U.S.A.
2:25 - 2:40 pm	Fertility treatment	**Dr. Michael Costello** Royal Hospital for Women, Australia
2:40 - 3:00 pm	**PANEL DISCUSSION**	
3:00 - 3:20 pm	**COFFEE BREAK**	
SESSION 5: AWARD LECTURE & ORAL PRESENTATIONS Chairs: Prof. Paolo Giacobini and Prof. Vasantha Padmanabhan		
3:20 - 3:35 pm	*Unsupervised Clustering-based Reclassified Subtypes of Polycystic Ovary Syndrome: a Large Cohort Study*	**Prof. Han Zhao** Shandong University, China
3:35 - 3:50 pm	*Activation of the HIF Pathway Allevaites Metabolic Defects in Pre-pubertal PCOS Mouse Model*	**Nikke Virtanen** University of Oulu, Finland
3:50 - 4:05 pm	*Abnormal Endometrial Calcium Signaling in PCOS-like Obese Mice Might Contribute to Subfertility in PCOS*	**Lena Luyckx** University of Oulu, Finland KU Leuven, Belgium
4:05 - 4:20 pm	*Circulating Anti-Müllerian Hormone Levels in Pre-Menopausal Women: Novel Genetic Insights From a GWAS Meta-Analysis*	**Natàlia Pujol-Gualdo** University of Oulu, Finland

4:20 - 5:00 pm	**Walter Futterweit Award in Clinical Research** (including 10 minute question time)	**Prof. Zi-Jiang Chen** Shandong University, China
5:00 - 6:30 pm	**POSTER SESSION**	
7:00 pm	**CONFERENCE DINNER** **Poster awards**	

DAY 3, SATURDAY, 7 OCTOBER 2023		
Time	**Event**	
EARLY CAREER SESSION		
8:00 – 9:00 am	Early career session – A guide to mentoring essentials ***Early career attendees***	**Dr. Anju Joham** Monash University, Australia **Prof. Helena Teede** Monash University, Australia
SESSION 6: THE 2023 PCOS EVIDENCE-BASED GUIDELINE WHAT DO WE STILL NEED TO KNOW? Chairs: Prof. Elisabet Stener-Victorin and Dr. Yvonne Louwers		
9:00 - 9:15 am	PCOS diagnosis	**Prof. Joop Laven** Erasmus MC, The Netherlands
9:15 - 9:30 am	Psychological features in PCOS	**Prof. Anuja Dokras** University of Pennsylvania, U.S.A.
9:30 - 9:45 am	Lifestyle management	**A/Prof. Lisa Moran** Monash University, Australia
9:45 - 10:00 am	Medical management	**Prof. Terhi Piltonen** University of Oulu, Finland
10:00 - 10:15 am	Infertility management	**Prof. Rob Norman** University of Adelaide, Australia
10:15 - 10:45 am	**PANEL DISCUSSION**	
10:45 - 11:00 am	**COFFEE BREAK**	

SESSION 7: ORAL PRESENTATIONS – CLINICAL Chairs: Prof. Alessandra Gambineri and Prof. Michael O'Reilly		
11:00 - 11:15 am	The Risk for Diabetic Complications in Women with Polycystic Ovary Syndrome and Matched Control Women	**Dr. Meri-Maija Ollila** University of Oulu, Finland
11:15 - 11:30 am	Hypertension and Hyperlipidaemia in Women with Polycystic Ovary Syndrome: a Population Based Multi-register Matched Cohort Study in Sweden	**Dr. Evangelia Elenis** Uppsala University, Sweden
11:30 - 11:45 am	The Effects of Maternal PCOS on the Cardiometabolic Risk and Liver Steatosis in Daughters and Sons	**Dr. Noel Ng** The Chinese University of Hong Kong, Hong Kong
11:45 - 12:00 pm	The Effect of 4 Months of Oral Semaglutide on Weight, Clinical, Metabolic and Reproductive Measures in Adolescents with Obesity and PCOS	**A/Prof. Melanie Cree** Children's Hospital, Colorado, U.S.A.
12:00 - 12:30 pm	**LUNCH**	
12:30 - 1:30 pm	**PATIENT ADVOCACY AND SUPPORT PANEL** Korento, Finland – Tiia Tuovinen PCOS Challenge, U.S.A. – Sasha Ottey PCOS Network, Sweden – Liselott Videla POSAA, Australia – Lorna Berry SOPK, Europe – Emelyne Heliun Verity, U.K. – Caroline Andrews *Supported by the Waterloo Foundation*	
SESSION 8: PARTERNING WITH WOMEN WITH PCOS Chairs: Prof. Anuja Dokras and Dr. Punith Kempegowda		
1:30 - 1:50 pm	Models of care in PCOS	**Dr. Jillian Tay** Monash University, Australia
1:50 - 2:10 pm	Consumer and health professional interaction	**A/Prof. Laura Cooney** University of Wisconsin, U.S.A
2:10 - 2:30 pm	Working in partnership with women with PCOS	**Rachel Morman** Verity U.K.
2:30 - 2:50 pm	**PANEL DISCUSSION**	
2:50 - 3:10 pm	**COFFEE BREAK**	

SESSION 9: WHAT'S IN A NAME? Chairs: Prof. Kathy Hoeger and Caroline Andrews		
3:10 - 3:25 pm	PCOS name change – caution needed	**Prof. Rob Norman** University of Adelaide, Australia
3:25 - 3:35 pm	The evidence for PCOS name change	**Prof. Helena Teede** Monash University, Australia
3:35 - 3:45 pm	The consumer voice	**Rachel Morman** Verity, U.K. **Lorna Berry** POSAA, Australia
3:45 - 4:45 pm	**PANEL DISCUSSION** **&** **SMALL GROUP DISUSSION** **FEEDBACK FROM SMALL GROUPS**	
4:45 - 4:55 pm	Wrap up and how to proceed	**Prof. Joop Laven** Erasmus MC, University Medical Center Rotterdam, The Netherlands
4:55 - 5:00 pm	**AE-PCOS SOCIETY UPDATE**	**Prof. Anuja Dokras** University of Pennsylvania, U.S.A.
5:00 - 5:10 pm	**AE-PCOS ANNUAL MEETING 2024 MEETING WRAP UP**	**Prof. Terhi Piltonen** University of Oulu, Finland **Prof. Elisabet Stener-Victorin** Karolinska Institutet, Sweden

Abstract ID #185 AZZIZ-BAUMGARTNER FAMILY EARLY CAREER INVESTIGATORS AWARD

Abstract Title: OVERACTIVATION OF GNRH NEURONS IS SUFFICIENT TO PROMOTE PCOS-LIKE CARDINAL TRAITS IN FEMALE MICE.

Silva, M.S.B. (1,2,3), Decoster, L. (1,2), Delpouve, G. (1,2), Lhomme, T. (1,2), Ternier, G. (1,2), Prevot, V. (1,2), and Giacobini, P. (1,2)

(1) Laboratory of Development and Plasticity of the Neuroendocrine Brain, FHU 1000 days for health, School of Medicine, Lille, France

(2) Univ. Lille, Inserm, CHU Lille, Lille Neuroscience & Cognition, UMR-S 1172, Lille, France

(3) Department of Medicine, Division of Endocrinology, Diabetes and Hypertension, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA.

Abstract: Objective: Neuroendocrine disturbances in brain circuitry enhancing the activity of gonadotropin-releasing hormone (GnRH) neurons might play a key role in the etiology of polycystic ovary syndrome (PCOS). Here, we focused on determining whether chronic overactivation of GnRH neurons using chemogenetic manipulations promotes the appearance and maintenance of the major PCOS-like traits in female mice as our disease model.

Methods: To activate GnRH neurons, we targeted the chemogenetic tool hM3D(Gq) expression in GnRH neurons. Using a Cre-loxP system approach, we unilaterally injected AAV9-DIO-hM3D(Gq)-mCherry into the median eminence (ME) of the hypothalamus in Gnrh1-cre female mice (Gnrh1hM3D(Gq)). Gnrh1hM3D(Gq) female mice were followed before, during, and after the cessation of chronic activation of GnRH neurons with i.p. 1 mg/kg clozapine-N-oxide (CNO) coupled with reproductive and neuroendocrine phenotyping for PCOS-like features. Luteinizing hormone (LH), testosterone (T), and anti-Müllerian hormone (AMH) blood levels were assessed using ELISA. Ovarian morphology was assessed using iDISCO+ technology and imaging with light-sheet microscopy. GnRH signaling requirement tests were carried out with Cetrorelix treatment (s.c. 0.5 mg/kg/48h).

Results: Viral transfection strategy effectively targeted nearly 60% of all hypophysiotropic GnRH neurons in the female mouse brain. Firstly, we found that 1 mg/kg CNO is sufficient to promote a 3.05-fold increase in LH secretion, a proxy of GnRH secretion, similar to other PCOS preclinical models. Chronic GnRH overactivation protocol promoted robust and long-lasting disruption of estrous cyclicity with a significant reduction of time spent in both proestrus and estrus ($P < 0.0001$) in Gnrh1hM3D(Gq) female mice (N = 15). During and after chemogenetic protocol, Gnrh1hM3D(Gq) had high circulating T levels ($P < 0.0001$) associated with high LH pulse frequency ($P < 0.0001$) secretion compared with control female mice. We also found that AMH levels in the blood were nearly 1.86-fold higher in Gnrh1hM3D(Gq) female mice compared with controls ($P < 0.0001$). Using iDISCO+ technology, we detected a robust alteration of the ovarian follicular dynamics in Gnrh1hM3D(Gq) female mice with an increase in the number of pre-antral follicles and a substantial reduction of pre-ovulatory follicles and corpora lutea counts compared with controls. Finally, we tested whether tempering GnRH signaling with Cetrorelix may offer a prospective therapeutic strategy. We discovered that GnRH-R blockade prevented neuroendocrine dysfunction in Gnrh1hM3D(Gq) female mice and rescued normal T and AMH concentrations in the blood similar to control levels.

Conclusions: Taken together, our results show that overactivation of hypothalamic GnRH neurons drives a vicious cycle of hormonal imbalance leading to robust reproductive and neuroendocrine dysfunction.

Abstract ID #206 AZZIZ-BAUMGARTNER FAMILY EARLY CAREER INVESTIGATORS AWARD

Abstract Title: UNSUPERVISED STEROID METABOLOME CLUSTER ANALYSIS TO DISSECT ANDROGEN EXCESS AND METABOLIC DYSFUNCTION IN 488 WOMEN WITH POLYCYSTIC OVARY SYNDROME – RESULTS FROM THE PROSPECTIVE DAISy-PCOS STUDY.

Thaís P. Rocha (1,2), Eka Melson(1), Roland J. Veen(3), Lida Abdi(1), Tara McDonnell(4), Veronika Tandl(5), James M. Hawley(1,6), Laura B. L. Wittemans(1,7), Amarah V. Anthony(1), Lorna C. Gilligan(1), Fozia Shaheen(1), Punith Kempegowda(1,8), Caroline D. T. Gillett(1,9), Leanne Cussen(4), Cornelia Missbrenner(5), Fannie Lajeunesse-Trempe(10), Helena Gleeson(11), D. Aled Rees(12), Lynne Robinson(13), Channa Jayasena(14), Harpal S. Randeva(15), Georgios K. Dimitriadis(10), Larissa G. Gomes(2), Alice J. Sitch(8,9), Eleni Vradi(16), Michael W. O'Reilly(4), Barbara Obermayer-Pietsch(5), Angela E. Taylor(1), Michael Biehl(3), Wiebke Arlt(1, 19, 20)

(1)University of Birmingham, Institute of Metabolism and Systems Research, United Kingdom,; (2)Disciplina de Endocrinologia e Metabologia, Faculdade de Medicina da Universidade de São Paulo, São Paulo; (3)University of Groningen, Bernoulli Institute for Mathematics, Computer Science and Artificial Intelligence; (4)Royal College of Surgeons in Ireland, Endocrinology Research Group, Department of Medicine, Dublin; (5)Medical University of Graz, Division of Endocrinology and Diabetology, Department of Internal Medicine, Graz; (6)Wythenshawe Hospital, Manchester University NHS Foundation Trust, Department of Clinical Biochemistry, Manchester; (7)University of Oxford, Big Data Institute, Oxford; (8)University of Birmingham, Institute of Applied Health Research, Birmingham,; (9)National Institute for Health and Care Research (NIHR) Birmingham Biomedical Research Centre, Birmingham, United Kingdom ; (10)King's College Hospital NHS Foundation Trust, Department of Endocrinology, London, United Kingdom; (11)Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Department of Endocrinology, Birmingham, United Kingdom,; (12)Cardiff University, Neuroscience and Mental Health Research Institute, School of Medicine , Cardiff, United Kingdom,; (13)Birmingham Women's Hospital, Birmingham Women's and Children's Hospital NHS Foundation Trust, Birmingham; (14)Imperial College London, Department of Metabolism, Digestion and Reproduction, London, United Kingdom; (15)University of Warwick, Warwick Medical School, Coventry, United Kingdom; (16)King's College London, Obesity, Type 2 Diabetes and Immunometabolism Research Group, Faculty of Cardiovascular and Metabolic Medicine & Sciences, School of Life Course Sciences, London, United Kingdom; (17)Bayer AG, Berlin, Germany; (18)University of Groningen, Bernoulli Institute for Mathematics, Computer Science and Artificial Intelligence, Gronigen, Netherlands; (19)Institute of Clinical Sciences, Faculty of Medicine, Imperial College London, London, United; Kingdom; (20)Medical Research Council Laboratory of Medical Sciences (MRC LMS), London, United Kingdom (18)University of Groningen, Bernoulli Institute for Mathematics, Computer Science and Artificial Intelligence, Gronigen,

Abstract: OBJECTIVE: Polycystic ovary syndrome (PCOS) affects 10% of women and is associated with a 2-3fold risk of type 2 diabetes (T2D), hypertension, fatty liver disease, and cardiovascular disease. Androgen excess has been implicated as a major contributor to metabolic risk in PCOS. We aimed to identify PCOS sub-types with distinct androgen profiles and compare their cardiometabolic risk.

METHODS: We prospectively recruited 488 treatment-naïve women with PCOS from UK & Ireland, Austria, and Brazil (Age 28[24-32] years; BMI 27.5[22.4-34.6] Kg/m2). Standardised assessments included blood before and during the 120min oral glucose tolerance test. We quantified eleven serum C19 classic and 11-oxygenated androgens by tandem mass spectrometry, followed by unsupervised k-means clustering of steroid data and statistical comparison of differences in clinical phenotype and metabolic parameters.

RESULTS: Machine learning identified three distinct PCOS subgroups characterised by gonadal-derived androgen excess (GAE; 21.5% of women; lead steroids testosterone, dihydrotestosterone), adrenal-derived androgen excess (AAE; 21.7%; 11-ketotestosterone, 11-hydroxytestosterone) and comparably mild androgen excess (MAE; 56.8%), with similar age and BMI. Compared to GAE and MAE, the AAE cluster had the highest rates of hirsutism (76% vs. 68% vs. 60%) and alopecia (32% vs. 14% vs. 22%) while the GAE cluster had the highest rates of acne (51% vs. 36% and 35% in AAE and MAE, respectively). The AAE cluster had the highest HOMA-IR and lowest Matsuda insulin sensitivity index (all $p<0.01$) and a 2-3fold higher incidence of impaired glucose tolerance (IGT) and newly diagnosed T2D. We achieved recruitment of 27% non-white women to the UK & Ireland cohort (n=208), with South Asian women more likely to be in the AAE cluster compared to white women (59% vs. 35%).

CONCLUSION: Unsupervised cluster analysis revealed three PCOS subtypes with distinct androgen excess profiles. The AAE cluster was characterised by the highest insulin resistance and prevalence of IGT and T2D, implicating 11-oxygenated androgens as associated with a high metabolic risk profile in women with PCOS. These results provide proof of principle for a novel metabolic risk prediction tool in PCOS and have the potential to guide future preventative and therapeutic approaches.

Abstract ID #96

Abstract Title: GLP-1 RECEPTOR AGONIST SEMAGLUTIDE IMPROVES TASTE SENSITIVITY IN WOMEN WITH POLYCYSTIC OVARY SYNDROME AND OBESITY

Jensterle M (1,2), Vovk A (2), Kovač J (3), Battelino S (2, 4), Ferjan S (1,2), Battelino T (2, 3), Janez A (1,2)

(1) Department of Endocrinology, Diabetes and Metabolic Diseases, Division of Internal Medicine, University Medical Centre Ljubljana, Zaloška cesta 7, SI-1000, Ljubljana, Slovenia

(2) Faculty of Medicine, University of Ljubljana, Vrazov trg 2, SI-1000, Ljubljana, Slovenia

(3) Department of Endocrinology, Diabetes and Metabolism, University Children's

Hospital, University Medical Centre Ljubljana, Bohoričeva 20, SI-1000, Ljubljana, Slovenia

(4) Department of Otorhinolaryngology and Cervicofacial Surgery, University Medical Centre Ljubljana, Zaloška cesta 2, SI-1000, Ljubljana, Slovenia

Abstract: OBJECTIVE: Obesity is associated with a reduced perception of taste. Reduced perception of taste has also been reported in polycystic ovary syndrome (PCOS). We aimed to assess the impact of semaglutide on the taste perception in women with PCOS and obesity. The primary endpoint was to measure an impact of semaglutide on taste sensitivity. The co-primary endpoint was to investigated alteration in transcriptomic profile of the tongue tissue induced by semaglutide. Secondary endpoint was to evaluated the changes in brain activation in response to sweet solution evoked by semaglutide.

METHODS: Thirty women with obesity and polycystic ovary syndrome, phenotype A (age 33.7 ± 6.1 years, BMI 36.4 ± 4.4 kg/m2, mean ± SD) were randomized in 1:1 ratio to once weekly semaglutide 1.0 mg s.c. or placebo in a 16-week, single-blind, placebo-controlled study. Taste sensitivity was evaluated by taste strips impregnated with 4 diffrent concentrations of sweet, sour, salty and bitter substances. All participants underwent paired biopsies of the tongue before and after treatment. The alteration of transcriptomic profile of tongue tissue was assessed as changes in expression level measured by RNA sequencing (NovaSEQ 6000 sequencer, Illumina). The change in neural response to sweet-tasting solution was assessed by functional MRI (fMRI). The neural responses to the sweet solution dripped directly on the tongue during fMRI was compared to the responses to distilled water, in fasting state and after the meal ingestion, at baseline and at study end.

RESULTS: Semaglutide significantly improved overall taste sensitivity and the sensitivity for all four basic tastes. A total of 1326 genes were differentially expressed in the tongue tissue between the groups with log FC > 0.7 or < -0.7 and FDR<0.05. Semaglutide upregulated WNT pahway that is involved in the renawal and diffrenetiation of the taste bud cells. It also significantly altered the expression of RNA for taste receptors and essential proteins in taste transduction, including TRPM5. In comparison with placebo, semaglutide increased activation of angular gyrus in response to sweet solution after the meal ingestion ($p<0.001$). Functionally, angular gyrus has an integrative role that includes reorienting the attentional system and giving the meaning to external stimuli based on stored memories and prior experiences.

CONCLUSIONS: Semaglutide improved taste sensitivity in women with PCOS and obesity along with transcriptomic alteration in signalling pathways involved in renewal and differentiation of taste bud cells and in taste transduction. In direct response to sweet solution, semaglutide evoked activation of an integrative hub in parietal cortex. The results provides a novel view of the functional mechanisms underlying the efficacy of semaglutide in the treatment of obesity.

(The study was supported by Slovenian Research Agency grants #P3-0298, #P3-0343.)

Abstract ID #97

Abstract Title: THE MAINTENANCE OF LONG-TERM WEIGHT LOSS AFTER SEMAGLUTIDE WITHDRAWAL IN WOMEN WITH OBESITY AND PCOS TREATED WITH METFORMIN: A 2-YEAR OBSERVATIONAL STUDY

Jensterle M (1,2), Ferjan S (1,2), Katja Goričar K (3), Janez A (1,2)

(1) Department of Endocrinology, Diabetes and Metabolic Diseases, University Medical Centre Ljubljana, Division of Internal Medicine, Zaloška cesta 7, SI-1000 Ljubljana, Slovenia;

(2) Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia, Vrazov trg 2, SI-1000 Ljubljana, Slovenia;

(3) Pharmacogenetics Laboratory, Institute of Biochemistry and Molecular Genetics, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia, Vrazov trg 2, SI-1000 Ljubljana, Slovenia;

Abstract: OBJECTIVE: Withdrawal of anti-obesity medication is frequently followed by weight regain due to compensatory biological changes that prevent the maintenance of long-term weight loss. In STEP 1 trial extension participants regained two-thirds of their prior weight loss during the 1-year off-treatment follow-up period after withdrawal of semaglutide 2.4 mg and discontinuation of active lifestyle intervention support. There are some studies implying that metformin might attenuate weight regain after weight loss in women with polycystic ovary syndrome (PCOS). To date, the amount of weight regain after semaglutide withdrawal in women with obesity and PCOS who continue treatment with metformin has not yet been evaluated. We explored changes in body weight, cardiometabolic and endocrine parameters in women with obesity and PCOS 2 years after semaglutide cessation.

METHODS: 25 women with obesity and PCOS (33.7 ± 5.3 years, body mass index (BMI) 36.1 ± 3.9 kg/m2, mean ± SD) were treated with once-weekly subcutaneous semaglutide 1.0 mg as an adjunct to metformin 2000 mg/day and lifestyle intervention for 16 weeks. At week 16, semaglutide was discontinued. Treatment with metformin 2000 mg/day and promotion of lifestyle intervention were continued during the 2- year follow up period. Weight, cardiometabolic and endocrine parameters were assessed to 2 years after semaglutide discontinuation.

RESULTS: During semaglutide treatment phase, weight decreased from 101 (90-106.8) kg to 92 (83.3-100.8) kg. 2 years after semaglutide withdrawal, weight was 95 (77-104) kg. The net weight loss 2 years after discontinuation of semaglutide remained significant when compared to baseline (-7 (-14.3 to -1.5) kg, p=0.001). Improvements in cardiometabolic parameters including decrease in total and LDL cholesterol, triglycerides and fasting glucose and glucose after OGTT that had seen during semaglutide-treatment phase, reverted towards baseline two years after semaglutide cessation. The reduction in free testosterone from 6.16 (4.07-9.71) to 4.12 (2.98-6.93) pmol/l (p=0.004) and in androstenedione from 6.62 (4.36-8.77) to 5.49 (3.78-6.84) nmol/l, (p= 0.002), observed during semaglutide treatment phase remained significant for 2 years (p=0.045 and p=0.023, respectively).

CONCLUSIONS: Two years after semaglutide withdrawal, women with PCOS regained one-third of their prior weight loss. Improvements of cardiometabolic variables reverted to baseline, whereas improvement of endocrine parameters achieved during semaglutide treatment phase persisted 2 years after semaglutide cessation. The role of metformin in attenuation of weight regain after semaglutide discontinuation needs to be explored in randomized controlled studies in different insulin resistant populations.

(This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.)

Abstract ID #98

Abstract Title: SEMAGLUTIDE REDUCES ACTIVATION OF A REWARD SYSTEM IN RESPONSE TO CALORIE DENSE FOOD CUES IN WOMEN WITH POLYCYSTIC OVARY SYNDROME AND OBESITY

Jensterle M (1,2), Vovk A (2), Kovač J (3), Battelino S (2, 4), Ferjan S (1,2), Battelino T (2, 3), Janez A (1,2)

(1) Department of Endocrinology, Diabetes and Metabolic Diseases, Division of Internal Medicine, University Medical Centre Ljubljana, Zaloška cesta 7, SI-1000, Ljubljana, Slovenia;

(2) Faculty of Medicine, University of Ljubljana, Vrazov trg 2, SI-1000, Ljubljana, Slovenia;

(3) Department of Endocrinology, Diabetes and Metabolism, University Children's

Hospital, University Medical Centre Ljubljana, Bohoričeva 20, SI-1000, Ljubljana, Slovenia;

(4) Department of Otorhinolaryngology and Cervicofacial Surgery, University Medical Centre Ljubljana, Zaloška cesta 2, SI-1000, Ljubljana, Slovenia;

Abstract: OBJECTIVE: Behavioral studies have suggested that exaggerated reactivity to food cues, especially those associated with calorie-dense food, may be one of the factors underlying obesity. This increased motivational potency of food in individuals with obesity appears to be mediated in part by a hyperactive reward system. GLP-1 receptor agonist semaglutide reduces preference for energy-dense food. We aimed to investigate the impact of semaglutide on the reward system in response to calorie-dense food cues in women with polycystic ovary syndrome and obesity.

METHODS: Thirty women with obesity polycystic ovary syndrome (age 33.7 ± 6.1 years, BMI 36.4 ± 4.4 kg/m2, mean ± SD) were randomized to once weekly semaglutide (SEMA) 1.0 mg s.c. or placebo in a 16-week, single-blind, placebo-controlled study. The change in neural response to visual food cues was assessed by functional MRI (Achieva 3.0T TX scanner (Philips Healthcare, Best, Netherlands). During fMRI, women were shown a series of calorie-dense, calorie-low food and non-food cues in fasting state and after the meal ingestion, at baseline and at the study end. Change in eating behaviour was evaluated by the Three-Factor Eating Questionnaire (TFEQ-R18).

RESULTS: After 16 weeks, semaglutide, as compared to placebo, significantly decreased activation of dorsolateral putamen in response to calorie dense food cues after high protein enriched nutritional drink intake (p<0.001). Complementary with this result, a significant decrease in body weight, waist circumference and visceral adipose tissue was observed in semaglutide group. Furthermore, the ability to resist emotional and uncontrolled eating was significantly greater in semaglutide group than in placebo group.

CONCLUSIONS: Putamen is involved in the reward processing of food. There are links between activation in the putamen and the future weight gain. Based on our results, we would assume that women with polycystic ovary syndrome and obesity find calorie dense food cues less rewarding while on semaglutide. Future research will evaluate the associations between fMRI outcome measures and weight loss as well as the importance of these measures in predicting treatment efficacy of anti-obesity medications in different populations living with obesity.

(The study was supported by Slovenian Research Agency grants #P3-0298, #P3-0343.)

Abstract ID #99

Abstract Title: HIPPOCAMPUS-DEPENDENT SPATIAL MEMORY AND COGNITION IS IMPAIRED IN DHEA INDUCED PCOS MICE MODEL.

Rao S (1), Johnson B S (1) and Laloraya M (1)*

(1) Female Reproduction and Metabolic Syndromes Laboratory, Division of Molecular Reproduction, Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram -695 014, Kerala, India.

Abstract: OBJECTIVE: Polycystic ovary syndrome (PCOS) is a metabolic disorder characterized by hyperandrogenemia, oligo/anovulation, and polycystic ovaries and it affects 5%–10% of women of reproducing age. Along with ovulatory dysfunction and other metabolic problems, psychological distress is also one of the co morbidity associated with PCOS. Gender variations in cognitive abilities are regulated by sex steroid to an extent along with other metabolic factors. In PCOS, hypothalamo-gonadal axis is impaired leading to high LH suggesting central neuro-endocrine defects contributing to PCOS. Hence, in this study we examined whether altered LH and sex steroid levels in PCOS affect brain function like memory and learning ability leading to cognitive impairment.

METHODS: To investigate the cognition proficiency in PCOS, we induced PCOS in prepubertal mice by injecting dehydroepiandrosterone (DHEA) sub-cutaneously for 20 consecutive days. PCOS mouse model were then subjected to various memory-dependent tests including Open Field Test (OFT), Novel object recognition paradigm (NOR) which is a hippocampus-independent object memory test and object location memory paradigm (OLM) which is an test of hippocampus-dependent spatial memory. We also analyzed the expression status of various short and long term memory markers and androgen receptor in hippocampus of mice model using qRT PCR.

RESULTS: Treatment of mice with DHEA resulted in a decrease in total distance traveled (P<0.007), and lesser time spent in central zones of the arena (P<0.03) when compared to the control group in open field test. DHEA treated mice also displayed a significant decrease in object location memory (P<0.03) as well as in the Novel object recognition test (P<0004) based on the discrimination index test. Transcript levels of short-term memory marker Npas4 were significantly reduced in DHEA-induced PCOS mice while Arc did not showed significant variation among groups. Expression levels of Egr1 and Egr2 were significantly up regulated in DHEA induced PCOS mice. Along with androgen receptor, expression levels of long-term memory marker Nmdar1 (Grin1) were also significantly up regulated in DHEA induced PCOS mice. Hippocampus Nmdar2a (Grin2a) transcript levels showed significant down regulation in DHEA induced PCOS mice.

CONCLUSION: Our data shows that DHEA administration in mice exhibited depression and anxiety-like behavior. Based on the behavioral experiments and expression of short- and long-term memory markers, a defective hippocampus-dependent spatial memory and cognition in terms of recognition memory was observed in DHEA induced PCOS mice model. Our work suggests, the need to assess spatial memory and cognition in PCOS women. Further studies in this respect would enable us to improve the well-being of PCOS women.

(Funding Support – DBT & ICMR)

Abstract ID #100

Abstract Title: UNSUPERVISED CLUSTERING-BASED RECLASSIFIED SUBTYPES OF POLYCYSTIC OVARY SYNDROME: A LARGE COHORT STUDY

Han Zhao1, Zi-Jiang Chen1, Shigang Zhao1, Xueying Gao1, Ziyi Yang1

1 State Key Laboratory of Reproductive Medicine and Offspring Health, Shandong University, Jinan, Shandong, China

Abstract: OBJECTIVE: Polycystic ovary syndrome (PCOS) is a complex disease with both endocrinal and metabolic disorders affecting over 10% reproductive-aged women. There is a lack of refined subtype classification for PCOS, and therefore no uniform protocol for the individualized treatment.

METHODS: Unsupervised clustering analysis was used to classify the PCOS diagnosed by the Rotterdam criteria in a main cohort China including more than 40,000 PCOS cases. Subtypes were based on nine commonly used clinical features. Replication was performed in five independent validation cohort from different areas. Prospective data on the regression and progression of PCOS characteristics and metabolic complications were compared between these subtypes.

RESULTS: To identify PCOS subtypes, we firstly included 29 clinical features, including age, height, weight, BMI, SBP, DBP, LH, FSH, E2, T, PRL, P, SHBG, AMH, DHEA-S, TSH, ALT, AST, GGT, ALB, TG, TC, HDL, LDL, fasting glucose, fasting insulin, ultrasound antral follicle counts, menstrual cycle, and age of menarche. After performing three different analysis, the following nine features were selected for further clustering: BMI, LH, FSH, T, AMH, DHEA-S, SHBG, fasting glucose, and fasting insulin. Using unsupervised clustering, we identified four subtypes within the discovery cohort China. The Jaccard scores of four subtypes were greater than 0.79. The clinical characteristics displayed by each subtype are distinct. First, the Hyper-androgenic PCOS subtype (HA-PCOS) was characterized by relative high levels of testosterone and DHEA-S, along with the mild metabolic disorder. Second, the Obesity-related PCOS subtype (OB-PCOS) had the relative high BMI, fasting glucose, and fasting insulin level, with the highest prevalence of T2DM, dyslipidemia, and hypertension, OB-PCOS was more inclined to a typical classic phenotype with the severe metabolic disorders. Third, the High SHBG PCOS subtype (SHBG-PCOS) was characterized by the highest SHBG among four subtypes. This subtype showed the relative mild phenotype. Fourth, the High LH/AMH PCOS subtype (LH-PCOS) was distinguished by high levels of LH, FSH, and AMH, which was mainly manifested as the high antral follicle counts.

CONCLUSIONS: We reclassified PCOS into four subtypes, which allow us to better understand the complex disease of PCOS.

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Abstract ID #102

Abstract Title: TRANSLATION OF THE MODIFIED POLYCYSTIC OVARY SYNDROME QUESTIONNAIRE (MPCOSQ) AND THE POLYCYSTIC OVARY SYNDROME QUALITY OF LIFE TOOL (PCOSQOL) IN DUTCH AND FLEMISH WOMEN WITH PCOS

Jiskoot G (1), Somers S (2), de Roo C (2), Stoop D (2) and Laven JSE (1)

(1) Dept. of Reproductive Medicine, Erasmus MC, Rotterdam, The Netherlands and

(2) Ghent University Hospital, Department of Reproductive Medicine, Corneel Heymanslaan 10, 9000 Ghent, Belgium

Abstract: OBJECTIVE:

This study aims to determine the test-retest reliability and to confirm the domain structures of the Dutch version of the modified polycystic ovary syndrome questionnaire (mPCOSQ) and the Polycystic Ovary Syndrome Quality of Life Scale (PCOSQOL) in Dutch and Flemish women with Polycystic Ovary Syndrome (PCOS).

METHODS:

Two independent translators performed a forward and backward translation of the original English mPCOSQ and PCOSQOL. PCOS patients were contacted with a request to complete both questionnaires (and some additional demographic questions) online in their home environment (T0). A test-retest design was applied to demonstrate stability over time by having all women complete the same questionnaires a second time after two to four weeks (T1). At both points in time participants were asked if they had a preference for one of the two questionnaires. The study was approved by the Ethics Committee of Erasmus Medical Centre and of Ghent University Hospital. Participants were included between January and December 2021.

RESULTS:

A total of 245 women participated in the study and completed the test-retest of both questionnaires; 64 women were included in Belgium and 181 in the Netherlands. The median age of the women who completed the mPCOSQ and the PCOSQOL assessments was 31 (IQR 27.0-34.0) years. The median weight was 79 (IQR 65.0-98.0) kg. The median BMI was 32.1 (IQR 27.7-39.2) kg/m2. Most women received their PCOS diagnosis one to five years ago (44.1%) and were not actively trying to become pregnant (63.7%). The mPCOSQ has excellent internal consistency (α: 0.95) and a high to excellent Intraclass Correlation Coefficient (ICC) for all six domains (ICC: 0.88 – 0.96). The PCOSQOL demonstrates excellent internal consistency (α: 0.96) and ICC (ICC: 0.91 – 0.96) for all four domains. The original six-factor structure of the mPCOSQ is partly confirmed. Based on the factor analysis of the PCOSQOL, an extra domain is added which included coping items. Most women have no preference for one of the two questionnaires (55.9%). Assuming that BMI played an important role in the difference between mPCOSQ and PCOSQOL scores in both countries, we performed additional analyses based on BMI and if women were trying to conceive. Women with a BMI below 30 had better QoL compared to women with a BMI above 30 on the mPCOSQ (4.48 vs. 3.93, p<0.002) and on the PCOSQOL (4.64 vs. 3.60, p<0.001). Also, women who were not trying to conceive had better QoL compared to women who were trying to conceive based on the mPCOSQ (4.38 vs. 3.68, p<0.001) and the PCOSQOL (4.14 vs. 3.68, p=0.002).

CONCLUSIONS:

In conclusion, The Dutch mPCOSQ and PCOSQOL are reliable and disease-specific QoL measures for women with PCOS. Both questionnaires are recommended for clinical practice.

This research received no external funding.

Abstract ID #103

Abstract Title: HEALTHCARE AND RESEARCH PRIORITIES FOR WOMEN WITH POLYCYSTIC OVARY SYNDROME IN THE UK NATIONAL HEALTH SERVICE: A MODIFIED DELPHI METHOD

Bassel H. Al Wattar1,2, Jhia Jiat Teh3, Sophie Clarke4, Ali Abbara5,6, Carole Percy7, Rachel Morman8, Alison Wilcox8, Vikram Talaulikar4

1. Beginnings Assisted Conception Unit, Epsom and St Helier University Hospitals, London, UK
2. Comprehensive Clinical Trials Unit, Institute for Clinical Trials and Methodology, University College London, London, UK
3 Department of Metabolism, Digestion and Reproduction, Imperial College London, London, UK
4. Reproductive Medicine Unit, University College London Hospitals, London, UK
5. Department of Metabolism, Digestion and Reproduction, Imperial College London, London UK.
6. Division of Diabetes and Endocrinology, Imperial College Healthcare NHS Trust, London UK.
7. School of Psychological, Social & Behavioural Sciences, Coventry University, Coventry, UK
8. The Verity PCOS Charity, London, UK

Abstract: Objective: Polycystic ovary syndrome (PCOS) is a chronic lifelong condition affecting up to 20% of women worldwide. There is limited input from affected women to guide the provision of healthcare services and future research needs. Our objective was to scope the healthcare and research priorities of women with PCOS in the UK.

Methods: A three-staged modified Delphi method of lay patient representatives of women with PCOS consisting of two Online e-questionnaires and a consensus meeting involving lay representatives and healthcare professionals. Participants were asked to identify and rank healthcare and research priorities for their importance.

Results: 624 lay participants took part in our Delphi method. Over 98% were diagnosed with PCOS (614/624, 98.4%). More than half experienced difficulties to receive a PCOS diagnosis (375/624, 60%), and the majority found it difficult to access specialised PCOS health services in the NHS (594/624, 95%).

Two domains were identified as high priority by more than 85% of our participants including better education for health professionals on the diagnosis and management of PCOS (238/273, 87.1%) followed by the need to set up specialist PCOS clinics to offer individualised care and routine monitoring (234/273, 85.7%).

Six domains were identified as high priority by more than 80% of participants including: reducing the waiting time to see a PCOS specialist (230/273, 84.2%), improving access to treatment of menstrual disorders (225/273, 82.4%), the need to improve access to rapid and reliable PCOS diagnosis (224/273, 82.0%), and the need to improve access to first-line treatment options in the community (223/273, 81.6%).

Out of fourteen research domains, seven were ranked as 'high priority' by more than 80% of participants. The top research priority was identifying better treatment for irregular periods (233/273, 85.3%) followed by developing better tests for early PCOS diagnosis (230/273, 84.2%). The remaining top PCOS research priorities included in descending order: reducing pregnancy complications (229/273, 83.9%), determining causes and pathophysiology of PCOS (226/273, 82.8%), identifying treatments for diabetes prevention and insulin resistance (226/273, 82.8%), improving fertility treatments (224/273, 82.1%), and weight loss interventions (220/273, 80.6%)

Conclusion: We identified 13 healthcare and 14 research priorities that reflect the current health needs of women with PCOS in the UK. Adopting these priorities in future healthcare and research planning will help to optimise the health of women with PCOS and increase patient satisfaction.

Abstract ID #105

Abstract Title: CLINICAL OUTCOMES OF DIFFERENT ENDOMETRIAL PREPARATION PROTOCOLS FOR EMBRYO TRANSFER IN WOMEN WITH POLYCYSTIC OVARY SYNDROME: A COMPREHENSIVE SYSTEMATIC REVIEW AND META-ANALYSES.

Jhia Jiat Teh(1), Hannah Denbigh(2), Michael P Rimmer(3), Peter Godolphine(7), Sophie Clarke(4), Vikram Talaulikar(4), Terhi Piltonen(5), Bassel H Al Wattar(6,7)

1 Department of Metabolism, Digestion and Reproduction, Imperial College London, London, UK.

2 Hull York Medical School, York UK

3 MRC Centre for Reproductive Health, Queens Medical Research Institute, Edinburgh BioQuarter, University of Edinburgh, Edinburgh, UK.

4 Reproductive Medicine Unit, University College London Hospitals, London, UK

5 Department of Obstetrics and Gynecology, Research Unit of Clinical Medicine and Medical Research Centre Oulu, Oulu University Hospital, University of Oulu, Oulu, Finland

6 Beginnings Assisted Conception Unit, Epsom and St Helier University Hospitals, London, UK.

7 Comprehensive Clinical Trials Unit, Institute for Clinical Trials and Methodology, University College London, London, UK

Abstract: Objective: Polycystic ovary syndrome (PCOS) affects up to a quarter of subfertile couples seeking assisted conception. Several protocols have been proposed to prepare the endometrium ahead of a planned embryo transfer (ET) to optimise the reproductive outcome of women with PCOS. Evidence on the most effective endometrial preparation method in this population is lacking. We aimed to compare the effectiveness and safety of different endometrial preparation protocols in PCOS women undergoing assisted conception by conducting a comprehensive systematic review and meta-analyses of randomised clinical trials (RCT).
Methods: We searched electronic databases (MEDLINE, EMBASE, Web of Science and Scopus) from inception until January 2023 for relevant studies of any design. We screened 819 citations and included 25 studies (6 RCTs, 16 retrospective and 3 prospective observational). Comparing six endometrial preparation protocols (fresh ET, frozen-thawed (FTET) with HRT only, HRT with GnRH agonist downregulation, mild stimulation, gonadotropins stimulation, and natural cycle FTET). Most studies suffered from a moderate to high risk of bias.
There was no significant difference in clinical pregnancy across all evaluated endometrial preparation protocols. Ongoing pregnancy was a higher with mild stimulation vs HRT only (n=6, 6302 women, RR 1.20; 95%CI 1.03–1.41; I2 60%). Live birth was higher with gonadotropins vs HRT only protocol (n=5, 7192 women, RR 1.15; 95%CI 1.07–1.24; I2 0%) and with HRT+GnRH agonist vs HRT only (n=4, 6696 women, RR 1.08; 95%CI 1.01–1.17; I2 21%). A fresh ET was associated with a lower live birth rate compared to FTET with HRT only (n=2, 1614 women, RR 0.86; 95%CI 0.77–0.96; I2 0%).
Compared to HRT only, a gonadotropins protocol (n=5, 4651 women, RR 0.75; 95%CI 0.60–0.93; I2 0%) and mild stimulation protocol (n=6, 4603 women, RR 0.52; 95%CI 0.42–0.65; I2 0%) showed lower risk of miscarriage. Network meta-analysis suffered from high variation between direct and indirect evidence especially across studies evaluating the use of gonadotropins highlighting reduced certainty in these effect estimates.
There was limited reporting for longterm obstetric outcomes in this cohort with limited evidence suggesting a lower risk for pre-eclampsia (one study, 861 women, RR 0.32; 95% CI 0.13-0.80) and a slight reduction in the average birth weight (one study, 1508 women, SMD -0.28; 95%CI 0.38 to -0.18) in fresh cycle transfer compared to FET with HRT only.
Conclusions: There is limited evidence to support the elective use of frozen over fresh embryo transfer in women with polycystic ovary syndrome undergoing assisted conception. Using mild-stimulation or gonadotropins frozen thawed embryo transfer may reduce the risk of miscarriage compared to hormone-replacement protocol, but it should not be offered routinely in practice pending larger randomised trials.
PROSPERO: CDR42021257212

Abstract ID #106

Abstract Title: FREE ANDROGEN INDEX MAY BE THE MOST USEFUL MARKER OF BIOCHEMICAL HYPERANDROGENISM FOR THE DETECTION OF PCOS

Hwang KR (1),(2), Kim JJ (1),(3), Choi YM(4)

(1)Department of Obstetrics and Gynecology, Seoul National University College of Medicine, Seoul Korea;

(2)Department of Obstetrics and Gynecology, SMG-SNU Boramae Medical Center, Seoul, Korea

(3)Healthcare System Gangnam Center, Seoul National University Hospital, Seoul, Korea;

(4)Department of Obstetrics and Gynecology, Grace Hospital, Goyang, Korea

Abstract: Objective: Hyperandrogenism is a core diagnostic criterion for polycystic ovary syndrome (PCOS). To decide what serum androgen measure should be used in clinical practice, it is essential to directly compare the diagnostic performances of androgen markers for PCOS. Therefore, we compared the performances of various serum androgens for predicting the diagnosis of PCOS in women with PCOS and matched controls in Korean women.

Methods: The receiver operating characteristic (ROC) curve analyses of androgens were performed for 195 (enrolled for age matching) and 104 (enrolled for age and BMI matching) women with PCOS and controls, respectively.

Results: There were significant differences in global AUCs in both age and age/BMI matched ROC models. The highest AUC was that of free androgen index (FAI) [0.818 (95% CI 0.764-0.853) in age matched model, and 0.715 (95% CI 0.644-0.785) in age and BMI matched model] as compared with those of total testosterone (T), bioavailable T, and calculated free T, even after the statistical significance was specified by Bonferroni correction. The AUCs of free T was not differ from that of FAI, but the performance of free T was not different from those of total T, bioavailable T, and calculated free T. FAI cutoff of 2.06 (age matched model) and 2.38 (age and BMI matched model) produced the highest combination of sensitivity and specificity.

Conclusions: Our findings suggest that FAI might be the most useful biochemical marker of hyperandrogenism for the detection of PCOS even eliminating the effect of age and obesity.

Abstract ID #108

Abstract Title: WOMEN WITH POLYCYSTIC OVARY SYNDROME AND SEVERE OBESITY HAVE HIGHER SCORES FOR COGNITIVE RESTRAINT EATING BEHAVIOR

Kataoka J (1,2), Stener-Victorin E (3), Larsson I (4,5)

(1) Institute of Neuroscience and Physiology, Department of Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden;

(2) Department of Obstetrics and Gynaecology, Sahlgrenska University Hospital, Gothenburg, Sweden;

(3) Department of Physiology and Pharmacology, Karolinska Institute, Biomedicum, Stockholm, Sweden;

(4) Department of Gastroenterology and Hepatology, Sahlgrenska University Hospital, Gothenburg, Sweden;

(5) Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

Abstract: OBJECTIVE: To investigate self-reported energy intake, physical activity, and eating behavior in women with severe obesity (BMI ≥ 35) with and without polycystic ovary syndrome (PCOS).

METHODS: In total, 246 women with severe obesity, referred to an obesity unit, were screened for PCOS with the NIH-criteria. Questionnaires used were Food frequency questionnaire (FFQ), International physical activity questionnaire (IPAQ), Three-factor eating questionnaire (TFEQ), and Questionnaire of eating and weight patterns revised (QEWPR). Binge eating disorder (BED) was identified according to DSM-5 criteria.

RESULTS: In women with severe obesity, self-reported energy intake, and physical activity did not differ between women with and without PCOS. Women with PCOS report higher scores in cognitive restraint eating compared to women without PCOS (p = 0.012). No differences were found between groups regarding emotional eating and uncontrolled eating. In both groups, cognitive restraint eating was negatively correlated to energy intake (PCOS: t-ratio -2.42, p=0.02; non-PCOS t-ratio -2.83, p=0.006). Uncontrolled eating was positively correlated to energy intake (PCOS: t-ratio 2.04, p=0.05; non-PCOS: t-ratio 5.69, p>0.001). For emotional eating, a positive correlation with energy intake was found in women without PCOS (t-ratio 5.67, p<0.0001). In women with PCOS, no correlation was found between emotional eating and energy intake (t-ratio -0.55 p=0.59). Prevalence of BED did not differ between women with and without PCOS (11.5% vs. 17.5%, Chi2, 1.22, p=0.27).

CONCLUSIONS: While no difference in prevalence of BED, women with severe obesity and PCOS report a greater degree of conscious control in relation to energy intake but no difference in emotional eating and uncontrolled eating, compared to women without PCOS. The three domains in eating behavior were correlated in different ways to energy intake in both groups.

Abstract ID #109

Abstract Title: ACTIVATION OF THE HIF -PATHWAY ALLEVIATES METABOLIC DEFECTS IN PREPUBERTAL PCOS MOUSE MODEL

Virtanen NV (1,2), Saarela U (1), Arffman RK (1), Karpale M (2), Koivunen P (2) Piltonen TT (1)

(1) Department of Obstetrics and Gynecology, Medical Research Center Oulu, Research Unit of Clinical Medicine, University of Oulu and Oulu University Hospital, Oulu, Finland;

(2) Faculty of Biochemistry and Molecular Medicine, University of Oulu, Oulu, Finland;

Abstract: OBJECTIVE: PCOS is a condition often accompanied by metabolic defects, which can also aggravate the general disease phenotype. Since activation of the Hypoxia inducible factor (HIF) -pathway has been shown to alleviate metabolic dysfunction, our study aims to investigate whether metabolic issues in PCOS could be countered with chemically induced HIF-pathway activation.

METHODS: Our study was conducted using a prepubertally induced letrozole mouse model. Female C57Bl/6J mice were outfitted, at three weeks' age, with subcutaneous pellets providing a daily continuous release of 50 µg of letrozole. Estrous cycles were monitored using vaginal smears. Ovaries were sectioned and H&E stained to allow morphological analysis. Glucose tolerance tests (GTTs) were performed and HOMA-IR values calculated to assess the metabolic health of the animals. ELISA was used to determine levels of blood testosterone and cholesterol, blood-, liver-, and white adipose tissue triglycerides, and muscle glycogen. HIF activation was induced with orally administered Roxadustat. Statistical analysis was performed with GraphPad.

RESULTS: Letrozole mice were completely anovulatory, while controls cycled normally. Ovarian morphology was affected, with letrozole mice showing multiple cystic follicles and hemorrhagic cysts. Blood testosterone values were higher in PCOS mice than controls. None of the above defects were alleviated by the Roxadustat treatment. In GTTs a difference was seen between controls and letrozole treated mice, with significantly increased area under the curve values in the letrozole group, indicating poor glucose tolerance, as well as increased HOMA-IR values signifying increased insulin resistance. Interestingly, these effects were completely reversed with Roxadustat treatment. Additionally, PCOS mice showed significant elevation in adipose tissue triglycerides and decrease in muscle glycogen, along with a trend, lacking statistical significance, of partial reversal by Roxadustat in both of these effects.

CONCLUSIONS: Our results show that HIF -pathway activation can counteract various metabolic defects caused by androgen excess. It should be noted that the letrozole mouse model is very potent in its effects, as it is maintained by the continuous letrozole release. Remedying these defects in this model could therefore be an excessive task and further studies with a different model would be in order, to investigate the effects of HIF activation on the reproductive aspects of PCOS. Besides providing proof of concept regarding the use of hypoxia response in alleviating PCOS, our study also provides insight into the specific qualities of the letrozole -induced PCOS mouse model, informing the choice of model for future studies.

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Abstract ID #110

Abstract Title: PATTERNS OF ANDROGEN EXCESS IN A POPULATION-BASED COHORT OF 24,435 PARTICIPANTS IN THE APPLE WOMEN'S HEALTH STUDY

Wang Z (1), Onnela JP (1), Jukic AM (2), Williams MA (1), Hauser R (1), Coull BA (1), Mahalingaiah (1, 3)*

(1) Department of Environmental Health/Biostatistics, Harvard T.H. Chan School of Public Health, Boston, MA, United States;

(2) National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC, United States.

(3) Department of OB/GYN, Massachusetts General Hospital, Boston, MA, United States

Abstract: OBJECTIVE: Androgen excess (AE) characterization has generally come from clinical studies which constrains generalizability of findings. We assessed AE patterns in a large, population-based cohort in the US, and we explored heterogeneity in these patterns by race and ethnicity.

METHODS: We evaluated self-reported AE features of 24,435 participants in the Apple Women's Health Study (AWHS) from 11/2019 to 12/2022. Details of the AWHS were described previously. We evaluated hirsutism (having thick, coarse, and dark hair on eight body locations, or relative to female family members), alopecia (severity, and relative to female peers), acne (severity, and relative to female peers), and clinician-diagnosed PCOS status. Self-reported race/ethnicity was grouped as non-Hispanic (NH) white (n = 18,233), NH Black (n = 1,169), Asian (n = 695), Hispanic (n = 1,521), multiple races (n = 2,273), or other (n = 544). Within Asians, participants reported South/East/Southeast Asian ancestries. Differences were evaluated using Kruskal-Wallis or Chi-square tests for continuous and categorical variables, respectively.

RESULTS: For hirsutism, among all 24,435 participants, excess hair growth on the chin was the most commonly reported (27%), while excess growth on the back was least commonly reported (2%). Hair growth on the upper lip and breasts were highest among Hispanic (25% and 20%, respectively) and lowest among NH Black participants (15% and 7%, respectively), while the percentage of hair growth on the chin was highest among NH Black (31%) and lowest among Asian participants (16%). There were also smaller differences at the other locations (chest, back, abdomen, upper arms, and upper thighs). Among Hispanic participants, 27% had more hair relative to female family members compared to 17% in NH white participants. For alopecia, the percentage of experiencing hair loss on top of the head was highest in Asians (13%) and lowest in NH white participants (7%). For acne, the percentage of having more acne compared to female peers was highest in NH white (31%) and lowest in NH Black (23%) participants. Lastly, the prevalence of PCOS was highest among those with multiple races (14%) and lowest among NH Black participants (10%). Within Asians, participants with South Asian ancestry had the highest hair growth on all locations, were most likely to have both more hair growth relative to female family members (36%) and more hair loss compared to females their age (36%), while those with Southeast Asian ancestry had a higher percentage of having acne with pus (22%) than East (18%) or South (16%) Asians. The p-values for all comparisons presented here were < 0.05. Several features were more severe among those with PCOS (data not shown).

CONCLUSIONS: We found notable racial and ethnic variation in hirsutism, alopecia, acne, and PCOS in this cohort, filling in the gap for self-assessed AE features from population-based studies.

Abstract ID #111

Abstract Title: EXPERIENCES AND EXPECTATIONS OF SUPPORT AMONG YOUNG WOMEN WITH PCOS AND THEIR MOTHERS IN INDIA

Lathia T (1), Chittem M (2), Chawak S (3), Akula N (4), Selvan C (5)

1. Department of Endocrinology, Apollo Hospitals, Navi Mumbai, India
2. Department of Liberal Arts, Indian Institute of Technology Hyderabad (IITH), Hyderabad, India
3. Jindal School of Psychology and Counselling, O P Jindal Global University, Sonipat, India
4. Rockwell International School, Hyderabad, India
5. Department of Endocrinology, Ramaiah Medical College, Bangalore, India

Abstract: Objective: Polycystic ovarian syndrome (PCOS) in India intersects with illness management and patriarchal notions of womanhood (e.g., interfering with one's marital prospects). A young woman's first source of support, therefore, is usually their mother who helps manage these social responses to PCOS. This study explored young women's and their mothers' experiences of managing PCOS-related symptoms, responses to their social network, and how the dyads were communicating with each other.

Methods: Individual, telephonic, semi-structured, audio-recorded interviews were conducted with 12 mother-daughter pairs (i.e., total n=24; mean age of daughters=22.4, mean age of mothers=49.5). The interviews were analysed using thematic analysis.

Results: Three themes were generated: (1) emotional turmoil and the emotional impact of having PCOS, (2) coming to terms with and adapting to the condition, and (3) need for communication between the mothers and daughters.

Conclusion: The dyads experienced immense emotional turmoil, with the former describing feelings of shame and the latter feelings of worry. The mothers played a crucial role in aiding their daughters in lifestyle management, although they preferred attempting at multiple alternate remedies while the daughters wanted to adhere to the physician-prescribed management choices. The dyads reported a need for effective empathic communication between one another, particularly in terms of lifestyle management. These findings highlight the need for (1) physicians to include mothers in PCOS-related discussions in their daily practice, (2) communication skills interventions for mothers and daughters, and (3) community outreach so as to improve sensitivity and awareness to the psychological aspects of having PCOS in India.

Abstract ID #112

Abstract Title: IS IT USEFUL TO MEASURE DHEAS LEVELS IN PCOS?

Catteau-Jonard S (1); Boucher H (1); Robin G (1)

(1) Lille Univ., CHU of Lille, Dept. of Medical Gynecology, 59000 Lille, France

Abstract: Objective : A high prevalence (around a third) of increased DHEAS levels has been reported in women with polycystic ovary syndrome PCOS. This excess of adrenal androgen remains a mystery in this ovarian pathology. It is well known that DHEAS production correlates negatively with age, and the studied populations of women with PCOS are generally young. To avoid this bias, a study was performed on a large population of women with PCOS and control women, using established DHEAS standards for each age group, in order to better assess prevalence and to better understand the link between PCOS and DHEAS.

Methods: A retrospective cross-sectional study was conducted within a university-affiliated reproductive endocrinology unit. A total of 1223 patients with PCOS according to the Rotterdam Criteria and 517 control women were included. Increased DHEAS levels was diagnosed according to the standards of the Institute of Biochemistry and Molecular Biology of the CHU, depending on the age of the patients. The prevalence of increased serum DHEAS levels was calculated in each population and according to the different PCOS phenotypes. Correlations were sought between serum DHEAS levels and clinical, hormonal and metabolic markers, with adjustment for age.

Results: In the PCOS group, the prevalence of higher DHEAS levels was significantly increased compared to control group : 8.1% vs 4.3% ; OR= 1.98 (95% CI : 1.23-3.19) , p=0.005 and OR =1.07 (95% CI : 1.05-1.09) , p= 0.014 without and after adjustment for BMI respectively. The prevalence of higher DHEAS levels was significantly increased in the phenotype A and C compared to control group : OR= 2.88 (95%CI : 1.76 to 4.72), p<0.001 and OR= 2.81 (95% CI : 1.39 to 5.67), p=0.004 respectively. The prevalence of higher DHEAS levels was not increased in B phénotype. A correlation was found between DHEAS levels and total testosteronemia (r=0.34, p<0.001), androstenedione (r=0.24, p<0.001), 17 hydroxyprogesteronemia (r=0.22, p<0.001) and age (r=0.25, p<0.001). No correlation was found with AMH, LH, FSH and a very weak positive correlation was found with BMI (r=0.15 ; p<0.001).

Conclusions: Using norms according to the age of the patients, the prevalence of increased DHEAS was found in "only" 8.1% of women with PCOS (11% in the case of phenotype A and C) compared with 4.3% in controls and women with PCOS of B phenotype. The DHEAS levels correlated only with other androgens, and not (or very little) with other ovarian, pituitary or metabolic markers. Therefore, the DHEAS assay does not appear to be of interest in the diagnosis and/or understanding of the pathophysiology of PCOS.

Abstract ID #113

Abstract Title: The impact of metformin on infections in PCOS-pregnancies and offspring allergy, asthma, and eczema

Mariell Ryssdal,1,2, Johanne Eikeland Skage,1,2, Guro F. Giskeødegård3 Live Marie T. Stokkeland,1,2 Anders Hagen Jarmund,1,2 Bjørg Steinkjer,1,2 Liv Guro Engen Hanem1 , Tone Shetelig Løvvik,1,4 Ann-Charlotte Iversen,1,2* and Eszter Vanky,1,4*

(1) Department of Clinical and Molecular Medicine, Norwegian University of Science and Technology (NTNU), 7491 Trondheim, Norway;

(2) Centre of Molecular Inflammation Research (CEMIR), Norwegian University of Science and Technology, 7491 Trondheim, Norway;

(3) K.G. Jebsen Center for Genetic Epidemiology, Department of Public Health and Nursing, Norwegian University of Science and Technology, 7491 Trondheim, Norway

(4) Department of Obstetrics and Gynecology, St. Olavs Hospital, Trondheim University Hospital, 7006 Trondheim, Norway;

*These authors contributed equally.

Abstract: Background: Polycystic ovary syndrome (PCOS) has wide implications for pregnancy, delivery, and long-term health for both mother and child. Metformin reduces preterm birth in PCOS-pregnancies. The potential effect of metformin on maternal infections in PCOS pregnancies and on long-term effects on the offspring is not explored.

Methods: Post-hoc analyses of two randomized controlled trials, the PregMet and PregMet2 studies (n=646), where women with PCOS were randomized to metformin or placebo from 1st trimester to delivery. Children from the PregMet study (n=153) were followed up at 8-years of age. Self-reported infections in pregnancy and clinical outcomes in the children were compared between the treatment groups.

Results: Women treated with metformin compared to placebo had less infections in pregnancy, 41% vs. 51% (p=0.01). In subgroup analyses, the prevalence of viral infections was significantly reduced 29% vs 37% (p=0.02), whereas reduction in bacterial infections was not significant (p=0.29). Children exposed to metformin in utero had higher prevalence of allergy (p=0.01) and eczema (p=0.004) at 8-years of age compared to those exposed to placebo. The prevalence of asthma did not differ (p=0.48).

Conclusion: Metformin-exposure during pregnancy seemed to reduce viral infections in pregnancy and increased the prevalence of allergy and eczema in the offspring at 8-years of age.

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Abstract ID #114

Abstract Title: ANTHROPOMETRICS OF NEONATES BORN TO MOTHERS WITH PCOS COMPARED TO A REFERENCE POPULATION – POOLED DATA FROM THREE RCTs AND THE NORWEGIAN MOTHER, FATHER, AND CHILD STUDY (MoBa)

Maren Sophie Aaserud Talmo med. Stud1#, Ingvild Skogedal Fløysand med. Stud1#, Guro Ørndal Nilsen MD1, Rønnaug Ødegård MD PhD2,3, Petur Benedikt Juliusson MD PhD4,5 Melanie Rae Simpson MD PhD5,6* and Eszter Vanky MD PhD1,7*,

*Shared last authorship

(1) Department of Clinical and Molecular Medicine, Norwegian University of Science and Technology (NTNU), 7491 Trondheim, Norway;

(2) Children's Clinic Centre for Obesity Research, St. Olavs Hospital, Trondheim University Hospital, Trondheim, Norway;

(3) Department of Health Registry Research and Development, National Institute of Public Health, Bergen, Norway;

(4) Department of Clinical Science, University of Bergen, Norway;

(5) Department of Public Health and Nursing, Norwegian University of Science and Technology, Trondheim, Norway;

(6) Clinical Research Unit Central Norway, St. Olavs Hospital, Trondheim, Norway;

(7) Department of Obstetrics and Gynaecology, St. Olavs Hospital, Trondheim University Hospital, 7006 Trondheim, Norway;

Abstract: Objective To explore the effect of polycystic ovary syndrome (PCOS) on newborn anthropometrics and the potential impact of body mass index (BMI), PCOS phenotype, and gestational diabetes mellitus (GDM).

Methods Post hoc analysis of data from three clinical trials conducted in Norway, Sweden and Iceland and the Norwegian mother, father, and child cohort study (MoBa). 390 PCOS pregnancies were compared to 68 925 reference pregnancies. Anthropometric measures were analyzed using multivariable linear regression, with adjustment for potential confounders. Regression analyses compared birth anthropometrics according to maternal BMI categories. Subgroups of PCOS phenotype and GDM were compared within the PCOS group. Main outcome measures were offspring birthweight, birth length, head circumference, and the respective z-scores. Ponderal index, placenta weight, and birthweight-to-placenta-weight (BWPW) ratio.

Results PCOS offspring were lighter, shorter and had a smaller head circumference. The estimated mean difference in z-scores were; birthweight -0.26 (95% CI -0.38 to -0.14); birth length -0.19 (-0.33 to -0.05); and head circumference -0.13 (-0.26 to -0.01). The PCOS group had a lower ponderal index and placenta weight, and higher BWPW-ratio. In the overweight and obese groups, the growth restrictive effect of PCOS was more apparent.

Conclusions PCOS has a growth restrictive effect on the fetus which is more pronounced in overweight and obese mothers.

(Funding: The Research Council of Norway, Novo Nordisk Foundation, St. Olavs University Hospital and the Norwegian University of Science and Technology.)

Abstract ID #115

Abstract Title: OVULATION INDUCED FROZEN EMBRYO TRANSFER REGIMENS IN WOMEN WITH PCOS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Voss KA (1), Chen YM (2), Castillo DA (3), Vitek WS (4) Alur-Gupta S (4)

1. Dept. of Obstetrics & Gynecology Residency, University of Rochester Medical Center, Rochester, NY, USA;

2. Dept. of Nursing & Public Health, Nazareth College School of Health and Human Services, Rochester, NY, USA;

3. Edward G. Miner Library, University of Rochester Medical Center, Rochester, NY, USA;

4. Strong Fertility Center, University of Rochester Medical Center, Rochester, NY, USA

Abstract: OBJECTIVE:

This is a systematic review and meta-analysis to evaluate whether the type of frozen embryo transfer (FET) regimen influences success rates and the risk of hypertensive disorders of pregnancy (HDP) in women with PCOS.

METHODS:

A systematic review was performed to compare ovulation induced regimens (letrozole and/or human menopausal gonadotropin) to a programmed regimen (HRT) in women with PCOS undergoing FETs. Primary outcomes were the relative risk (RR) of live birth and HDP. Secondary outcomes included RR of clinical pregnancy, miscarriage and ectopic pregnancies. All studies in PubMed, Embase, Web of Science, Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov were searched up until February 2, 2023 using a combination of MeSH terms and keywords. Searches were not limited by date or language but conference and meeting abstracts as well as ongoing trials without data were excluded.

A random effects meta-analysis was then performed for each outcome using relevant included studies. Dichotomous data were presented as RR with 95% confidence intervals (CI). Statistical analysis was performed using Stata.

RESULTS:

Two independent researchers (KV, SAG) screened 1614 titles and abstracts in Covidence, of which 43 publications met inclusion criteria for full text review. 20 of these studies were relevant, however additional data was needed from 9 of them. After two unsuccessful attempts to contact each study author for additional data, these publications were excluded. Therefore, for the final review 11 studies were included in the meta-analysis.

Ovulation induced regimens were associated with a higher live birth rate (8 studies, RR 1.14 [95% CI 1.08, 1.21]) and lower miscarriage rate (9 studies, RR 0.67 [95% CI 0.59-0.76]) compared to programmed regimen. Rates of clinical pregnancy (10 studies, RR 1.05 [95% CI 0.99, 1.11]), ectopic pregnancy (7 studies, RR 1.40 [95% CI 0.84, 2.33]), and HDP (3 studies RR 0.78 [95% CI 0.53, 1.15]) were not significantly different between the regimens.

CONCULSIONS:

For women with PCOS, ovulation induced FET regimens are associated with higher live birth rates and lower rates of miscarriage compared to HRT. Given this, ovulation induced FET regimens should be considered as first line in women with PCOS. Although prior literature suggests that HRT regimens are associated with higher rates of HDP, possibly due to the absence of a corpus luteum, this meta-analysis did not find a significant difference between the 2 regimens. However more research in the form of RCTs is needed to confirm this finding.

Abstract ID #116

Abstract Title: SHOULD THE OVARIAN MARKERS FOR THE DIAGNOS OF PCOS BE REVISED?

van der Ham K (1), Schilfgaarde E (1), Louwers YV (1), Laven JSE (1)

(1) Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

Abstract: OBJECTIVE: PCOS is characterized by three features: ovulatory dysfunction, hyperandrogenism and polycystic ovary morphology (PCOM). PCOM is detected by ultrasound. The definition of PCOM according to the 2003 Rotterdam criteria was 12 or more follicles measuring 2 - 9mm throughout the entire ovary or an ovarian volume ≥ 10 cc. This was based on a single report on sensitivity and specificity in PCOS compared to controls. In the international PCOS guideline, published in 2018, the thresholds for antral follicle count to define PCOM was increased due to improvement of accuracy of ultrasound devices. The threshold for ovarian volume (OV) was maintained. Therefore, in this study we investigated and compared OV and follicle number per ovary (FNPO) in a large cohort of well-phenotyped women with PCOS and in controls. We redefined the cut-off values of both diagnostic criteria for PCOM.

METHODS: This retrospective cross-sectional study contains data of 2723 women with PCOS (after excluding missing ultrasound data or the presence of corpora lutea, dominant follicles and cysts) and 200 controls. Control women had regular menstrual cycles, hormone values within the normal range, and no diagnosis of PCOS. In the PCOS group, 52 women underwent a transabdominal ultrasound (TAUS) and were compared to women who underwent a transvaginal ultrasound (TVUS).

RESULTS: We found significantly higher mean FNPO and mean OV in women with PCOS compared to age-matched controls (22.5 IQR (15.5 - 31.5) versus 12.0 (IQR 7.3 - 16.5) and 8.7 mL (IQR 6.6 - 11.6) versus 5.28 mL (IQR 3.4 - 7.2) respectively). Mean OV was similar between TAES and TVUS (9.8 mL (IQR 6.6 – 12.7) versus 8.7 mL (IQR 6.6 - 11.6), p = 0.84) , but mean FNPO was significantly lower in TAUS compared to TVUS (13 (IQR 9 - 16) versus 22.5 (IQR 15.5 - 31.5), p < 0001). ROC analysis showed an AUC of 0.781 (left ovary) and 0.798 (right ovary) for FNPO, using a cut-off value of 20 and using an ultrasound probe >8 MHz. ROC analysis for OV, using a cut-off value of 10 mL, showed an AUC of 0.733 (left ovary) and 0.782 (right ovary). The ideal cut-off value appears to be between 5.0 and 8.0 mL. Only 19/2559 (0.7%) women would not have received the PCOS diagnosis if OV > 10mL was not included in the diagnostic criteria.

CONCLUSIONS: We can conclude that TAUS can be used for establishing PCOM through OV, but does appear not to be accurate enough for FNPO, even with an ultrasound probe >8 MHz. Furthermore, FNPO seem to be a better marker for PCOM than OV and the cut-off value for diagnosing PCOM through ovarian volume should be revised or abolished. It seems that using FNPO alone as a diagnostic marker for PCOM does not result in underdiagnoses.

Abstract ID #117

Abstract Title: Evolution of cardiovascular risk markers and the risk for cardiovascular events in polycystic ovary syndrome: results from a long-term monocentric cohort study

Gambineri A (1,2), Pandurevic S (1,2), Cecchetti C (1,2), Dionese P (1,2), Belardinelli E (1,2), Rotolo L (1,2), Rucci P (3), Fanelli F (1,2), Bergamaschi L (4), Pizzi C (4), Uberto P (1,2)

(1) Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy.

(2) Department of Medical and Surgical Sciences (DIMEC), University of Bologna, Italy

(3) Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy

(4) Unit of Cardiology, Department of Specialist, Diagnostic and Experimental Medicine, University of Bologna, Italy

Abstract: OBJECTIVE: Aim of this cohort study was to evaluate the long-term evolution of cardiovascular (CV) risk markers and the risk for CV events in a population of women with polycystic ovary syndrome (PCOS).

METHODS: A total of 120 Caucasian PCOS patients diagnosed by NIH criteria at our Unit during the reproductive age were evaluated in 2009 for CV risk markers (hypertension, type 2 diabetes mellitus-DM, dyslipidaemia, obesity, carotid intima media thickness-cIMT, and epicardial fat thickness-EFT) and for major and minor CV events. All patients were subsequently reevaluated in 2020. 1:5 Matched controls by age and type 2 DM at baseline (total number 600) were included to estimate odds ratio of major and minor CV events by conditional logistic regression analysis.

RESULTS: Mean age of PCOS was 39.9±7.6 years at baseline and 51.9±7.6 years at follow-up, with a prevalence of menopausal state of 7.5% and 40.8%, respectively. At baseline, no major (acute myocardial infarction or stroke) or minor CV events were detected in PCOS. At follow-up, no major CV events were detected in PCOS, but 3 cases of arterial revascularization (2.5%), 1 case of transient ischaemic attack-TIA (0.8%), 2 cases of exercise-induced ischemia (1.7%) and 1 case of NYHA heart failure (0.8%) were documented. Odds ratios (95% CI) of minor CV events in PCOS vs. matched controls were 1.844 (0.525-6.474); 2.710 (0.392-18.763) for revascularization, 1 (0.104-9.464) for TIA, 1.250 (0.136-11.422) for heart failure.

Prevalence of hypertension, type 2 DM, dyslipidaemia, and obesity were 25.8%, 11.7%, 53.3% and 30.8% at baseline, and 40.0%, 20.8%, 83.3% and 42.5% at follow-up ($p<0.001$, $p<0.01$, $p<0.001$, $p>0.05$, respectively). cIMT was significantly increased at follow-up (0.58±0.16mm vs. 0.81±0.27mm, $p<0.001$), and the % of patients with cIMT≥ 1mm or with carotid plaques with no critical stenosis passed from 1.7% to 34.1% ($p<0.001$). In contrast, a significant decrease in EFT was detected from baseline to the follow-up (0.86±0.35cm and 0.41±0.23cm, respectively; $p<0.001$).

CONCLUSIONS: This cohort study shows that PCOS is characterized by a high prevalence of cardiovascular risk markers, with a tendency to increase over time; nonetheless, not all cardiovascular risk markers worsen, with some interesting beneficial variations occuring in EFT in the late reproductive or early post-menopausal years. Minor and major CV events seems not to be increased in PCOS.

Funding: This study was supported by PRIN 2017 Prot. 2017ATZ2YK

Abstract ID #118

Abstract Title: SEXUAL DYSFUNCTION IN WOMEN WITH PCOS: A CASE CONTROL STUDY

Pastoor, H. (1), Both, S. (2), Laan, E.T. (2), Laven, J.S. (1)

corresponding author: Pastoor, H., h.pastoor@erasmusmc.nl, 0031-6-17048767;

(1): Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Erasmus University Medical Centre, Rotterdam, The Netherlands;

(2): Department of Sexology and Psychosomatic Gynecology, Amsterdam University Medical Centers, Amsterdam, the Netherlands;

Abstract: OBJECTIVE: The literature shows that women with Polycystic Ovary Syndrome (PCOS) report lower levels of sexual function and sexual satisfaction and more sexual distress. Contributing factors seem to be obesity, alopecia, hirsutism, acne, infertility, anxiety, depression and low self-esteem. In women with PCOS clinical and/or biochemical hyperandrogenism is common, its relationship with sexual function is however inconclusive.

The purpose of this study is to assess the relationship of sex steroid levels with sexual function in women with and without PCOS.

METHODS: This observational prospective case control study with 135 women (68 PCOS, 67 control) was conducted from March 2017 until March 2020. Heterosexual women with and without PCOS, aged 18 – 40 years, in a steady relationship and without any comorbidities underwent an extensive medical and endocrine screening using liquid chromatography – tandem mass spectrometry (LC-MS/MS) and they filled in two validated sexual function questionnaires Female Sexual Function Index (FSFI) and Female Sexual Distress Scale Revised (FSDS-R). Means and percentages were calculated and compared between the two groups with ANOVA, Chi square tests or Mann-Whitney U tests. Linear and logistic regression analysis to determine associations between log transformed endocrine values and sexual function outcomes were performed with adjustment for confounders.

RESULTS: Women with PCOS reported significantly lower sexual function ($P<0.001$, partial $\eta2 = 0.104$; FSFI total score), higher levels of sexual distress ($P<0.001$, partial $\eta2 = 0.090$; FSDS-R total score) and they more often complied with the definition of sexual dysfunction (41.2% vs 11.9%, $P<0.001$, Phi V = 0.331; FSFI<26.55& FSDS-R≥15) and clinical sexual distress (51.5% vs 19.4%, $P<0.001$, Phi V = 0.335; FSDS-R≥15).

Regression analysis adjusted for confounders showed only few and weak associations between androgen levels and sexual function, with each model explaining maximum 15% in sexual function. Following significant Group X Hormone interactions, analyses for both groups separately showed no significant associations in the PCOS group. The control group showed only weak negative associations between testosterone and FSFI pain (β=-6.022, P=0.044, Adj R2=0.050), Free Androgen Index and FSFI orgasm (β=-3.360, P=0.023, Adj R2=0.049) and androstenedione and clinical sexual distress (β=-7.293, P=0.036, exp(β)=0.001).

CONCLUSIONS: Sexual function is impaired in women with PCOS and should be discussed. Endocrine perturbations seem to have minimal direct impact on sexual function and are not clinically useful as diagnostic indicators. Performing a thorough biopsychosocial assessment is necessary to determine factors that influence sexual function in a specific case. Offering tailor made treatment including psychosexual counselling is important in the clinical care for women with PCOS.

FUNDING: (1) & (2)

Abstract ID #119

Abstract Title: EMOTIONAL AND COGNITIVE UNDERPININGS OF WOMEN WITH POLYCYSTIC OVARY SYNDROME ACROSS THE URBAN, RURAL AND TRIBAL INDIA

Redkar, Maitreyi (1), Khan, Azizuddin (2)

(1) Psychophysiology Laboratory, Humanities and Social Sciences Department, Indian Institute of Technology – Bombay, Maharashtra, India

(2) Psychophysiology Laboratory, Humanities and Social Sciences Department, Indian Institute of Technology – Bombay, Maharashtra, India

Abstract: OBJECTIVE: To investigate the emotional and cognitive underpinnings of women with Polycystic Ovary Syndrome (PCOS) from areas of residence. The study evaluated whether the Westernized urban lifestyle, agrarian rural lifestyle and forest-dwelling tribal lifestyle affected the psychological experience of PCOS. As per our knowledge, this study is among the first to look at the cross-sectional psychological impact of PCOS on Indian women from not just urban but also rural and tribal areas.

METHODS: Two questionnaires were administered to 566 participants from India (195 PCOS and 271 non-PCOS; overall mean age = 25.60), of which 162 were from urban areas (78 PCOS and 84 non-PCOS), 222 from rural areas (128 PCOS and 94 non-PCOS) and 182 from tribal areas (89 PCOS and 93 non-PCOS). The first questionnaire was the Cognitive Failures Questionnaire (CFQ) which explored the cognitive impairments experienced; the second questionnaire was the Beck's Depression Inventory (BDI) which evaluated the depressive tendencies experienced. This study used a 2 (conditions - PCOS vs Non-PCOS) x 3 (areas of residence - urban vs rural vs tribal) mixed factorial design.

RESULTS: The one-way ANOVA for cognitive failures among the conditions was $F (1, 560) = 2287.46$, $p=0.01$, $n2= 0.80$, and for areas of residence, was $F (2, 560) = 52.23$, $p=0.01$, $n2= 0.16$. The interaction effect between the area of residence and condition for CFQ total was $F (2, 560) = 15.67$, $p=0.01$, $n2= 0.05$. The three subscales of CFQ - Forgetfulness at $F (2, 560) = 9.03$, $p=0.01$, $n2= 0.031$, Distractibility at $F (2, 560) = 11.09$, $p=0.01$, $n2= 0.038$ and False Trigger at $F (2, 560) =14.69$, $p=0.01$; $n2= 0.05$ were all statistically significant.

One-way ANOVA for the main effect of depressive tendencies between the two conditions was at $F (2, 560) = 71.94$, $p=0.01$, $n2= 0.114$ and the main effect between the areas of residence was at $F (2, 560) = 8.54$, $p=0.01$, $n2= 0.030$. Like the main effects, the interaction effect between the area of residence and condition was also statistically significant $F (2, 560) = 11.77$, $p=0.01$, $n2= 0.040$.

CONCLUSIONS: Women with PCOS had higher scores on cognitive failures and depressive tendencies compared to the non-PCOS healthy participants across the urban, rural and tribal areas of India. In cognitive failures, the urban areas reported higher cognitive failures than the rural and tribal. The rural participants reported higher levels of depression compared to the urban and tribal. Though this study establishes that area of residence impacts the cognitive failures and depressive tendencies of women with PCOS, further experimental work is required to understand these neurocognitive markers better.

Abstract ID #120

Abstract Title: VALIDATION OF THE ELECSYS ANTI-MÜLLERIAN HORMONE (AMH) PLUS IMMUNOASSAY CUT-OFF FOR POLYCYSTIC OVARIAN MORPHOLOGY (PCOM) IN THE DIAGNOSIS OF POLYCYSTIC OVARY SYNDROME (PCOS): THE HARMONIA STUDY

Piltonen T (1), Kinnunen J (1), Kangasniemi MH (1), Luiro K (2), Rajecki M (2), Jokelainen J (3) , Kiviniemi E (3), Allegranza D (4), Hund M (4), Olziersky A(4), Logan CA (5), Buck K (5), Savukoski SM (1), Arffman RK (1).

(1) Department of Obstetrics and Gynecology, Oulu University Hospital and Research Unit of Clinical Medicine, Medical Research Center, Oulu University Hospital, University of Oulu, (MRC Oulu, Finland), Oulu, Finland

(2) Department of Obstetrics and Gynecology, University of Helsinki, Helsinki, Uusimaa, Finland

(3) Northern Finland Birth Cohorts, Arctic Biobank, Infrastructure for Population Studies, Faculty of Medicine, University of Oulu, Oulu, Finland

(4) Roche Diagnostics International Ltd, Rotkreuz, Switzerland

(5) Roche Diagnostics GmbH, Penzberg, Germany

Abstract: OBJECTIVE: PCOS diagnosis per Rotterdam criteria requires ≥2 of the following criteria be met: oligo- and/or anovulation (OA), clinical and/or biochemical hyperandrogenism (HA) and polycystic ovarian morphology (PCOM). Per the 2023 update of the International Evidence-Based PCOS Guideline, serum AMH can substitute the antral follicle count (AFC) in the PCOM diagnosis. Previously, an Elecsys® AMH Plus (Roche Diagnostics) cut-off of 3.2 ng/mL to detect PCOM was derived and validated in the case-control APHRODITE study. This study aimed to validate the 3.2 ng/mL cut-off in the large, population-based HARMONIA study.
METHODS: The prospective, multi-center, population-based HARMONIA study (NCT05527353) based at Oulu and Helsinki University Hospitals in Finland enrolled women born in the Northern Finland area between July 1, 1985 - June 31, 1989. The Ethical Committee of the Northern Ostrobothnia Hospital District provided ethical approval (EETTMK 47/2019).
Each participant completed one study visit including serum sampling (any menstrual cycle stage), clinical data collection, and a gynecological examination with TVUS. All data were collected by trained midwives and gynecologists. For the analysis, PCOS cases were defined per Rotterdam criteria as PCOS positive (phenotypes A-D). PCOS phenotype B cases being PCOM negative were excluded from the primary analysis. OA was defined as cycles >35 days or less than 8 cycles/year, clinical HA as modified Ferriman-Gallway score >4, biochemical HA as serum testosterone >1.77 nmol/L (LCM-MS) and PCOM as AFC≥20 and/or ovarian volume ≥10 mL. Controls were PCOM-negative women with an AFC <20, ovarian volume <10 mL and no PCOS diagnosis.
The minimum sample size for the study's primary analysis was calculated to achieve a lower 95% confidence limit greater than 65% for sensitivity and greater than 70% for specificity with 80% joint probability. The estimated minimum sample size was 55-88 cases and 164-262 controls, respectively.
RESULTS: In total, 1798 subjects were included in the primary analysis. Study data is currently under analysis and the results will be available at the AE-PCOS Annual Meeting in Rotterdam.
Results will include:
- Patient characteristics (age, BMI, waist, testosterone, SHBG, FAI, LH, FSH) and subject grouping (including phenotype grouping)
- Median AMH levels
- Correlation of AMH to AFC and ovarian volume (Spearman correlation coefficients)
- Validation of the AMH cut-off of 3.2 ng/mL for PCOM (Receiver Operator Characteristic-analysis) with sensitivity and specificity.

CONCLUSIONS:
The validation of the Roche Elecsys® AMH Plus cut-off in HARMONIA will confirm the utility of a simple serum AMH blood test to identify PCOM as part of PCOS diagnosis. This would enable faster, less expensive and more accurate diagnostic workup compared to PCOM assessment with ultrasound.

Abstract ID #122

Abstract Title: UTILIZING A DIGITAL COHORT STUDY TO UNDERSTAND THE PREVALENCE OF POLYCYSTIC OVARY SYNDROME AND RELATED HEALTH FACTORS

Wang Z (1), Scalise AL (1), Onnela JP (1), Baird DD (2), Jukic AM (2), Williams MA (1), Hauser R (1), Coull BA (1), Mahalingaiah S (1, 3)*

(1) Department of Environmental Health/Biostatistics, Harvard T.H. Chan School of Public Health, Boston, MA, United States; (2) National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC, United States; (3) Department of OB/GYN, Massachusetts General Hospital, MA, United States.

Abstract: OBJECTIVE: We evaluated demographics, BMI, behaviors and health outcomes among individuals with diagnosed or presumed polycystic ovarian syndrome (PCOS) in the Apple Women's Health Study (AWHS), a nationwide, population-based digital cohort study in the United States (US).

METHODS: Among 71,733 eligible AWHS participants (11/2019-7/2023) who completed a Medical History Survey at enrollment, we evaluated the prevalence of self-reported physician-diagnosed PCOS. Among those without diagnosed PCOS, we then evaluated a subset of participants (n = 30,027) who provided reproductive history and hormonal symptoms data to identify those with presumed PCOS. Presumed PCOS was defined as experiencing irregular cycles after menarche for at least 5 years, still irregular at enrollment, or only regular with hormone use, and having androgen excess (self-reported hirsutism or severe acne). Those without diagnosed PCOS or presumed PCOS were considered not to have PCOS. Across these three groups, we evaluated the distributions [n (%) or mean] of demographics (age, race/ethnicity), BMI, health outcomes (overall health rating, cardiometabolic, reproductive, or pregnancy complications) and behavioral factors (physical activity, diet), and we used Chi-square/Kruskal-Wallis tests to determine statistical significance (the non-PCOS group as the referent group).

RESULTS: Among the 71,733 participants, 8,734 (12%) had clinician diagnosed PCOS. Among the subset without diagnosed PCOS and with reproductive history and hormone symptom data, 4,230 had presumed PCOS and 21,453 did not. Compared to those without PCOS, those with diagnosed/presumed PCOS were on average younger at enrollment (34 years/31 years vs. 37 years, $p < 0.01$) and were more likely to identify as more than one race (11%/12% vs. 9%, $p < 0.01$). Those with diagnosed PCOS were more likely to have BMI > 30 kg/m2 (61%) than the presumed PCOS (35%) or non-PCOS (35%) groups ($p < 0.05$). Similar trends were noted for infertility (PCOS vs. non-PCOS: 17% vs. 4%). Compared to those without PCOS, those with diagnosed/presumed PCOS had poorer overall self-rated health (12%/8% vs. 5% that reported "much worse health" compared to their peers, $p < 0.05$), higher prevalence of health conditions such as stroke (1.0%/0.8% vs. 0.7%, $p < 0.01$), arrhythmia (5.6%/4.2% vs. 4.0%, $p < 0.01$), endometrial hyperplasia (1.6%/0.8% vs. 0.4%, $p < 0.01$), and any pregnancy complications (among those who had been pregnant, 43%/40% vs. 32%, $p < 0.01$), as well as reported less vigorous physical activity (20%/26% vs. 30%, $p < 0.01$) and different dietary choices (e.g. 16%/7% vs. 11% with a low carb diet, $p < 0.01$).

CONCLUSIONS: Participants with diagnosed or presumed PCOS were more likely to have multiple adverse health outcomes. Further analysis is needed to examine associations both cross-sectionally and longitudinally as participants continue to be followed. (Funding: Apple Inc.)

Abstract ID #123

Abstract Title: SEX HORMONE-BINDING GLOBULIN AS A BIOMARKER FOR METABOLIC DISTURBANCES IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

van der Heijden DMB (1), van Bree BE (1, 2), van Golde RJT (1, 2), Brouwers MCGJ (3, 4), Spaanderman MEA (1, 2), Valkenburg O (1, 2)

(1) Department of Gynaecology and Obstetrics, Maastricht University Medical Centre+, Maastricht, Limburg, The Netherlands;

(2) GROW School for Oncology and Reproduction, Maastricht University, Maastricht, Limburg, The Netherlands;

(3) Department of Internal Medicine, Maastricht University Medical Centre+, Maastricht, Limburg, The Netherlands.

(4) CARIM School for Cardiovascular Diseases, Maastricht University, Maastricht, Limburg, The Netherlands

Abstract: OBJECTIVE: Sex hormone-binding globulin (SHBG) can be regarded as a biomarker for metabolic distress. Hyperandrogenism, obesity and insulin resistance are common features of women with polycystic ovary syndrome (PCOS). Low SHBG levels result in a higher fraction of free testosterone, that may be causally related to clinical features such as hirsutism and ovulatory dysfunction. We hypothesize that the evaluation of SHBG in the study of PCOS phenotype may allow for better individual risk appraisal and possibly targeted intervention strategies. The aim of this study is to examine SHBG as a biomarker for metabolic disturbances in European women with PCOS in relation to hyperandrogenaemia.

METHODS: Retrospective data was collected from the outpatient clinic for menstrual cycle disorders at Maastricht University Medical Centre +. A structured interview, physical examination and vaginal ultrasound evaluation took place. Endocrine evaluation was performed after overnight fast and encompassed fasting glucose and insulin levels, total cholesterol, SHBG, testosterone, gonadotropic hormones, and Estradiol. PCOS was diagnosed according to the 2018 ESHRE guideline. Mann Whitney U test was used to determine significant differences between women with low (<40 nmol/L) and normal (≥40 nmol/L) SHBG levels. Linear regression analyses were used to study associations between metabolic features, SHBG level and hyperandrogenaemia.

RESULTS: 208 women were included. As expected, women with low SHBG level (n=84) showed significantly poorer metabolic outcomes (HOMA-IR, dyslipidaemia, blood pressure) compared to women with normal SHBG level (n=124). BMI was inversely associated with SHBG ($p<0.001$; beta -0.597; 95% CI [-0.708, -0.486]). The inverse relation of waist and SHBG level remained after correction for BMI and HOMA-IR ($p<0.05$, beta -0.344 [-0.646, -0.046]). SHBG showed associations with metabolic outcomes, i.e., Triglycerides (Tg; beta -0.396 [-0.532, -0.261]), HDL-cholesterol (HDL-C; beta 0.541 [0.432, 0.659]), and LDL-cholesterol (LDL-C, beta -0.140 [-0.277, -0.002]). Only HDL-C remained significant after correction for BMI, waist and HOMA-IR. Testosterone was associated with insulin (beta 0.161 [0.012, 0.310]), Tg (beta 0.222 [0.079 to 0.365]), and LDL-C (beta 0.158 [0.021, 0.295]), but not HDL-C. Significant associations remained after correction for BMI, waist and HOMA-IR.

CONCLUSIONS: SHBG level and total Testosterone are indicative for metabolic dysregulation in women with PCOS. Hyperandrogenaemia is related to insulin resistance and dyslipidaemia in PCOS patients. We hypothesize that SHBG reflects metabolic dysregulation driven by visceral adiposity. Its association with non-alcoholic fatty liver disease might play an important role in the expression of SHBG and aetiology of PCOS, which can be the subject of future research.

Abstract ID #124

Abstract Title: WOMEN WITH POLYCYSTIC OVARY SYNDROME HAVE INCREASED RISK FOR CARDIOVASCULAR EVENTS – A NATION-WIDE REGISTER STUDY

Koskenkari N. (1), Ollila MM. (1), Arffman RK. (1), Morin-Papunen L. (1), Pesonen P. (2), Gissler M. (3), Junttila J. (4), Piltonen TT. (1)

(1) Department of Obstetrics and Gynaecology, Medical Research Center Oulu, Research Unit of Clinical Medicine, University of Oulu and Oulu University Hospital, Oulu, Finland;

(2) Infrastructure of Population Studies, Faculty of Medicine, University of Oulu, Oulu, FI-90014, Finland;

(3) THL Finnish Institute for Health and Welfare, Department of Knowledge Brokers, Box 30, 00271 Helsinki, Finland;

(4) Research Unit of Internal Medicine, Medical Research Center Oulu, University of Oulu and Oulu University Hospital, Oulu, Finland;

Abstract: OBJECTIVE: Polycystic ovary syndrome (PCOS) is a common endocrinopathy among reproductive aged women and it is associated with cardiovascular disease (CVD) risk factors and thus, possibly with higher risk for CVD events. The main aim of our study was to investigate the incidence of CVD events, procedures, and use of medications among PCOS women.

METHODS: A 1:3 matched case-control study using nation-wide register-based data (1.1.1995 to 31.12.2018). Women with PCOS (based on the International Classification of Diseases, Revisions 8–10 codes) were compared to age- and residential area matched controls.

The follow-up started at the diagnosis for PCOS and ended to death, emigration, or to 31.12.2018. The main outcome was the occurrence of any CVD event (including atrial fibrillation [AF], angina pectoris [AP], myocardial infarction [MI] and ischemic coronary disease, heart failure [HF], transient ischemic attack [TIA], stroke, aortic valve stenosis [AS], atherosclerosis, pulmonary embolism [PE], venous thrombosis [VT]) or CVD death. Moreover, we analyzed the occurrence of major adverse cardiovascular events (MACE) (including MI and ischemic heart disease, HF, TIA, stroke, CDV death) and venous events (including PE and VT). Crude and education-adjusted Cox proportional hazard models were applied, and the results were reported as hazard ratio (HR) with 95% confidence intervals.

RESULTS: This study included 8,821 women with PCOS and 25,451 controls. The mean follow-up time was 10.2 ± 6.1 years and the mean age at the end of the follow-up was 36.9 ± 8.8 years. Women with PCOS had increased risk for the development of any CVD event (HR= 1.77 [1.56–2.01]), MACE (HR=1.73 [1.41–2.12]), and venous events (HR=1.74 [1.42–2.13]) in the education-adjusted analyses. As for individual CVD events, prevalence of AF, AP, MI and ischemic coronary disease, HF, TIA, AS, PE, and VT were significantly increased. Moreover, women with PCOS had undergone diagnostic coronary artery angiograms significantly more often than control women. The use of cardiovascular system medications, such as antihypertensives, antithrombotics, and lipid modifying agents were higher in PCOS women compared to controls.

CONCLUSION: Women with PCOS have increased risk for developing cardiovascular events, which also translated to increased use of cardiovascular disease medications. PCOS should be considered as a major CVD risk factor. Moreover, it is important to enhance prevention and treatment of women with PCOS and cardiovascular diseases to prevent CVD events.

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Abstract ID #125

Abstract Title: GUT BACTERIOME AND VULNERABILITY TO MOOD DISORDERS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

Lee S (1,2), Tejesvi MV (3), Hurskainen E (1), Aasmets O (4), Herzig KH (5,6), Plaza-Díaz J (7,8), Franks S (9), Morin-Papunen L (1), Tapanainen JS (1,10), Altmäe S (2,11,12), Tapiainen T (2,13), Org E (4), Salumets A (2,14,15), Piltonen TT (1)*, Arffman RK (1)*

(1) Dept. of Ob/Gyn, Oulu University Hospital, University of Oulu, Oulu, Finland;

(2) Dept. of Ob/Gyn, University of Tartu, Tartu, Estonia;

(3) Biocenter Oulu, University of Oulu, Oulu, Finland;

(4) Institute of Genomics, University of Tartu, Tartu, Estonia;

(5) Research Unit of Biomedicine, Oulu University Hospital, University of Oulu, Oulu, Finland;

(6)Dept. of Paediatric Gastroenterology and Metabolic Diseases, Poznań University of Medical Sciences, Poznań, Poland;

(7)Dept. of Biochemistry and Molecular Biology II, University of Granada, Granada, Spain;

(8)Children's Hospital of Eastern Ontario Research Institute, Ottawa, Canada;

(9)Dept. of Metabolism, Imperial College London, London, United Kingdom;

(10)Dept. of Ob/Gyn, Helsinki University Hospital, University of Helsinki, Helsinki, Finland;

(11)Dept. of Biochemistry and Molecular Biology, University of Granada, Granada, Spain;

(12)Instituto de Investigación Biosanitaria ibs GRANADA, Granada, Spain;

(13)Research Unit of Clinical Medicine, University of Oulu, Oulu, Finland;

(14)Competence Centre on Health Technologies, Tartu, Estonia;

(15)Dept. of Clinical Science, Karolinska University Hospital, Karolinska Institut, Stockholm, Sweden

Abstract: OBJECTIVE: To investigate the influence of the gut microbiome on mood disorders in women with PCOS, we aimed to 1) identify mood disorder-specific bacteria, 2) characterize the gut microbial community in relation to mood disorders within the context of PCOS, and 3) further explore the associations between the gut microbiome and PCOS-related clinical characteristics.
METHODS: This study is a prospective and case-control study utilizing the longitudinal Northern Finland Birth Cohort 1966 (NFBC 1966). Classification of PCOS and clinical measurements were performed at ages 31 and 46, resulting in 103 women with PCOS and 208 BMI-matched non-PCOS controls were identified at age 46. The subjects were then categorized based on mood disorder status, using questionnaires; non-mood disorder (NMD) or mood disorder (MD). Thus, the final sample size was 84 PCOS NMD, 18 PCOS MD, 180 control NMD, and 25 control MD. The gut microbiome was collected from fecal samples at age 46 and was sequenced in the V3-V4 region of the 16S rRNA (Illumina MiSeq).
RESULTS: We observed substantial differences in clinical parameters related to glucose metabolisms, such as HOMA-IR ($P=0.031$), fasting glucose ($P=0.013$), and fasting insulin ($P=0.040$), depending on mood disorders within the PCOS group. Next, using machine learning, we identified differentiating bacterial features based on mood disorder status in the entire cohort, regardless of PCOS diagnosis. The log frequency of Actinomycetaceae F0332 ($P=0.045$) and Aggregatibacter ($P=0.038$) was significantly higher in the MD group than in the NMD group. PCOS MD showed decreased alpha diversity (Pobserved features=0.028, Pshannon=0.032) and significantly higher relative abundance of Sutterella ($P<0.001$) compared to PCOS NMD, whereas control subjects did not show these changes in the gut bacterial community. Furthermore, Sutterella showed positive correlations with the PCOS-related clinical parameters linked to obesity, glucose metabolisms, and gut barrier integrity, such as BMI ($P=0.011$), waist circumference ($P=0.015$), fasting glucose ($P<0.001$), and fasting insulin ($P=0.045$), and zonulin ($P=0.033$).
CONCLUSION: Our findings suggest that i) obesity and inflammation may act synergistically in the development and manifestation of both PCOS and mood disorder and ii) certain bacteria could potentially exacerbate the conditions. In conclusion, the gut microbiome may serve as a potential nexus linking the pathology of PCOS to mood disorders via immunological, metabolic, and endocrinological factors.
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Abstract ID #126

Abstract Title: SUBCUTANEOUS ADIPOSE TISSUE REGULATING GENES AS PREDICTION OF WEIGHT LOSS BY LIFESTYLE INTERVENTION IN OVERWEIGHT/OBESE WOMEN WITH POLYCYSTIC OVARY SYNDROME

Hellberg A (1), Salamon D (1), Ujvari D (1,2) , Rydén M (3), Hirschberg AL (1,4)

(1) Department of Women's and Children's Health, Karolinska Institutet, Solna, Sweden

(2) Department of Microbiology, Tumor and Cell Biology, National Pandemic Centre, Centre for Translational Microbiome Research, Karolinska Institutet, Solna, Sweden

(3) Department of Medicine, Karolinska Institutet, Huddinge, Sweden

(4) Department of Gynecology and Reproductive Medicine, Karolinska University Hospital, Solna, Sweden

Abstract: OBJECTIVE: Overweight/obese women with polycystic ovary syndrome (PCOS) have varying difficulties in achieving weight loss by lifestyle intervention. Subcutaneous adipose tissue regulation may predict individual successful weight loss in these women. The purpose of the present study was to investigate baseline subcutaneous adipose tissue regulating genes as prediction of successful weight loss by lifestyle intervention in obese/overweight women with PCOS.

METHODS: The study was based on a randomized controlled trial of behavioral modification treatment (intervention) compared to minimal intervention (control) in overweight/obese women with PCOS performed at Karolinska University Hospital, Stockholm, Sweden. Sixty-eight obese/overweight women, 18-40 years of age and body mass index (BMI) ≥ 27, fulfilling all three Rotterdam criteria of PCOS were selected for the 4-month intervention. Fifty-five of these women provided baseline abdominal subcutaneous adipose tissue samples. In subgroups of five individuals that had lost most weight (weight loss group) and five individuals that had gained weight (weight gain group), adipose tissue gene expression was analyzed by microarray. Genes found to differ in expression between the subgroups were processed in a pathway analysis. Real-time RT-PCR on 55 subjects was used to validate gene expressions. Results were related to weight change after lifestyle intervention. Spearman correlations, one-way ANOVA and multiple logistic regression analyses were performed.

RESULTS: Forty genes differed significantly between the subgroups of weight loss and weight gain by microarray analysis. Among those, ten genes (RRM2, ANLN, ANPEP, STMN1;MIR3917, PFKB1, H3C2 (HISTH3B), TOP2A, ACLY, PC and GSTM5) were involved in metabolic pathways. The results were confirmed by real-time RT-PCR in all 55 subjects. Baseline gene expressions of ANLN and GSTM5 correlated negatively with weight change (R = -0.3, P = 0.03 and R = -0.41, P < 0.01, respectively). Gene expressions of H3C2 and GSTM5 explained 24% of the variation in body weight change (P < 0.001) in the multiple regression analysis. The strongest predictor of weight loss was GSTM5 explaining 17.5% of change in body weight (%) after lifestyle intervention (P < 0.001).

CONCLUSIONS: This study shows that baseline subcutaneous adipose tissue regulating genes can predict weight change by lifestyle intervention in overweight/obese women with PCOS. GSTM5, a gene involved in glutathione metabolism and in glutathione-mediated detoxification was the strongest predictor of weight change in these women.

(Swedish Research Council (2017-02051), Stockholm County Council (2019-0248))

Abstract ID #127

Abstract Title: COMPOSITIONAL ASSOCIATIONS OF 24-HOUR ACTIVITY CYCLE AND CARDIOMETABOLIC HEALTH IN WOMEN WITH PCOS

Pesonen E (1,2,3), Farrahi V (3,4), Brakenridge CJ (5), Ollila MM (1,3), Morin-Papunen LC (1,3), Jämsä T (3,4) Korpelainen R (2,3,6), Moran LJ (7), Piltonen TT (1,3), Niemelä M (4,8)

(1) Department of Obstetrics and Gynecology, Research Unit of Clinical Medicine, University of Oulu and Oulu University Hospital, Oulu, Finland;

(2) Department of Sports and Exercise Medicine, Oulu Deaconess Institute Foundation sr., Oulu, Finland;

(3) Medical Research Center Oulu, Oulu University Hospital and University of Oulu, Oulu, Finland;

(4) Research Unit of Health Sciences and Technology, University of Oulu, Oulu, Finland;

(5) Active Life Lab, South-Eastern Finland University of Applied Sciences, Mikkeli, Finland;

(6) Research Unit of Population Health, University of Oulu, Oulu, Finland;

(7) Monash Centre for Health Research and Implementation, Monash University, Clayton, Victoria, Australia;

(8) Centre for Wireless Communications, University of Oulu, Oulu, Finland;

Abstract: OBJECTIVE: Lifestyle modification, including increasing physical activity (PA), is recommended as a first-line treatment for PCOS. However, it is not known if the affected women need more tailored physical activity guidelines. Our objective was to determine the association of 24-hour composition of sedentary behavior (SB), light PA (LPA), moderate-to-vigorous PA (MVPA), and sleep with cardiometabolic health in women with PCOS.

METHODS: The study used data from the 46-year follow-up of the Northern Finland Birth Cohort 1966. Participants filled questionnaires and their waist circumference, blood pressure, fasting blood sample and oral glucose tolerance were measured. Participants wore a waist-worn accelerometer for 14 days, from which time spent in SB, LPA, and MVPA were determined. Sleep duration was self-reported. The PCOS group (n=192) consisted of women with two of the following criteria: oligo/amenorrhea, hirsutism or biochemical hyperandrogenism, AMH level ≥3.2 ng/ml, while controls did not exhibit any PCOS criteria (n=665). Compositional regression analysis and isotemporal time reallocations in 15-min intervals were used to study associations between 24-hour movement composition and cardiometabolic health while adjusting for sociodemographic factors, smoking, alcohol use, psychological distress, and medication. Percentage differences with 95% confidence intervals (CI) were reported.

RESULTS: There was no difference in the overall 24-h movement composition between women with PCOS and controls (p=0.192). More time in MVPA relative to other behaviors was associated with better cardiometabolic health in both groups, although the associations with fs-glucose, 2-h glucose, 2-h insulin, and mean arterial pressure were not significant in women with PCOS. Notably, more time in SB or LPA in relation to other behaviors was not associated with cardiometabolic markers in women with PCOS, in contrast to controls. In women with PCOS, reallocating 15 minutes from SB to MVPA was associated with favorable waist circumference (-1.9%Δ [95% CI -3.1 to -0.7%Δ]), triglycerides (-5.1%Δ [95% CI -8.5 to -1.6%Δ]), and HOMA-IR (-6.4%Δ [95% CI -11.0 to -1.6%Δ]) estimates. Conversely, reallocating 15 minutes from MVPA to SB was associated with unfavorable waist circumference (2.9%Δ [95% CI 1.0 to 4.7%Δ]), triglycerides (8.1%Δ [95% CI 2.5 to 14.0%Δ]), and HOMA-IR (10.6%Δ [95% CI 2.7 to 19.1%Δ]) estimates. In controls, the magnitude of the percentage differences and the confidence intervals were smaller in the corresponding time reallocations.

CONCLUSIONS: The findings suggest that maintaining and increasing MVPA at the expense of other activity behaviors is important for cardiometabolic health in women with PCOS, while the relevance of SB and LPA may differ from controls.

(Funding: Jenny and Antti Wihuri Foundation, Sigrid Juselius Foundation, Academy of Finland, Ministry of Education and Culture, Roche)

Abstract ID #128

Abstract Title: PELVIC FLOOR MUSCLE THICKNESS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

Melo MH (1), Micussi MT (2), Medeiros R (3), Cobucci RN (4), Maranhão TM (3), Gonçalves AK (3).

(1) Health Sciences Graduate Program of the Federal University of Rio Grande do Norte, Natal, Brasil

(2) Department of Physical Therapy of the Federal University of Rio Grande do Norte, Natal, Brasil

(3) Department of Gynecology and Obstetrics of the Federal University of Rio Grande do Norte, Natal, Brasil

(4) Department of Gynecology and Obstetrics of the Potiguar University, Natal, Brasil

Abstract: Scientific literature has indicated the presence of androgen receptors in the levator ani muscles and pelvic fascia.The existence of androgen receptors in the vaginal wall can play an essential role in the development of pelvic floor disorders in women. Thus, androgen-related disorders may interfere with the function of pelvic floor muscles. By the way, polycystic ovary syndrome (PCOS) is one of the most heterogeneous disorders in women of reproductive age, which is associated with hyperandrogenism. The aim of the present study was to evaluate and compare the thickness levator ani muscles of women with PCOS and in normal menstrual cycle women. Methods:The sample was composed by recruited voluntaries, 10 (ten) women with PCOS (PCOS group) and 10 women with normal menstrual cycle (control group). The evaluation of all the volunteers women were completed by a transperineal 3D ultrasound, using a variable frequency volumetric transducer (4-8 Hz) and Minitab 11.0 software.The axial plane was used to assess the thickness of the levator ani muscles on the right and left sides. Descriptive statistics and the Mann Whitney test were used to characterize the sample and to compare the groups. Results:The obtained data showed that women mean age was 25.1 (± 2.1) and 24.2(± 1.9) in the SOP and control groups, respectively (p> 0.05). There is no significant difference between the thickness of the pelvic floor muscles on the right (SOP group:Right 1.12 (± 0.5); Left 1.08 (± 0.6) and Control Group: Right 0.89 (± 0.6), Left 0,94 (±0,4). There was no intergroup difference. Conclusions: It was concluded that young women with PCOS and normal menstrual cycle did not show differences in the thickness of the pelvic floor muscles identified by ultrasound. However, the PCOS group showed a tendency to present a greater thickness. Perhaps, this fact may be due to the state of hyperandrogenism or abdominal overload in this group.

Abstract ID #129

Abstract Title: Thyroid autoimmunity and hypothyroidism in the different phenotypes of polycystic ovary syndrome

Sciarroni E (1), Benetti Z (1), Benelli E (1), Bagattini B (1), Simoncini T (2), Tonacchera M (1), Fiore E (1)

(1) Department of Clinical and Experimental Medicine, Section of Endocrinology, University Hospital of Pisa, Pisa, Italy;

(2) Department of Obstetrics and Gynecology, University Hospital of Pisa, Pisa, Italy;

Abstract: OBJECTIVE: Polycystic ovary syndrome (PCOS) is the most common female endocrine disorder. According to the ESHRE-ASMR 2003 diagnostic criteria, patients can be divided into 4 phenotypes: phenotype 1 (hyperandrogenism, oligo-anovulation, and polycystic ovarian morphology (PCOM) at ultrasound), phenotype 2 (hyperandrogenism and oligo-anovulation), phenotype 3 (hyperandrogenism and PCOM) and phenotype 4 (oligo-anovulation and PCOM). A higher frequency of autoimmune thyroid diseases has been described in patients with PCOS. This study aimed to evaluate the prevalence of anti-thyroglobulin (AbTg) and anti-thyroperoxidase (AbTPO) antibodies and hypothyroidism in the different phenotypes of PCOS.

METHODS: A total of 448 patients with PCOS were recruited and divided into the 4 phenotypes: 58,0% (260/448) in phenotype 1, 26,6% (119/448) in phenotype 2, 8,5% (38/448) in phenotype 3, 6,9% (31/448) in phenotype 4.

RESULTS: Thyroid antibodies (TAb) were found in 20,1% of patients (90/448). TAb positivity was significantly higher in regrouped phenotypes 1-2 (83/379, 21.9%) than in regrouped phenotypes 3-4 (7/69, 10.1%). Patients were then subdivided according to serum level of TgAb. Low titer (<100 U/mL) TgAb frequency did not differ significantly among the 4 phenotypes, but high titer (>100 U/mL) TgAb were significantly more frequent in regrouped phenotypes 1-2 (39/379, 10,3%) than in regrouped phenotypes 3-4 (0/69, 0,0%) (p=0,005). Analogously, low titer TPOAb frequency did not differ significantly among phenotypes, while high titer TPOAb were more frequent in regrouped phenotypes 1-2 (39/379, 10,3%) than in regrouped phenotypes 3-4 (2/69, 2,9%), although without statistical significance (p=0,11). Hypothyroidism was present in 53/439 patients and was defined as the presence of a TSH > 4 mU/L (21 patients) or euthyroidism under thyroid hormone replacement therapy (32 patients). It was significantly more frequent in TAb-positive patients (23/87, 26,4%) than in TAb-negative patients (30/352, 8,5%) (p>0,01), and more common in regrouped phenotypes 1-2 (46/372, 12.4%) than in regrouped phenotypes 3-4 (7/60, 10.4%), although no statistical significance was found (p=0.657). According to binary logistic regression analysis, hypothyroidism was significantly associated with TAb presence (OR 4,19; CI 2,25-7,79; p<0,01), but not to phenotype (OR 1,29; CI 0,97-1,76; p=0,109).

CONCLUSIONS: We found different TAb prevalence and serum levels in patients with distinct PCOS phenotypes. This variability may be related to the subtle imbalances among estrogens, androgens, and progesterone levels typical of this syndrome, more conspicuous in patients with phenotypes 1 and 2 ("classical PCOS"), who presented indeed a higher frequency of TAb. Hypothyroidism was significantly related to Tab presence.

Abstract ID #130

Abstract Title: Gut microbiota influents PCOS-like traits of mice induced by letrozole

Yushan Li (1), Yuchen Zhu (1), Dan Li (2), Wen Liu (1), Yi Zhang (1), Wei Liu (1), Chenhong Zhang (2), Tao Tao (1)

1 Department of Endocrinology and Metabolism, Renji Hospital, School of Medicine, Shanghai JiaoTong University, Shanghai 200127, China

2 State Key Laboratory of Microbial Metabolism, School of Life Sciences and Biotechnology, Shanghai Jiao Tong University, Shanghai, 200240, China

Abstract: OBJECTIVE: Polycystic ovary syndrome (PCOS) is a complex disorder that affects metabolism, reproduction, as well as endocrine function, characterized by hyperandrogenism and insulin resistance. The gut microbiota has been implicated in the pathogenesis of PCOS. However, the underling mechanism of gut microbiota in PCOS needs further elucidation. Thus, we aim to investigate regulation of development of metabolic and reproductive phenotypes of PCOS induced by letrozole using a pseudo germ-free PCOS mouse model

METHODS: The PCOS mouse model was established through the administration of letrozole to both conventional and antibiotics-treated mice. The evaluation of glucose metabolism, sex hormone levels, and ovarian morphology was conducted. Additionally, 16S rRNA gene sequencing was performed on fecal samples from each group of mice, and functional prediction of gut microbiota was conducted using PICRUSt2 to explore potential mechanisms.

RESULTS: By using letrozole-induced PCOS mice model, we manifested that antibiotic intervention significantly reduced the serum total testosterone level and glucose intolerance. Antibiotic treatment reduced the number of amplicon sequence variants (ASVs), as well as the Shannon and Simpson index. Meanwhile, letrozole induced a significant increase in the Shannon and Simpson index instead of ASVs. Through random forest model analysis, the results revealed significant alterations in three distinct groups of microbiota, namely Clostridia_vadinBB60_group, Enterorhabdus, and Muribaculaceae after letrozole treatment . Further correlation analysis found that the changes of these bacteria were positively correlated with serum total testosterone levels and AUC of blood glucose in IPGTT. Antibiotic treatment resulted in a reduction of the absolute abundance of 5 ASVs belonging to unclassified Clostridia_vadinBB60_group, unclassified Enterorhabdus, , and unclassified Muribaculaceae, which were positively correlated with mice serum total testosterone levels and AUC of blood glucose in IPGTT. Moreover, 25 functional pathways of gut microbiome were significantly different between the letrozole-treated mice with and without antibiotics.

CONCLUSIONS: These results suggest that dysbiosis of the gut microbiota may take participate in the development of PCOS and that modulation of the gut microbiota may be a potential treatment for PCOS.

Abstract ID #131

Abstract Title: CELL-TYPE-SPECIFIC DISEASE SIGNATURES AND MECHANISMS REGULATING SKELETAL MUSCLE IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

Gorsek Sparovec T (1), Congru LI (1), Gustaw Eriksson (1), Haojiang Lu (1), Sanjiv Risal (1), Eva Lindgren (1), Damdimopoulou P (4), Angelica Lindén Hirschberg (2,3) , Qiaolin Deng (1), Elisabet Stener-Victorin (1)

1. Department of Physiology and Pharmacology, Karolinska Institutet
2. Department of Women's and Children's Health, Karolinska Institutet
3. Department of Gynecology and Reproductive Medicine, Karolinska University Hospital, Stockholm
4. Division of Obstetrics and Gynaecology, Karolinska Institutet

Abstract: Objective: Polycystic ovary syndrome (PCOS) is associated with a high degree of metabolic comorbidities. Lifestyle management including diet and exercise is the first-line treatment, followed by prescription of antidiabetic drugs (metformin) to regulate blood glucose levels. Skeletal muscle plays a central role in energy and glucose metabolism, and its function is impaired in PCOS due to elevated testosterone and insulin levels. Fibrosis, low-grade inflammation, and mitochondrial dysfunction in muscle further exacerbate insulin resistance. How cellular complexity and heterogeneity are altered in skeletal muscle dysfunction and in PCOS with insulin resistance and whether the changes can be reversed by lifestyle/metformin remain unclear.

Methods: We aim to uncover the cell-type specific fingerprint in the skeletal muscle of healthy women and hyperandrogenic and insulin-resistant women with PCOS using single-nuclei RNA sequencing (snRNA-seq). In addition, women with PCOS are randomized to a 16-week lifestyle management intervention, with or without metformin, allowing us to uncover whether identified alterations can be reversed. In a subset of participants, muscle satellite cells are isolated, cultured and will be used to validate cellular and molecular mechanisms of the cell-type-specific disease signatures identified by snRNA-seq. To define the myogenic capacity and mitochondrial function of satellite cells and myotubes in vitro, we will perform bulk RNA-seq, Seahorse metabolic flux assays, and glucose uptake with fluorescent D-glucose analog (2-NBDG). Transcriptomic data from the in vitro studies will be deconvoluted with snRNA-seq data to explain the phenotypic fingerprint of PCOS.

Results: This project is just getting started, and we have already optimized a nuclei extraction protocol for 10X single nuclei 3' RNA sequencing. We have successfully sequenced 28 samples and will present preliminary analyzes, along with preliminary results from in vitro experiments.

Conclusion: The comprehensive analyzes proposed in this project will greatly enhance our understanding of the cellular complexity and specific cell types underlying skeletal muscle dysfunction associated with insulin resistance and hyperandrogenism in PCOS and define their response to current first-line treatment.

Abstract ID #132

Abstract Title: EFFECTS OF METFORMIN ON PLASMA OXYNTOMODULIN LEVELS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME: SECONDARY ANALYSIS OF RANDOMIZED CLINICAL TRIAL.

Damasceno R, Oliveira FR, Cândido AL, Gomes KB, Bizzi M, Azevedo R, Comim FV, Reis FM, Rocha AL.

Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

Abstract: OBJECTIVE: An abnormal secretion of incretins, especially Glucagon-like peptide 1 (GLP-1), glucose-dependent insulinotropic polypeptide (GIP), and oxyntomodulin, has been described in subjects with Type 2 diabetes mellitus and polycystic ovary syndrome (PCOS). Oxyntomodulin has important actions in the metabolism including the ability to reduce food intake and improve insulin secretion reducing the liver fat accumulation. Metformin is an insulin-sensitizing hypoglycemic drug and is widely used in the treatment of PCOS. Whether treatment with metformin may affect circulating levels of oxyntomodulin is not known and is the subject of this study.

METHODS: This is a secondary analysis of a randomized clinical trial. Forty-five participants with PCOS were randomly assigned to receive metformin (1500mg/day, n=21) or placebo (n=24) for 60 days. Plasma samples were obtained before and after the treatments and the levels of oxyntomodulin were evaluated by an enzyme immunoassay.

RESULTS: The baseline clinical characteristics of the metformin and the placebo groups were similar. There was a small increase in plasma oxyntomodulin levels both in the metformin group (from 23.7 ± 9.9 to 27.3 ± 9.3 pg/ml) and in the placebo group (21.6 ± 7.3 to 23.9 ± 12.0 pg/ml), but with no significant difference between treatments.

CONCLUSION: In women with PCOS, the use of metformin for 60 days did not alter oxyntomodulin levels compared to placebo.

FUNDING: Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG, grant APQ-02798-16) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

Abstract ID #133

Abstract Title: THE ROLE OF THE VISCERAL ADIPOSITY INDEX IN THE ASSESSMENT OF METABOLIC SYNDROME IN POLYCYSTIC OVARY SYNDROME PATIENTS: A NEW ANTHROPOMETRIC INDEX

Rocha AL, Baeta T, Nazare, I, Costa J, Caporalli J, Oliveira M, Couto M, Azevedo R, Comim F, Reis FM, Cândido AL.

Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

Abstract: OBJECTIVE: Polycystic ovary syndrome (PCOS) is a frequent endocrine disorder commonly associated with metabolic syndrome (MS) and increased risks of cardiovascular disease and type II diabetes. Some indexes such as lipid accumulation product (LAP) and homeostatic model assessment for insulin resistance (HOMA-IR) can predict MS in PCOS patients. This study aimed to assess the role of visceral adiposity index (VAI) as a predictor of MS in PCOS patients, compared to LAP and HOMA-IR indexes.

METHODS: We performed a cross-sectional study comprising 317 consecutive women diagnosed with PCOS and referred for multidisciplinary care in a teaching hospital. VAI, LAP, and HOMA-IR indexes were calculated. To compare indexes accuracy, participants were divided into the following two groups: PCOS patients with MS and PCOS patients without MS. Data were analyzed in a ROC curve.

RESULTS: Among women with MS, 92.3% had abnormal VAI results, 94.5% had abnormal LAP results, and only 50.5% of MS patients had abnormal HOMA-IR results. However, most women without MS presented a normal HOMA-IR (64.6%). The comparison of indexes in ROC curve showed that VAI is the most accurate index (area under the curve [AUC] = 0.868, 95% confidence interval 0.821-0.914), followed by LAP (AUC = 0.842) and HOMA-IR (AUC = 0.649).

CONCLUSION: The VAI index was a better predictor of metabolic MS in women with PCOS when compared to other indexes.

Abstract ID #134

Abstract Title: CORRELATION OF INTRAHEPATIC FAT AND β CELL FUNCTION IN PCOS AS MEASURED BY mDIXON TECHNOLOGY

Jie Yu, Yushan Li, Siyu Lin, Tao Tao

Department of Endocrinology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University,

Shanghai, China.

Abstract: OBJECTIVES: The predisposition to abnormal glucose metabolism in patients with polycystic ovary syndrome (PCOS) may be related to visceral fat deposition and decreased β-cell function. mDIXON Quant magnetic resonance technology was used to quantify hepatic fat deposition, which could lead to early indication and prevention of some metabolic risks.

METHODS: In this cross-sectional study, 160 patients with PCOS were enrolled, and all subjects underwent an upper abdomen magnetic resonance plain scan and glucose tolerance test.

RESULTS: Patients with PCOS were classified into 3 groups according to different glucose metabolic states: normal glucose tolerance (NGT), impaired glucose regulation (IGT), and type 2 diabetes mellitus(T2DM). Compared to patients with NGT, patients with abnormal glucose metabolism showed significantly higher overall liver fat and fat deposits in the left lobe of the liver and the right lobe of the liver (P<0.01). Further analyzing the fat in each lobe of the liver, the proportion of the right anterior lobe of the liver in abdominal visceral fat was significantly decreased and that of the right posterior lobe in abdominal visceral fat was significantly increased in patients with abnormal glucose metabolism (P<0.05). Using disposition index (DI) to assess the decline of β-cell function in PCOS patients, the PCOS patients were divided into four groups. Q1~Q4 indicated the decline of β-cell function. Compared with the first quartile, all the lobes of liver and the overall fat of the liver were significantly higher (p all<0.001). The left lobe of liver, the right lobe of liver and the overall fat of liver were significantly higher (p all<0.001). Left lobe, right lobe, and overall liver fat were significantly negatively correlated with DI levels (r=-0.3894,-0.3672,-0.3907 respectively; p<0.001). The AUC of DM predicted by combining mean liver fat with BMI and SHBG was 78.1%.

CONCLUSIONS: Liver lobar fat is significantly elevated in PCOS with glucose metabolism and is associated with decreased β-cell function. Changes in fat content of different lobes of the liver are present in PCOS with glucose metabolism. Lobular fat and overall liver fat were significantly associated with DI; left lobe, right lobe, and overall liver fat were independent risk factors for decreased DI. To some extent, the combination of age, BMI and overall liver fat could predict the occurrence of DM in PCOS patients.

Abstract ID #135

Abstract Title: NECK CIRCUMFERENCE AS A METABOLIC HEALTH MARKER AMONG WOMEN WITH PCOS: A SYSTEMATIC REVIEW

Haapakangas S (1), Koskenkari N (1), Ollila MM (1), Arffman RK (1), Piltonen TT (1)

(1) Department of Obstetrics and Gynaecology, Medical Research Center Oulu, Research Unit of Clinical Medicine, University of Oulu and Oulu University Hospital, Oulu, Finland

Abstract: OBJECTIVE: Neck circumference (NC) has been recognized as a compelling and convenient anthropometric index to identify metabolic health abnormalities, such as metabolic syndrome (MetS) and insulin resistance (IR) among women with PCOS. Neck circumference reflects the ectopic fat deposit in the upper body that contributes to excessive free fatty acid levels and metabolic disorders. Both MetS and IR are more common among women with PCOS than in the general population and are closely related to increased rates of long-term morbidity and mortality. Therefore, it is increasingly important to develop and evaluate simple and reliable clinical tools for early identification of MetS, IR and related metabolic abnormalities among PCOS women. Aim of this study was to summarize the associations of NC with MetS, IR or related outcomes among PCOS women.

METHODS: A systematic search was conducted through Pubmed/Medline and Scopus until first of June 2023 based on the search terms of neck circumference and PCOS to find relevant English-language papers. The PICO method was used to define the study question for the systematic review. Studies that examined associations of NC and anthropometric measurements, overweight, obesity, MetS, IR, dyslipidemia, hypertension, or related disorders among women with PCOS were included. The methodological quality of the included studies was assessed using the Newcastle-Ottawa scale.

RESULTS: Of the 97 publications 7 full texts that met the selection criteria were included for the systematic review. There was a large heterogeneity among the study results. Neck circumference had a positive correlation with PCOS and several metabolic abnormalities in majority of the studies. Women with PCOS had a higher NC and were more insulin resistant based on HOMA-IR or HOMA%S values, when compared to women without PCOS. PCOS women with MetS or IR had a significantly higher NC compared to PCOS women without MetS or IR. Subjects with a higher NC had a higher waist circumference. Neck circumference cut off values for MetS among PCOS women varied from 33 cm to 34.25 cm and for IR 34.25 cm up till 42 cm. Majority of the studies were done with Asian population.

CONCLUSIONS: Neck circumference correlated significantly with insulin resistance and metabolic syndrome related outcomes among PCOS women. Data considering NC cut off values for metabolic syndrome and insulin resistance among PCOS women is scarce. Further studies are needed especially among wider ethnic population.

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Abstract ID #136

Abstract Title: CHARACTERISATION OF THE DAILY RHYTHM OF SALIVARY ANDROGENS IN HEALTHY WOMEN AND IN WOMEN WITH POLYCYSTIC OVARY SYNDROME BY LIQUID CHROMATOGRAPHY-TANDEM MASS SPECTROMETRY

Rotolo L (1,2), Gambineri A (1,2), Bissi V (2), Zauli F (1,2), Galante G (2), Cecchetti C (1,2), Dionese P (1,2), Belardinelli E (1,2), Solmi B (1,2), Pagotto U (1,2), Fanelli F (2).

(1) Dept. of Medical and Surgical Sciences, University of Bologna - Endocrinology and Prevention and Care of Diabetes Unit, IRCCS Azienda Ospedaliero-Universitaria, Bologna, Italy;

(2) Center for Applied Biomedical Research, Dept. Of Medical and Surgical Sciences, Alma Mater Studiorum - Bologna University, Bologna, Italy.

Abstract: OBJECTIVE: Excess testosterone in PCOS is accompanied by increased levels of other ovarian and adrenal androgens. Obesity is strictly connected with androgen excess and with the derangement of hormone circadian rhythmicity. To date, it has not been clarified whether hyperandrogenism in PCOS, either complicated by obesity or not, is accompanied by the dysregulation of androgen rhythm. The aim of our study was to investigate androgen daytime rhythmicity and overall androgen daily exposure by measuring testosterone (T), androstenedione (A4) and dehydroepiandrosterone (DHEA) in saliva of healthy women (HW) and of women with PCOS fulfilling the three Rotterdam diagnostic criteria, according to their BMI status.

METHODS: HW (n=24) were aged 23-37y and showed no PCO morphology (PCOm), menstrual irregularity or hyperandrogenism. PCOS patients (n=18) were aged 15-38y and showed oligo-amenorrhea, PCOm and either clinical (hirsutism) or biochemical (elevated serum T) hyperandrogenism. Both groups were subdivided in normal weight (NW, BMI <25kg/m2; HW: n=20, PCOS: n=5) and overweight/obese (OW/OB, BMI ≥25kg/m2; HW: n=4, PCOS: n=13). All were in follicular phase (days 1-5), had standardised meals at 8, 13 and 20 am, and self-collected saliva every hour from 7 until 23 am. T, A4 and DHEA were measured by a validated LC-MS/MS method.

RESULTS: All women displayed high androgen levels at awakening, decreasing until bedtime (all p<0.001). Compared to HW, PCOS women showed higher T and A4 levels at each time point, and higher DHEA at 9, 11 and 16 am (all p<0.050). Throughout the day, small androgen spikes were detected at 14 (A4 and DHEA), 18 (DHEA) and 23 (T, A4 and DHEA) am in HW, and at 11 (T, A4 and DHEA), 17 (T, A4 and DHEA) and 23 (T) am in PCOS. The area under the curve (AUC) of T and A4 daily profiles was significantly higher in PCOS compared to HW independently of BMI classification, whereas DHEA AUC was higher in OW/OB PCOS compared to NW PCOS and to both NW and OW/OB HW (all p<0.050). Multiple regression, including androgen AUC as dependent variable and age, BMI and PCOS status as covariates, showed an independent impact of PCOS over T and A4 (both p<0.001) and of BMI over DHEA (p=0.031).

CONCLUSIONS: Our study provides new and detailed information on androgen circadian regulation in health and in PCOS as allowed by novel, highly sensitive and specific LC-MS/MS technology. While overall day/night androgen rhythmicity was maintained, a specific time-dysregulation of small surges was described in PCOS. Excess T and A4 in PCOS was detectable in saliva throughout the day, whereas DHEA excess was only detectable in mid-morning and in the afternoon. Finally, while increased T and A4 secretion specifically characterized the PCOS condition independently of BMI, excess DHEA specifically characterized the obese PCOS phenotype, thereby suggesting a specific adrenal contribute to the dysmetabolic sequelae of PCOS.

Abstract ID #137

Abstract Title: GENE EXPRESSION REGULATION IN CUMULUS CELLS OF WOMEN WITH POLYCYSTIC OVARY SYNDROME

Moolhuijsen LME (1), van Marion E (2), de Oliveira Santos Goular A (1), van der Hout – van Vroonhoven M (3), Gregoricchio S (4), van IJken WFJ (3), Zwart W (4), Laven JSE (5), Baart E (2), Visser JA (1)

(1) Department of Internal Medicine, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands;

(2) Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynaecology, Erasmus MC, University Medical Centre, PO Box 2040, 3000 CA, Rotterdam, the Netherlands;

(3) Center for Biomics, Erasmus MC, University Medical Center Rotterdam, Rotterdam, Netherlands;

(4)Division of Oncogenomics, Oncode Institute, The Netherlands Cancer Institute, 1066CX Amsterdam, The Netherlands;

(5) Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands.

Abstract: OBJECTIVE: Polycystic Ovary Syndrome (PCOS) is the most common endocrine disorder in women, affecting reproductive and metabolic function. A subset of anovulatory PCOS patients require ovarian stimulation and in vitro fertilization (IVF) to treat their subfertility. Yet, this group of patients shows a reduced chance to achieve a pregnancy due to impaired oocyte developmental competence. This impaired oocyte competence is linked with abnormal follicle development and altered cumulus cell-oocyte environment in PCOS. However, the molecular mechanisms affecting oocyte competence in PCOS are still unknown. Moreover, PCOS is considered a complex genetic disorder, yet the etiology remains to be elucidated. Also epigenetic and environmental factors contribute to the disease, suggesting that these factors may interact with the genetic architecture to influence oocyte competence. Here we aim to identify PCOS-associated changes in the open chromatin landscape of cumulus granulosa cells (CGCs), i.e. the cells surrounding the oocyte, and determine how this is affected by associated metabolic comorbidities.

METHODS: Women with PCOS diagnosed according to the Rotterdam criteria were compared to normo-ovulatory women with a regular cycle (25 – 35 days). As BMI has been shown to introduce epigenetic marks, we stratified both groups in normal BMI (20 – 25 kg/m2) and high BMI (> 25 kg/m2). CGCs were collected after oocyte retrieval procedures. CGCs were isolated and fresh samples were analyzed by ATAC-sequencing to assess chromatin structure. Genome-wide differences in chromatin accessibility between groups were generated via matrices containing peak scores. Additionally, candidate gene analysis was performed on a list of genes linked to PCOS pathophysiology.

RESULTS: Samples of 48 women were analyzed, of which 23 were from women with PCOS and 25 from normo-ovulatory women (age range 30 – 35 years). No differences were found in peak distribution between PCOS women and normo-ovulatory women in our genome-wide analysis. Likewise, BMI did not influence peak distribution in CGCs, neither in women with PCOS nor in normo-ovulatory women. In addition, focusing on 11 specific candidate genes showed no differences in women with PCOS compared to normo-ovulatory women.

CONCLUSIONS: This is the largest study on chromatin accessibility in women with PCOS. In this study, no differences in chromatin structure were found between cumulus cells of PCOS and normo-ovulatory women undergoing IVF treatment. This suggests that gene regulation at the level of CGCs is not altered in PCOS. However, we cannot rule out that the stimulation protocol erases potential differences in epigenetic signatures present in granulosa cells of preovulatory follicles. Follow-up analysis will focus on differences on the level of single nucleotide polymorphisms identified by genome wide association studies between PCOS and controls.

Abstract ID #138

Abstract Title: CLUSTERING IDENTIFIES DISTINCT SUBTYPES OF PCOS – TOWARDS A RATIONALE APPROACH TO PCOS CLASSIFICATION

K van der Ham (1), LME Moolhuijsen (2), K Brewer (3), R Sisk (4), YV Louwers (1), JV Visser (2), A Dunaif (3), JSE Laven (1)

(1) Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Erasmus University Medical Center, Dr. Molewaterplein 40, 3015 GD, Rotterdam, The Netherlands;

(2) Department of Internal Medicine, Erasmus University Medical Center, Dr. Molewaterplein 40, 3015 GD, Rotterdam, The Netherlands;

(3) Division of Endocrinology, Diabetes and Bone Disease, Icahn School of Medicine at Mount Sinai, New York, NY, USA;

(4) Division of Endocrinology, Metabolism, and Molecular Medicine, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, USA.

Abstract: OBJECTIVE: Different criteria that are used to diagnose polycystic ovary syndrome (PCOS) reflect the heterogeneity of the syndrome. However, PCOS diagnosed by NIH or Rotterdam criteria has a similar genetic architecture. Using Hierarchical Clustering (HC) in a cohort of ~900 NIH PCOS cases from the United States (US), we have previously identified discrete PCOS clusters, which were designated “reproductive subtype” (high LH, FSH and SHBG) and “metabolic subtype” (high BMI, insulin and glucose); cases that did not belong to these clusters were designated “indeterminate subtype”. The subtypes appeared to capture biologically meaningful differences, as assessment by a genome-wide association study indicated that they were characterized by distinct and novel genome-wide significant loci.

METHODS: In the current study, we applied HC to the same traits (BMI, LH, FSH, DHEAS, SHBG, testosterone, fasting insulin and fasting glucose) in an independent cohort from the Netherlands. We then assessed whether additional traits differed between the obtained subtypes: anti-Müllerian hormone (AMH), total follicle count, DHEA, androstenedione, LDL, HDL, triglycerides, cholesterol, systolic and diastolic blood pressure. We also applied K-means clustering in addition to HC to assess cluster stability.

RESULTS: We replicated discrete subtypes in this large independent cohort of women with PCOS defined by the Rotterdam criteria, with a lower BMI (mean 27 kg/m2) compared to the US cohort (mean BMI 35 kg/m2). There were 1026 cases in the metabolic subtype, 450 cases in the reproductive subtype and 1026 in the indeterminate subtype. Cases in the reproductive subtype had significantly (all P<0.001) higher serum AMH levels, follicle counts, and HDL levels compared to the metabolic and indeterminate subtypes. These findings suggest that the reproductive subtype captures affected women with alterations in folliculogenesis, without using PCOM to define this subtype. In contrast, the cases in the metabolic subtype had significantly (all P<0.001) higher triglyceride and LDL levels and higher systolic and diastolic blood pressure compared to the other subtypes. This provides further evidence that the metabolic subtype identifies cases with higher cardiometabolic risk. Combining two cluster methods resulted in a consensus and a non-consensus group. The non-consensus group showed a less profound metabolic and reproductive subtype.

CONCLUSIONS: Overall, our findings suggest that clustering algorithms capture etiologically distinct subtypes of PCOS diagnosed by both NIH and Rotterdam criteria, in an overweight as well as in a normal-weight cohort. Furthermore, our findings provide an example of the power of modern disease classification based on objective biologic differences rather than expert opinion.

FUNDING: R01 HD100812

Abstract ID #139

Abstract Title: METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE IN MIDDLE-AGED WOMEN WITH PCOS

van Zwol – Janssens, C. (1), van der Ham, K. (1), van de Sanden, J. (1), Velthuis, B.K. (2), Budde, R.P.J. (3), Franx A. (4), Fauser B.C.J.M. (5), Boersma E. (6), Laven J.S.E. (1), Bos D. (3), Louwers, Y.V. (1), and on behalf of the CREW consortium

(1) Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynaecology, Erasmus University Medical Center, Rotterdam, the Netherlands.

(2) Department of Radiology, University Medical Center Utrecht, University of Utrecht, Utrecht, The Netherlands.

(3) Department of Radiology and Nuclear Medicine, Erasmus University Medical Center, Rotterdam, the Netherlands.

(4) Department of Obstetrics and Gynaecology, Erasmus University Medical Center, Dr. Molewaterplein 40, 3015 GD, Rotterdam, the Netherlands.

(5) Department of Reproductive Medicine and Gynaecology, Department of Obstetrics and Gynaecology, University Medical Center Utrecht, University of Utrecht, Heidelberglaan 100, 3584 CX, Utrecht, The Netherlands.

(6) Department of Cardiology, Erasmus University Medical Center, Dr. Molewaterplein 40, 3015 GD, Rotterdam, the Netherlands.

Abstract: OBJECTIVE: Women with polycystic ovary syndrome (PCOS) often present with cardiometabolic risk factors which are also associated with metabolic dysfunction-associated steatotic liver disease (MASLD), such as obesity, insulin resistance, dyslipidemia and hyperandrogenism. With this study we aim to investigate the prevalence of MASLD in middle-aged women with PCOS and to determine if cardiovascular, hepatic or endocrine parameters in women with PCOS are associated with liver fat content.

METHODS: Middle-aged women with a previous diagnosis of PCOS according to the Rotterdam criteria underwent a coronary CT scan, a blood withdrawal and filled in a questionnaire for cardiovascular screening in the CREw-IMAGO study. In this secondary analysis, we used the non-enhanced CT scans to measure the mean attenuation of three regions of interest in different parts (at least two different segments) of the liver. The attenuation is expressed in Hounsfield units (HU), and measures of <48 HU are defined as steatosis and <40 HU as severe steatosis.

RESULTS: In total, 91 women with a mean age of 50 years underwent a CT scan, nine (10%) women had MASLD. Three of these women had mild steatosis and six (6%) severe steatosis. When comparing women with MASLD to those without MASLD, fasting insulin (228 vs 86 pmol/L, p = 0.01), alanine aminotransferase (ALAT) (38.8 vs 22.9 U/L, p <0.001) and alkaline phosphatase (ALP) (93.9 vs 73.1, p = 0.02) was significantly higher in women with MASLD. BMI (32.0 vs 28.3 kg/m2, p = 0.09), triglycerides (2.14 vs 1.01 mmol/L, p = 0.07), and free androgen index (2.3 vs 1.9, p = 0.48) were not significantly different between the two groups. Furthermore, BMI, triglycerides, insulin, gamma GT and ALP were positively associated to liver fat content, and insulin and gamma GT were also independent predictors of liver fat content. Testosterone and FAI were not associated with liver fat content.

CONCLUSION: Our results show a prevalence of 10% of MASLD in middle-aged women with PCOS, which is lower than described in reproductive aged women with PCOS and lower than the described prevalence of 20% in European middle-aged women without PCOS. This seems in line with previous findings were the increased presence of cardiometabolic risk factors women with PCOS during their reproductive age do not necessary lead to MASLD later in life.

(Funding: The CREw-IMAGO study is funded by the Dutch Heart Foundation (grant 2013T083). The Dutch Heart Foundation had no role in the collection, analysis, and interpretation of data, nor in the decision to submit the article for publication.)

Abstract ID #140

Abstract Title: DYSLIPIDEMIA AND POLYCYSTIC OVARY SYNDROME ACCORDING TO AGE

Benetti Z (1), Sciarroni E (1), Benelli E (1), Falcetta P (1), Bagattini B (1), Simoncini T (2), Fiore E (1), Tonacchera M (1)

Smith JG (1), Jones EB(2)

(1) Departement of Clinical and Experimental Medicine, Section of Endocrinology, University Hospital of Pisa, Pisa, Italy

(2) Departmen of Obstetrics and Gynecology, University Hospital of Pisa, Pisa, Italy

Abstract: OBJECTIVE

Polycystic ovary syndrome (PCOS) is the most common endocrine disease in women of reproductive age. Dyslipidemia is recurrent in PCOS, although some studies have shown various differences. The purpose of this study was to evaluate the lipid profile in women with PCOS according to their age at diagnosis and to better understand if it can be

influenced by hyperandrogenism or only by the body mass index (BMI).

METHODS

In this retrospective study, 712 consecutive PCOS patients were recruited at the

Department of Endocrinology of Pisa from February 1, 2014, to October 31, 2020. The diagnosis of PCOS was made following the International PCOS Network Guidelines, thus including women with two of the three following findings: clinical and/or biochemical hyperandrogenism; chronic ovulatory dysfunction; polycystic ovarian morphology (PCOM) at ultrasound. Patients were divided into three different groups according to their age: group A ≤20 years, group B 21-30 years, and group C >30 years. Anthropometric, hormonal, and metabolic parameters, focusing on lipid profile, were collected and compared between the different age groups.

RESULTS

The prevalence of dyslipidemia varied between age groups (p 0.019), with a tendency to increase with aging. The atherogenic lipid pattern, defined as the presence of both low

HDL cholesterol (HDL-C <50 mg/dl) and high triglycerides (TG >50 mg/dl), was significantly higher in group C (9.2%) than in group A (5.1%) and B (3.1%; p 0.031). Total cholesterol (TC), LDL-C, and TG were significantly higher in group B [respectively 180.4±29.2, 113.7±23.9 and 72.1 (55-99.2)] and C [193.2±32.6, 123.3±33.1 and 87 (66-140)] than in

group A [172.1±35.2, 106±28.9 and 72 (57-102)], while HDL-C was lower in group A (58±13.8) than in group B (61.3±17.1). Hyperandrogenism was more commonly found in group A (88.9%) than in groups B and C (81.8 and 81%, respectively; p 0.011) and its prevalence tended to decrease with aging. Obesity was more frequently encountered in group C, than in groups A and B (53% vs 40.1% and 33.9%, respectively; p 0.006). Since BMI differed significantly between age groups, a partial correlation analysis adjusted for BMI was performed and the positive relationship between age and total and LDL-C and the negative association with hyperandrogenism was maintained. We did not find any association between hyperandrogenism and lipid abnormalities.

CONCLUSIONS

Clinical and biochemical features of women affected by PCOS change with aging.

Advanced age and high BMI are both independent risk factors for dyslipidemia, while hyperandrogenism had not been demonstrated to influence lipid profile.

Abstract ID #142

Abstract Title: INFORMING AN ONLINE PCOS HEALTH COACHING PROGRAM: A PROTOCOL

Pirotta S (1,2), Avery J (3), Laven J.S.E (4), Ayton D (1)

(1)Health and Social Care Unit, School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC Australia

(2) Womanly Nutrition and Dietetics Clinic, online, Melbourne, Australia

(3) Robinson Research Institute, University of Adelaide, North Adelaide, Australia

(4) Erasmus MC University Medical Center, Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynaecology, Rotterdam, the Netherlands

Abstract: OBJECTIVE: Women need multidisciplinary, personalised lifestyle and medical care to best manage their PCOS to improve quality of life and reduce disease risk, yet very few multidisciplinary randomised control trials have been conducted in real-world settings and none have been online or taken a personalised approach to PCOS management. This study aims to develop an online, person-centred, multidisciplinary PCOS health coaching program using co-design workshops.

METHODS: Two online 2-hour workshops will be conducted with women diagnosed with PCOS (n=10) and 2 x 1-hour workshops with clinicians (n=5) and researchers (n=2) working in the PCOS discipline via ZoomTM. Workshop 1 will incorporate ranking exercises and process mapping to identify the most important proposed program modules and PCOS risk factors/symptoms and gather feedback on language use to optimise program engagement. Workshop 1 feedback will inform PCOSBetter program adaptation and an implementation plan will be developed. Workshop 2 will present the implementation plan. Small group discussion will focus on finalising program characteristics and module delivery according to the TiDieR Framework and will identify possible challenges to participant engagement according to the Extended Technology Acceptance Model (ETAM).

RESULTS: Data will finalise the PCOSBetter program design and characteristics. This project is stage 1 of 3 across the implementation and evaluation process of PCOSBetter. Stage 1 includes co-design and finalised program development. Stage 2 sees program piloting through a community-based randomised control trial. Stage 3 see program evaluation and efficacy to inform adaptation and scale-up, if successful.

CONCLUSION: PCOSBetter will act as ‘connector’ to the current fragmented PCOS healthcare services, removing the barrier of location and accessibility. People will be better able to meet their complex needs through easy-to-access health coaching and referral to relevant community services.

(Funding: CRE WHIRL Project Support Grant 2023 awarded to Dr Stephanie Pirotta)

Abstract ID #143

Abstract Title: AGE-RELATED CURVES OF ANTI-MÜLLERIAN HORMONE USING THE PICOAMH AND THE GEN II ASSAYS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

Barbagallo F (1,2), Van der Ham K (1), Louwers YV (1), Willemsen SP (1,3), Laven JSE (1)

(1) Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Erasmus University Medical Center, Rotterdam, Netherlands.

(2) Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy.

(3) Department of Biostatistics, Erasmus MC, University Medical Center, Rotterdam, The Netherlands.

Abstract: OBJECTIVE: The measurement of anti-Müllerian hormone (AMH) has gained widespread use in clinical practice, and it has also been proposed as a substitute for polycystic ovary morphology (PCOM). The replacement of ultrasound (US) with a single blood test for AMH would be clinically advantageous, especially in situations in which US is not available or feasible. However, the lack of international standard for AMH measurement, as well as cut-off values, strongly limits the adoption of AMH as a marker of PCOM. Different evaluations of age- and assay-specific reference ranges have been published in the last years, nevertheless these studies have mainly been conducted in normo-ovulatory or infertile women. Little is known in conditions where serum AMH levels are in the high range, especially in patients with PCOS. On this basis, the primary aim of this study was to develop an age-specific percentile distribution of AMH in patients with PCOS measured by two different assays [picoAMH (Ansh Labs) and Gen II (Beckman Coulter)]. The secondary aim of this study was to explore the association between AMH and endocrine and ultrasound parameters in women with PCOS.

METHODS: A cohort of 3,610 women aged 20 to 40 years with PCOS diagnosis according to the Rotterdam Criteria were included. AMH levels were measured by the picoAMH (Ansh Labs) assay in 1,854 women and Gen II (Beckman Coulter) assay in 1,756 women. Age-specific centile curves were constructed for the picoAMH and the Gen II assays using the LMS method. The correlations between AMH, clinical, hormonal, and ultrasound characteristics were evaluated by Spearman test.

RESULTS: The age specific percentile AMH distributions were developed and the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles were calculated for both assays used. AMH levels were significantly different between PCOS phenotypes for both the assays. In detail, serum AMH levels were significantly higher in patients with phenotype A compared to all other phenotypes for both picoAMH and Gen II assays. We also found a statistically significant positive correlation between AMH levels (for both assays) and luteinizing hormone (LH), LH/follicular stimulating hormone (FSH) ratio, testosterone, androstenedione, free androgen index, mean follicular number, and mean ovarian volume. In contrast, AMH levels were significantly negatively correlated with body mass index in both assays.

CONCLUSIONS: To our knowledge this is the first study reporting age specific percentile nomograms of serum AMH levels measured by the picoAMH and the Gen II assays in a large population of PCOS women. These findings may help to interpret AMH levels in PCOS patients and in turn, facilitate the use of AMH as a diagnostic tool for PCOM across age ranges.

Abstract ID #144

Abstract Title: FACE VALUE: EXPERIENCES OF HAVING HIRSUTISM AMONG YOUNG WOMEN DIAGNOSED WITH PCOS AND THEIR MOTHERS IN INDIA

Selvan C(1),Chittem M(2) Lathia T (3), Chawak S (4)

1.Department of Endocrinology, Ramaiah Medical College, Bangalore, India

2.Department of Liberal Arts, Indian Institute of Technology Hyderabad (IITH), Hyderabad, India

3.Department of Endocrinology, Apollo Hospitals, Navi Mumbai, India

4.Jindal School of Psychology and Counselling, O P Jindal Global University, Sonipat, India

Abstract: Objective: Hirsutism brought on by polycystic ovarian syndrome (PCOS) can lead to low self-confidence, embarrassment, and body dissatisfaction. Given the family-centeredness of health-seeking in India, and owing to the limited research, this study explored the experiences of, needs from and communication between young Indian women diagnosed with PCOS-related hirsutism and their mothers.

Methods: Using a cross-sectional design, individual, telephonic, semi-structured, audio-recorded interviews with young women diagnosed with PCOS-related hirsutism (n=27; mean age=22.4) and their mothers (n=12, mean age=49.5) were conducted. The interviews were analysed using thematic analysis. Results: The themes generated for the young women were: (i) “my face is covered with hair and managing it is a fulltime job”: shame and low self-confidence, finding solutions for managing hirsutism and (ii) “a mother who understands”: experiences of having an emotionally (un)supportive mother. Themes for the mothers included: (i) “it was difficult for her and it was difficult for me”: desire to emotionally support their daughter and (iii) “I’m always there with her”: introducing mechanisms to manage excessive hair versus restricting any action towards hair removal.

Conclusions: The study highlighted incongruences in terms of what daughters wanted from their mother (emotional and instrumental support, empathy and decisional independence) and what mothers believed they were providing their daughters (daily/overall and decisional support). Therefore, the study findings indicate a need for sensitivity interventions for daughters and their mothers (e.g., empathic communication skills), young women and their friends (e.g., improving peer awareness), and doctors (e.g., sensitizing mothers, providing decision aids) in India.

Abstract ID #145

Abstract Title: PRECLINICAL STUDIES WITH HSD17B5 INHIBITOR OG-7191 TO INVESTIGATE A POTENTIAL NOVEL TREATMENT OF HYPERANDROGENISM IN PCOS

Janhunen SK (1), Saarinen-Aaltonen N (1), Hakkarainen J (1), Lewandowski L (1), Järvikare T (1), Graziano M (2), Koskimies P (1)

(1) Organon R&D Finland Ltd, Turku, Finland

(2) Organon LLC, Jersey City, NJ, USA

Abstract: OBJECTIVE: The objective was to characterize the pharmacodynamic properties of a novel HSD17B5 inhibitor, OG 7191 in vitro and in vivo. HSD17B5 (also known as AKR1C3 enzyme) efficiently catalyzes the reduction of weakly active androgens to highly active androgens, 11-ketoandrostenedione (11KA4) to 11-ketotestosterone (11KT) and Δ4-androstene-3,17-dione (A4) to testosterone (T). Inhibition of the formation of highly active androgens has potential to reduce hyperandrogenism related symptoms in the polycystic ovary syndrome (PCOS). The objective of this study was to evaluate the inhibition of HSD17B5 in cells and tissues relevant for androgen production in PCOS, including HSD17B5-expressing human cell line, human adipocytes, human adipose and ovarian tissue.

METHODS: In vitro assays included human colon carcinoma cell line transfected to stably express human HSD17B5 (HCT116-AKR1C3), adipocytes differentiated from primary human subcutaneous preadipocytes, human subcutaneous adipose tissue and ovarian samples. Commercially obtained human tissue samples were originally derived from healthy premenopausal females under informed consent and with approval from the institutional review board. The samples were treated with substrates 11KA4 or A4, with and without OG-7191, and analyzed for 11KT and T by UPLC or LC-MS/MS. Due to species selective differences a mouse model was developed expressing human HSD17B5 to study the activity in vivo. The inhibition efficacy of OG-7191 on the HSD17B5 activity in tumors was investigated by injecting a HSD17B5 substrate (11KA4 or A4) into tumor and measuring the amount of product (11KT or T) formed at 1 to 24 h after oral administration of OG-7191 (0.1 to 10 mg/kg) or vehicle.

RESULTS: OG-7191 dose-dependently inhibited formation of 11KT and T at low nanomolar levels in cell-based assays. In intact human adipocytes and subcutaneous adipose tissue homogenate, OG-7191 inhibited the 11KT and T formation up to 85% and 44% at concentrations of 300-500 nM. In a human ovarian sample, OG-7191 inhibited 11KT and T formation by about 50% at 1 µM. OG 7191 dose-dependently inhibited the intratumoral production of 11KT and T in vivo and the effects of oral doses ≥1 mg/kg reached statistical significance (P<0.0001).

CONCLUSIONS: OG-7191 is a potent and selective inhibitor of the human enzyme HSD17B5. In vitro OG-7191 dose-dependently inhibits the formation of highly active androgens in human adipose and ovarian tissue. Upon oral dosing of OG-7191 in a mouse model the human enzyme can be inhibited thereby demonstrating a pharmacodynamic effect and potential for reducing symptoms that are related to hyperandrogenism in PCOS.

(The studies were conducted and sponsored by Organon R&D Finland Ltd (previously known as Forendo Pharma Ltd).)

Abstract ID #146

Abstract Title: MATERNAL HYPERANDROGENISM CAUSES PREGNANCY FAILURE THROUGH IMPROPER PLACENTATION VIA ANDROGEN RELATED PATHWAY

Lu H (1), Jiang H (1), Li C (1), Pui H (1), Lindgren E (1), Pei Y (1), Risal S (1), Torstensson S (1), Eriksson G (1), Ohlsson C (2), Benrick A (3,4), Stener-Victorin E (1), Deng Q (1)

(1) Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden

(2) Centre for Bone and Arthritis Research, Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

(3) Department of Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

(4) School of Health and Education, University of Skövde, Skövde, Sweden

Abstract: OBJECTIVE: The hyperandrogenic in utero environment in pregnant women with polycystic ovary syndrome (PCOS) affects placenta and embryo development and predisposes their offspring to adverse health status later in life. Moreover, PCOS jeopardizes pregnancy to miscarriage, preterm delivery, and perinatal mortality. We set out to understand the underlying molecular mechanism(s) of pregnancy complications associated with PCOS and the consequence of a hyperandrogenic intrauterine environment on the offspring.

METHODS: We used a peripubertal PCOS-like mouse model induced by continuous exposure to dihydrotestosterone (DHT) that develops obesity, anovulation, and dysfunctional ovarian morphology, to study the effects of maternal hyperandrogenism during pregnancy. To explore molecular mechanisms contributing to the developmental defects, whole genome bisulfite and RNA sequencing of primordial germ cells and placenta were performed at embryonic day 10.5 and 13.5, two critical developmental stages. To validate the finding in a human setting, human trophoblast organoid culture system was applied to further evaluate the effects of hyperandrogenism in the proliferation and differentiation of placenta trophoblast cell lineage.

RESULTS: Maternal hyperandrogenism severely reduced the pregnancy rate and led to impaired formation of the placenta labyrinth zone with reduced trophoblast precursor cells proliferation and differentiation capacity. The compromised placentation led to miscarriage at the mid-gestation stage thus no offspring was born from the PCOS lineage. All adverse effects acted through the androgen-related pathway, as co-treatment of androgen receptor blocker flutamide prevented the development of all embryonic phenotypes and gave rise to first-generation offspring. Such detrimental effects of utero androgen exposure also hold true when human trophoblast organoids are exposed to high androgen levels, and impaired differentiation and invasion of trophoblast cells were observed. In addition, in human trophoblast organoids, the addition of prolactin partially prevented the diminished differentiation capacity.

CONCLUSIONS: We here show that maternal hyperandrogenism results in a low pregnancy rate and early miscarriage because of compromised placental trophoblast cell differentiation, which led to implantation failure and impaired transportation of nutrients. Such effects are driven by androgen receptor pathways, and blockage of this pathway shows no adverse effects on offspring health. This research sheds light on the molecular mechanisms of pregnancy complications in women with PCOS and could pave the ways in the development of future treatment options.

(We would like to thank the support from the Swedish Research Council, Strategic Research Programme of Diabetes and Novo Nordisk Foundation.)

Abstract ID #147

Abstract Title: DECREASED NUMBER OF ADIPOSE STEM AND PROGENITOR CELLS IN PCOS-LIKE MICE.

Perian C (1), Vujičić M (1), Benrick A (1), Wernstedt Asterholm I (1)

(1) Department of Physiology, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, 40530 Gothenburg, Sweden

Abstract: OBJECTIVE: Visceral adiposity is associated with the metabolic syndrome, chronic inflammation, and increased risk for cardiovascular diseases. In contrast, healthy subcutaneous adipose tissue (SAT) expansion maintains metabolic health during weight gain. Prepubertal exposure of female mice to dihydrotestosterone (DHT) leads to weight gain, and reproductive and metabolic disturbances that closely resemble polycystic ovary syndrome (PCOS). In contrast to healthy states, PCOS drives visceral adiposity. We aim to determine mechanisms for this shift in fat distribution in PCOS.

METHOD: Vehicle control- or DHT-pellets were implanted in prepubertal female mice. Cell proliferation was measured after bi-weekly intraperitoneal injections of 5-ethynyl-2′-deoxyuridine (EdU). Flow cytometry was used to evaluate macrophage polarization, adipose progenitor cells and proliferation over a six-week course in both SAT and gonadal white adipose tissue (GWAT).

RESULTS: PCOS-like mice developed mild hyperglycemia and hyperinsulinemia, increased fat mass and increased adipocyte size in both SAT and GWAT. This change in adiposity was accompanied by a reduced pre-adipocyte population, and a smaller pool of M2-like macrophages. Therefore, we hypothesized that early androgen exposure impairs adipogenesis. Flow cytometry analysis showed that the density of adipose progenitor cells (Lin-Sca1+) was decreased in GWAT of DHT-exposed animals, and this cell population had lower proliferation both in SAT and GWAT. This was mainly due to reduced proliferation of (Lin-Sca1+)CD34low adipocyte progenitor cell subset in both fat depots of DHT-exposed females. Finally, PDGFRb+ preadipocyte cell population showed decreased proliferation in SAT. The EdU incorporation in mature adipocytes was very low and similar between groups indicating that the reduced pool of progenitor cells in PCOS-like mice is not due to increased adipogenesis.

CONCLUSIONS: Prepubertal DHT exposure induces metabolic dysregulation. Smaller amounts of total and proliferation adipocyte precursors suggest that the capacity for adipogenesis is lower. This alteration could contribute to the accelerated adipocyte hypertrophy and dysfunction of adipose tissue that frequently is seen in women with PCOS. We plan on investigating the implication of the altered macrophage polarization in the regulation of adipocyte precursors and adipose tissue homeostasis.

(This study is funded by the Swedish Research Council.)

Abstract ID #148

Abstract Title: SIGNIFICANT RACIAL AND SOCIOECONOMIC DIFFERENCES IN PROVISION OF PRESCRIPTIONS FOR PATIENTS WITH POLYCYSTIC OVARY SYNDROME AND INFERTILITY

Applebaum JC (1), Kim EK (2), Sharp M (1), Dokras A (3), Shah DK (3)

(1) Department of Obstetrics and Gynecology, Hospital of the University of Pennsylvania, Philadelphia, PA, USA;

(2) Division of Urogynecology and Reconstructive Pelvic Surgery, Brigham and Women's Hospital, Boston, MA, USA;

(3) Division of Reproductive Endocrinology and Infertility, Hospital of the University of Pennsylvania, Philadelphia, PA, USA;

Abstract: OBJECTIVE: While there are known racial and socioeconomic disparities in the provision of infertility treatment in the United States, those specific to individuals with polycystic ovary syndrome (PCOS) are understudied. Our objective was to assess whether provision of infertility treatment for patients with PCOS seeking fertility care varies by patient and physician level demographics.

METHODS: We conducted a retrospective study using the electronic medical record at a tertiary academic health system from 2007-2021 for patients who sought care for PCOS and infertility. Patient age, BMI, race, estimated household income, primary insurance payor, and prescriptions for fertility treatment (clomiphene citrate, letrozole, and injectable gonadotropins) were extracted. Dates of encounter and sex and medical specialty of the physician were also extracted. Differences in patient and physician demographics between patients who received and did not receive a prescription were identified with univariable analysis. Multivariable logistic regression was performed to determine associations between patient and physician demographics and likelihood of prescription receipt.

RESULTS: 3,435 unique patients with PCOS and infertility were identified with a mean age of 31.1 +/- 5.7 years. Of the 68.8% of patients who received a prescription, 47.8% were clomiphene citrate, 38.6% letrozole, and 13.7% injectable gonadotropins. Multivariable logistic regression demonstrated lower odds of prescribing any medication for Black patients compared to White patients (aOR 0.69, 95% CI 0.55-0.86), those with estimated household income below the federal poverty level (FPL) compared to above the national median (aOR 0.82, 95% CI 0.68-0.99), and those with public compared to commercial insurance (aOR 0.56, 95% CI 0.39-0.79). These disparities persisted in a subanalysis of patients prescribed oral medications only with lower odds of receiving a prescription for Black compared to White patients (aOR 0.75, 95% CI 0.59-0.93), those with estimated household income below the FPL compared to above the national median (aOR 0.74, 95% CI 0.56-0.98), and those with public compared to commercial insurance (aOR 0.65, 95% CI 0.49-0.85). Patients also had lower odds of receiving any prescription from general obstetrician-gynecologists (aOR 0.78, 95% CI 0.64-0.96), family medicine physicians (aOR 0.42, 95% CI 0.29-0.59), and general internal medicine physicians (aOR 0.63, 95% CI 0.49-0.80) compared to reproductive endocrinologists.

CONCLUSION: This large cohort study is the first to show significant racial and socioeconomic disparities in the provision of infertility treatments for patients with PCOS who seek fertility care. Moreover, fewer primary care physicians engaged in first-line fertility treatment, indicating a significant opportunity for physician education to improve access to fertility care.

Abstract ID #149

Abstract Title: Maternal androgenized induce hepatic lipid metabolic dysfunction in the male offspring

Shuting Ning(2), Enting Ji(1), Chunren Zhang(1), Min Hu(1)(3), Yingxia Ning(2)(3), Hongxia Ma(1)(3)

(1)Dept. of Traditional Chinese Medicine, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China;

(2)Dept. of Gynaecology and Obstetrics, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China;

(3) Institute of Integration of Traditional Chinese Medicine and Western Medicine, Guangzhou Medical University, Guangzhou, China;

Abstract: OBJECTIVE: For women of reproductive age, polycystic ovarian syndrome (PCOS) is one of the most prevalent metabolic and reproductive condition. First-degree female relatives to PCOS patients have been known to experience metabolic and reproductive problems due to heritable factors. In a manner similar to that of sisters with PCOS, brothers have altered gonadotrophin and steroidogenic production, as well as a metabolic phenotype and an elevated risk of cardiovascular disease and other conditions, which is suggestive of a male PCOS analogue. However, the evidence is limited that maternal androgen excess influence the male offspring, particularly the impact of hepatic lipid metabolism. Therefore, the aims of the present study was to determine that an excess of androgens in dams during pregnancy may cause lipid metabolic dysfunction in liver in adult male offspring in a prenatal androgen (PNA) mouse model, which mimics the elevation of androgens in women with PCOS during pregnancy.

METHODS: Pregnant C57BL/6 mice were randomly assigned to two groups and treated with daily subcutaneous injections of 5α-dihydrotestosterone (sesame oil containing 250 μg of DHT with benzyl benzoate) or vehicle (sesame oil with benzyl benzoate) from gestational day 16 to 18. Male pups were weighed as adult. An oral glucose tolerance test (OGTT) was used to evaluate the PNA males' glucose metabolism at 25 weeks old. On the 26 weeks, the animals were deeply anesthetized and decapitated. Trunk blood was collected and liver was dissected and wet weighed. Both tissues and blood samples were collected for histological, molecular, and biochemical analyses.

RESULTS: Adult PNA mice exhibited greater body weight and a larger percentage of liver mass, as well as increased levels of serum triglycerides and LDL-C, elevated levels of ALT and AST, higher fasting glucose and insulin. Whilst, the serum testosterone and estradiol were decreased in the adult male offspring. Next, we found the upregulated expression of lipid synthesis genes (Pparg, Acc1, Fasn, Scd1) and downregulated expression of lipid breakdown genes (Ppara, Cpt1a) in the livers of male offspring in adult compared to the control group by qPCR analysis. In line, the expression of inflammatory Il33 was higher and Il10 was lower than the controls. Further, western blot analysis revealed that the expression of PPARG, which related to lipid storage, was also increased in the liver of male offspring compared to control mice.

CONCLUSIONS: Maternal androgen excess contribute to de novo lipogenesis abnormal and inflammatory responses in the liver in the adult male offspring. Our finding suggests that PCOS pregnancy with hyperandrogenism is impact to the hepatic lipid metabolism, resulting in hepatic steatosis in the male offspring. (Supported by the Fundamental Research Funds for the National Natural Science Foundation of China, 16008024)

Abstract ID #150

Abstract Title: BLOCKING FSH ACTION PREVENTS DEPRESSION-LIKE BEHAVIOR INDUCED BY HIGH FAT DIET

Sims S(1)(2), Cheliadinova U(1)(2), Korkmaz F(1)(2), Gimenez-Roig J (1)(2), Frolinger T(1)(2), Lizneva D(1)(2), Yuen T(1)(2), Zaidi M(1)(2)

(1)Center for Translational Medicine and Pharmacology, Icahn School of Medicine at Mount Sinai, New York, NY USA

(2)Department of Medicine and of Pharmacological Sciences, Icahn School of Medicine at Mount Sinai, New York, NY USA

Abstract: OBJECTIVE: Multiple studies across the globe have reported a positive association between PCOS and depression or anxiety symptoms. Moreover, PCOS women with depression and anxiety symptoms have a higher body mass index (BMI) than women without these symptoms, as obesity is associated with the development of depression in the general population. Pathogenesis of depression and anxiety in patients with reproductive abnormalities, i.e. PCOS and menopausal woman, is poorly understood. However, gonadotropin (LH and FSH) signaling have been implicated into its development and progression. Here we evaluate the effect of blocking FSH signaling on the prevention and treatment of depression and anxiety. To answer this question, we utilized High Fat Diet (HFD) feeding - and ovariectomy (OVX) to induce depression-like behavior in mice and tested the effect of an FSH binding monoclonal mouse antibody (HF2) on the behavioral phenotype.

METHODS: C57BL/6 mice were fed on HFD for 11 weeks, and received continues HF2 (100μg) / Veh treatment (i.p injections) starting on the second HFD feeding week. Depression-like behavior was evaluated in the Forced Swim Test (FST) with immobility time a measure of behavioral despair. The Dark-light box was utilized to screen for anxiety. For further evaluation of the role of FSH on depression and anxiety. We tested C57BL/6 mice, which were OVX at 9 weeks of age and treated with HF2 (100 μg) / Veh treatment, (i.p injections) for 4 weeks, starting 3 weeks following OVX. A separate group HF2 / Veh treated mice, were exposed to 28-days of chronic stress, utilized as another model to induce depression in both sham and OVX.

RESULTS: C57BL/6 mice fed on HFD and injected with HF2 showed a reduction in FST immobility time compared to veh treated HFD feeding mice, suggesting a prevention of HFD-induced depression-like behavior. We found no effect of HFD feeding or HF2 treatment mice on anxiety-like behavior, tested in the Dark-light box. In addition, we showed OVX induced depression-like behavior, but not anxiety, in compared to shame operated mice. However, HF2 (100 μg) treatment failed to reverse the OVX-induced phenotype, including under the context of 28-days of chronic stress.

CONCLUSIONS: Together, our results provide first-time evidence, that blocking FSH action can prevent development of depression in a HFD - induced depression model but not reverse the depression – like behavior, induced by OVX suggesting a preventative rather than curative therapeutic strategy for FSH blockage.

Abstract ID #151

Abstract Title: THE RISK FOR DIABETIC COMPLICATIONS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME AND MATCHED CONTROL WOMEN

Ollila MM (1), Hautakoski A (1), Arffman M (2), Morin-Papunen L (1), Sund R (3), Piltonen TT (1)

(1) Dept. of Obstetrics and Gynaecology, Medical Research Center Oulu, Research Unit of Clinical Medicine, University of Oulu and Oulu University Hospital, Oulu, Finland;

(2) Department of Public Health and Welfare, Finnish Institute for Health and Welfare, Helsinki, Finland;

(3) School of Medicine, Institute of Clinical Medicine, University of Eastern Finland, Kuopio, Finland.

Abstract: OBJECTIVE: Women with PCOS have increased risk for type 2 diabetes (DM2). The objective of the present study was to investigate, for the first time, whether women with PCOS and DM2 have increased risk for diabetic complications, such as retinopathy, neuropathy, nephropathy, cardiovascular complications, cerebrovascular complications, foot complications, and death compared to non-PCOS control women with DM2.

METHODS: A nested 1:5 matched case-control study within the nationwide database of the Diabetes in Finland. The database includes all Finnish individuals with diabetes. Women with PCOS were identified using ICD-codes. Women with PCOS and DM2 (n=925) were compared to control women (n=4600) with matching time of the diabetes diagnosis and the age of diabetes onset. The characteristics of women with PCOS were also evaluated against all women with DM2 (n=180 219). The risk for diabetic complications (i.e., a composite variable including retinopathy, neuropathy, nephropathy, cardiovascular, cerebrovascular or foot complication) and diabetes-related death were analysed using Cox regression with competitive event approach and adjustments for education, year of DM2 diagnosis and age at DM2 diagnosis. The follow-up started at the DM2 diagnosis and ended to the first complication or death.

RESULTS: The median age at DM2 diagnosis was 62 years (interquartile range [IQR]: 53–71) in all women with DM2, whereas it was only 35 years (IQR: 28–45) in women with PCOS. The median follow-up time was 7.8 years (IQR: 4.0–11.6) in women with PCOS and DM2, 6.6 years (IQR: 3.6–9.9) in matched control women, and 5.8 years (IQR: 2.7–9.7) in all women with DM2.

Overall, 14.4% (n=131) women with PCOS and DM2 had developed some diabetic complication compared to 17.3% (n=794) of matched control women during the follow-up time. In addition, twelve women with PCOS and DM2 had died compared to 97 matched control women. In the Cox regression analysis, women with PCOS and DM2 had smaller hazard ratio (HR=0.77 with 95% confidence interval [95% CI] of 0.63–0.93) for the occurrence of diabetic complications, whereas the hazard for diabetes-related death (HR=0.59 [95% CI: 0.32–1.07]) did not differ from control women.

CONCLUSIONS: Women with PCOS develop DM2 at markedly younger age than majority of women and thus women with PCOS are burdened with DM2 longer. When compared to women with matching diabetes duration and age at disease onset, women with PCOS had slightly smaller risk for diabetic complications, whereas the risk for diabetes-related death did not significantly differ. Women with PCOS were rather young at the end of follow-up and there were only few deaths, so a longer follow-up may be required to see if the risk of diabetic complication differs between women with PCOS and matched controls.

(This study was funded by the Sakari Alhopuro Foundation and Finnish Diabetes Research Foundation).

Abstract ID #152

Abstract Title: The role of adiponectin on the development of anxiety-like behavior in females.

Samad M(1), Joakim Ek(1), Krieger JP(1), Perian C(1), Skibicka K(1), Stener-Victorin E(2), Wernstedt Asterholm I(1), Benrick A(1)

(1) Department of Physiology, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, 40530 Gothenburg, Sweden.

(2) Department of Physiology and Pharmacology, Karolinska Institute, 17177 Stockholm, Sweden.

Abstract: OBJECTIVE: Women with polycystic ovary syndrome (PCOS) have more symptoms of moderate to severe anxiety and depression. Elevated levels of androgens during pregnancy can increase the risk of anxiety and depression in daughters from women with PCOS. The mechanism behind the development of these symptoms is poorly understood, but elevated androgens and lower levels of the adipose tissue hormone adiponectin may play important roles, which we will elucidate in this project. We have tested the hypothesis that elevated levels of adiponectin in female mice can protect against the development of androgen-induced anxiety-like behavior in the offspring.

METHODS: Pregnant adiponectin transgenic female mice that overexpress adiponectin and wild-type controls were injected with inactive solution or dihydrotestosterone to induce prenatal androgenization (PNA) in the offspring. Behavioral tests were performed in 4 months old adiponectin transgenic and wt offspring using open field and elevated plus maze test to measure signs of anxiety.

RESULTS: PNA offspring spent more time in the closed arms in the elevated plus maze, indicating an anxiety-like behavior. Adiponectin overexpression in the dam or the offspring did not prevent the development of an anxiety-like behavior in PNA offspring. However, the adiponectin overexpression in the dam had metabolic imprinting effects on the offspring leading to lower fat mass and improved insulin sensitivity. Serum adiponectin levels were higher in adiponectin overexpressing mice but there was no difference in cerebrospinal fluid (CSF) levels compared to wildtypes.

CONCLUSIONS: Adiponectin overexpression does not have anxiolytic effects in PNA offspring. The low molecular forms of adiponectin that can pass the blood-brain-barrier and mediate anxiolytic effects were unaltered in the CSF and can thus explain the lack of central effects. A model that increases CSF adiponectin levels is likely needed to establish anxiolytic effects. Next, we will investigate if low levels of adiponectin increase anxiety-like symptoms in PNA offspring.

Abstract ID #153

Abstract Title: ABNORMAL ENDOMETRIAL CALCIUM SIGNALING IN PCOS-LIKE OBESE MICE MIGHT CONTRIBUTE TO SUBFERTILITY IN PCOS.

Luyckx L (1,2), Arffman R (1), Piltonen T (1), Vriens J (2)

(1) Dept. of Obstetrics and Gynecology, University of Oulu, Oulu, North Ostrobothnia, Finland;

(2) Dept. of Development and Regeneration, KU Leuven, Leuven, Vlaams-Brabant, Belgium

Abstract: OBJECTIVE: Calcium is an important signalling molecule in the endometrium, hence abnormal calcium signalling can cause defective endometrial function during key reproductive events. This explorative study used a prenatally androgenized (PNA) mouse model to investigate whether endometrial calcium signalling is abnormal in polycystic ovary syndrome (PCOS), the most common endocrine disorder in women characterized by reproductive defects such as subfertility and pregnancy complications.

METHODS: PNA PCOS-like mice were generated by daily injection of pregnant dams with 250 µg dihydrotestosterone (DHT) during E16.5-E18.5. PNA female offspring received a high-fat high sugar (HFHS) diet to induce obesity followed by isolation of endometrial epithelial cells (EECs) and analysis of intracellular calcium concentrations [Ca2+]i using calcium microfluorimetry. Additionally, PNA obese mice were ovariectomized and received estrogen and progesterone injections to induce window of implantation (WOI) stage followed by isolation of the uterus and transcriptomic analysis with RNAseq. Transcriptome data was corrected for multiple testing. Two-Way ANOVA was used for analysis of microfluorimetry data, minimal 3 replicates per experiment were used.

RESULTS: Measurement of [Ca2+]i of isolated mouse EECs showed that PNA combined with excessive body weight causes increased basal [Ca2+]i levels compared to normal weight controls. Furthermore, preliminary transcriptome data showed aberrant expression of genes related to calcium signalling in uteri of hormonally primed PNA mice. More specific, the expression of Phospholipase C (Plc) and Stim1, both involved in intracellular calcium homeostasis, and Cacna1, a voltage-gated calcium channel, were reduced in obese PNA mice compared to obese controls.

CONCLUSIONS: PCOS affects up to 1 in 10 women but details about the pathophysiology of endometrial dysfunction in PCOS are still lacking. This preliminary data shows that endometrial calcium signalling might be negatively affected by PCOS and excess body weight. Further investigation of this topic using human samples can increase our understanding of PCOS-related endometrial dysfunction and could contribute to the improvement of fertility treatments of women with PCOS.

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Abstract ID #154

Abstract Title: Spatial memory and learning in a prenatally-androgenized rat model of polycystic ovary syndrome

MAHSA NOROOZZADEH

Reproductive Endocrinology Research Center,

Research Institute for Endocrine Sciences,

Shahid Beheshti University of Medical Sciences, Tehran, Iran,

Abstract: Objectives:Alzheimer's disease (AD) a progressive neurodegenerative disease is the most common cause of dementia worldwide. AD is clinically characterized by impaired memory and cognition and changes in thinking and unconscious behavior.

Polycystic ovary syndrome (PCOS) the most common endocrine disorder in reproductive-aged women is associated with hormonal and metabolic disturbances, inflammation, depression, and gut microbiota dysbiosis in affected women, all of which may adversely affect cognitive function, learning and memory and then predispose them to AD in their later life. In the present study, we aimed to examine special memory and learning in a prenatally-androgenized rat model of polycystic ovary syndrome.

Method: Pregnant Wistar rats in the experimental group (n=8) received 5 mg of testosterone (s.c. injection) on the 20th day of pregnancy, while controls received solvent. Female offspring who exposed to androgen during their prenatal life were considered as the rat model of PCOS. Morris water maze evaluations of spatial memory and learning were conducted on prenatally-androgenized rat model of PCOS and their controls at 12 month of age for five days (training and probe days). Generalized Estimating Equation Model and t-student unpaired test results were used to compare the findings documented between two groups. P values < 0.05 were considered statistically significant.

Results: During the training sessions, the results of GEE model showed statistically significant increases in the latency, duration and frequency variables in the rat model of PCOS compared to controls. No significant differences were observed between two groups in any mentioned variables in prob test.

Conclusion: Special memory and learning were impaired in our prenatally-androgenized rat model of PCOS. This may be considered a risk factor for AD and dementia in later life. This rat model of PCOS may contribute to us to better understanding involved mechanisms in impaired memory in PCOS status. However more studies are needed to confirm our results.

Abstract ID #156

Abstract Title: HYPERTENSION AND HYPERLIPIDEMIA IN WOMEN WITH POLYCYSTIC OVARY SYNDROME: A POPULATION BASED MULTI-REGISTER MATCHED COHORT STUDY IN SWEDEN

Elenis E (1,2), Turkmen S (3), Sundström Poromaa I (1), Persson S (1).

(1) Dept. of Women's and Children's Health, Uppsala University, Uppsala, Sweden;

(2) Reproduction Center, Women's Clinic, Uppsala University Hospital, Uppsala, Sweden;

(3) Dept. of Clinical Sciences, Obstetrics and Gynecology, Sundsvall Research Unit, Umeå University, Umeå, Sweden.

Abstract: OBJECTIVE: Polycystic ovary syndrome (PCOS) is an established risk factor for insulin resistance and hyperinsulinemia. However there is still uncertainty what regards the relationship to the rest of the metabolic syndrome risk factors. The primary purpose of the current study was therefore to explore the impact of PCOS and secondarily of its phenotypes on the risk to develop hypertension and hyperlipidemia.

METHODS: This is a national multiregister matched cohort study, performed in Sweden between January 1, 1997 to December 31, 2016. Study participants were selected from the entire population of women born between 1950-1999 and residing in Sweden. Data was obtained after linkage of six validated national registers (i.e. the Swedish National Patient Register, the Medical Birth Register, the Prescribed Drug Register, the Total Population Register, the Education Register and the Register on Causes of Death). Study exposure was defined as having an ICD-10 diagnosis of PCOS, androgen excess or anovulatory infertility. All women with PCOS identified (50 969) were compared with an age- and residence- matched cohort of women without PCOS (246 246). Exposed women were further classified into being hyperandrogenic (HA) or normoandrogenic (NA) depending on the presence or not of hyperandrogenism (either through the ICD-10 diagnosis of androgen excess or the prescription of antiandrogenic medications). The outcomes of hypertension and hyperlipidemia were defined either by their ICD-10 diagnoses or by the prescription of anti-hypertensive or lipid-lowering drugs. Multivariable adjusted Cox regression-derived hazard ratios (HRs) for hypertension and hyperlipidemia were performed. All risk estimates were adjusted for the participants' birth period, country of birth and education, as well as obesity (or BMI for the women that birthed a child).

RESULTS: Women with PCOS, regardless of obesity, faced a two times higher risk for hypertension compared to women without PCOS [aHR 2.25, 95% CI 2.13-2.39], with similar risk estimates seen after adjusting for BMI. When stratifying exposed women according to their PCOS phenotype, it was demonstrated that hyperandrogenism further inflated the risk to almost 6-times [i.e. aHR 5.51, 95% CI 4.97-6.10 for HA-PCOS women and aHR 1.94, 95% CI 1.83-2.07 for NA-PCOS women respectively]. In regard to hyperlipidemia, PCOS women had, independently of obesity, a twofold risk compared to non-PCOS women [aHR 2.29, 95% CI 1.96-2.66], with comparable risk estimates between the PCOS phenotypes.

CONCLUSIONS: PCOS is an independent risk factor for the development of hypertension and hyperlipidemia with the effect seen being further increased in women with the hyperandrogenic PCOS phenotype. We therefore recommend that PCOS diagnosis and especially hyperandrogenism be added among the risk factors included in the algorithms for the long-term cardiovascular disease risk assessment in women.

Abstract ID #155

Abstract Title: ARE WE MISSING DIMINISHED OVARIAN RESERVE (DOR)? LOW ANTI-MULLERIAN HORMONE (AMH) LEVELS AND REPRODUCTIVE SUCCESS IN WOMEN FROM THE PREGNANCY IN POLYCYSTIC OVARIAN SYNDROME TRIAL (PPCOS I)

Hughes LH (1), Komorowski AS (1), Aaby DA (2), Kalra B (3), Kumar A (3), Legro RS (4), Boots CE (1)

(1) Div. of Reproductive Endocrinology and Infertility, Northwestern University Feinberg School of Medicine, Chicago, IL, USA;

(2) Northwestern University Feinberg School of Medicine, Chicago, IL, USA;

(3) Ansh Labs, Webster, TX, USA;

(4) Dept. of Obstetrics and Gynecology, Pennsylvania State College of Medicine, Hershey, PA, USA;

Abstract: OBJECTIVE: To examine patient characteristics and reproductive outcomes in women with low serum AMH levels and polycystic ovarian syndrome (PCOS) who underwent ovulation induction.

METHODS: Cryopreserved serum samples were obtained from the PPCOS I trial 1. This study was a multi-institutional, randomized control trial of 626 infertile women with PCOS defined by Rotterdam criteria treated with clomiphene citrate plus placebo, metformin plus placebo, or a combination of metformin and clomiphene. Fasting serum was collected before randomization and at study completion (confirmation of a pregnancy or up to 7 treatment cycles). AMH concentration was measured using an enzyme-linked immunosorbent assay (PCOCheck ELISA, AL-196, Ansh Labs LLC). Ovulation/pregnancy success and characteristics of women with an AMH ≤ 1 ng/ml (DOR) were compared to patients with AMH >1ng/ml.

RESULTS: Serum from a total of 322 patients was obtained from PPCOS 1 (N=118 clomiphene group, N=82 metformin group, N=122 combined group). Six women (1.9%) had DOR as defined by baseline AMH ≤ 1 ng/ml. Two of these patients underwent 7 induction cycles and never ovulated. Only one of the women ultimately conceived and was the youngest of the six (24 years old). Although there were no statistically significant differences, patients with DOR tended to be older (31.8 vs 28.0 years, p=0.12), had a higher body mass index (BMI) (36.7 vs 34.6 kg/m2, p=0.47), were less androgenic (free androgen index 6.8 vs 9.6, p= 0.30; hirsutism score 12.5 vs 14.3, p=0.65), and had less insulin resistance (Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) score 4.2 vs 5.3, p=0.26). Four women with DOR had a prior diagnosis of "ovulatory dysfunction", one was a tobacco smoker, and none had additional infertility diagnoses (i.e., endometriosis, uterine, tubal, male, or unexplained). Although bilateral ovarian volume was lower in patients with DOR compared to those with AMH >1 ng/ml (14.2 vs 23.3 cm3, p=0.04), 3 women with DOR were indicated to have polycystic ovary morphology on at least one ovary.

CONCLUSIONS: AMH measurement identified patients with DOR that were previously diagnosed with PCOS by the Rotterdam Criteria. Patients with DOR had poor success achieving pregnancy with oral ovulation induction and may have benefited from DOR counseling and more aggressive fertility treatment with the potential for fertility preservation to achieve their ideal family size. Therefore, measurement of AMH should be considered essential in the evaluation of PCOS, not only to confirm the diagnosis of polycystic ovaries, but perhaps more importantly, to rule-out a DOR diagnosis and guide fertility treatment. (Funded by Northwestern University Dept. of OBGYN Biostatistical Support Grant)

REFERENCE: 1. Legro RS, Barnhart HX, Schlaff WD, et al. Clomiphene, metformin, or both for infertility in the polycystic ovary syndrome. N Engl J Med 2007;356:551-66.

Abstract ID #157

Abstract Title: CIRCULATING ANTI-MÜLLERIAN HORMONE LEVELS IN PRE-MENOPAUSAL WOMEN: NOVEL GENETIC INSIGHTS FROM A GWAS META-ANALYSIS

Pujol-Gualdo N. (1,2), Karjalainen M.K. (3,4), Võsa U. (1), Arffman R. (2), Mägi R. (1), Ronkainen J. (3), Laisk T. (1), Piltonen T.T. (2)

(1) Estonian Genome Centre, Institute of Genomics, University of Tartu, Tartu, Estonia;

(2) Department of Obstetrics and Gynecology, Research Unit of Clinical Medicine, University of Oulu, Oulu, Finland;

(3) Research Unit of Population Health, Faculty of Medicine, University of Oulu, Oulu, Finland;

(4) Northern Finland Birth Cohorts, Arctic Biobank, Infrastructure for Population Studies, Faculty of Medicine, University of Oulu, Oulu, Finland;

Abstract: OBJECTIVE: AMH is expressed by preantral and small antral ovarian follicles in women, and variation in age-specific circulating AMH levels has been associated with several health conditions. In this study, we aim to conduct the largest genome-wide association study (GWAS) meta-analysis to identify novel genetic variants for circulating anti-Müllerian hormone (AMH) levels and provide insights into biological pathways and tissues involved in AMH regulation.

METHODS: We performed a GWAS meta-analysis in which we combined 2,619 AMH measurements (at age 31 years old) from a prospective founder population cohort (Northern Finland Birth Cohort 1966, NFBC1966) to a previous GWAS meta-analysis that included 7,049 pre-menopausal women (spanning age range 15-48). NFBC1966 AMH measurements were quantified using an automated assay (Elecsys® AMH Plus (Roche)). We annotated the genetic variants, combined different data layers to prioritise potential candidate genes, described significant pathways and tissues enriched by the GWAS signals, defined plausible regulatory roles using colocalization analysis and leveraged publicly available summary statistics to assess genetic and phenotypic correlations with multiple traits.

RESULTS: Three novel genome-wide variants were identified. One of these is in complete linkage disequilibrium with c.1100delC in CHEK2, which is found to be 4-fold enriched in the Finnish population compared to other European populations. We propose a plausible regulatory effect of some of the GWAS variants linked to AMH, as they colocalise with SNPs associated with gene expression levels of BMP4, TEX41 and EIF4EBP1. Gene set analysis highlighted significant enrichment in renal system vasculature morphogenesis and tissue enrichment analysis ranked the pituitary gland as the top association.

CONCLUSIONS: Our results highlight the increased power of founder populations and larger sample sizes to boost the discovery of novel trait-associated variants underlying variation in AMH levels, which aided to characterise novel biological pathways and plausible genetic regulatory effects linked with AMH levels variation for the first time

(Study funding / competing interest(s): This work has received funding from the European Union's Horizon 2020 research and innovation programme under the MATER Marie Sklodowska-Curie grant agreement No. 813707 (N.P.-G.), Academy of Finland, Sigrid Jusélius Foundation, Novo Nordisk, University of Oulu, Roche (T.T.P). This work was supported by the Estonian Research Council grant 1911 (R.M.). J.R. was supported by the European Union's Horizon 2020 research and innovation program under grant agreements No. 874739 (LongITools), 824989 (EUCAN-Connect), 848158 (EarlyCause) and 733206 (LifeCycle). U.V. was supported by Estonian Research Council grant PRG (PRG1291).)

Abstract ID #158

Abstract Title: DO DEPRESSION AND/OR ANXIETY INCREASE THE RISK OF METABOLIC SYNDROME IN POLYCYSTIC OVARY SYNDROME? A LONGITUDINAL STUDY

Lee IT [1], Rees J [2], King S [2], Kim AE [1], Cherlin T [2], Mumford S [1, 3], Hinkle S [1, 3], Dokras A [1]

[1] Department of Obstetrics and Gynecology, University of Pennsylvania, Philadelphia, PA, USA;

[2] Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA;

[3] Department of Biostatistics, Epidemiology and Informatics, University of Pennsylvania, Philadelphia, PA, USA

Abstract: Objectives: PCOS is associated with a high prevalence of both mood and metabolic disorders. In the general population, history of depression is associated with increased risk of metabolic syndrome (MetSyn), with some studies finding similar associations for anxiety. However, it is unknown whether preexisting mood disorders increase risk of MetSyn in patients with PCOS. We therefore aimed to evaluate the association between history of depression and /or anxiety and incidence of MetSyn in a longitudinal cohort of patients with PCOS.

Methods: We evaluated a longitudinal, single-center cohort of patients with hyperandrogenic PCOS by Rotterdam criteria and at least two evaluations for MetSyn three years apart (2008-2022). The primary exposure was depression and/or anxiety, defined by diagnosis codes or prescriptions for antidepressants or anxiolytics at a given visit. The primary outcome was risk of developing MetSyn, defined by the Adult Treatment Panel III. Mixed-effect Cox regression was performed, allowing multiple occurrences of MetSyn per participant while accounting for the random effect of the participant, to estimate hazard ratios (HR) for developing MetSyn adjusting for age, race, ethnicity, and free testosterone. For patients with MetSyn at a given visit, probability of having persistent MetSyn at a subsequent visit was estimated by mixed-effects modified Poisson regression adjusting for confounders as above.

Results: Among 321 participants, baseline characteristics did not differ between those with depression/anxiety (33.0%, n=105) and those without (n=216). Median follow-up was 7 years (IQR 4-9), median age at study entry was 28 years (IQR 23-31), and median baseline BMI was 33.2 kg/m2 (IQR 26.3-39.4). Adjusted prevalence of MetSyn at baseline was higher in those with depression/anxiety compared to those without (45.8% versus 36.6%, p=0.10). More importantly, depression/anxiety was associated with increased risk of incident MetSyn (adjusted HR=1.91, p=0.03) during the study period. Median age of first MetSyn incidence was 30 (IQR 26.5-33.5), with no difference between groups. Increased incidence of MetSyn was similar in subgroup analyses of patients with only depression or only anxiety. Among patients with MetSyn at a given visit, persistence of MetSyn at subsequent visits was similar between groups (71.7% versus 77.1%, p=0.32).

Conclusions: In our large longitudinal PCOS cohort, we show for the first time that risk of developing MetSyn is higher in patients with depression and/or anxiety compared to those without. While the international PCOS guidelines recommend that all patients undergo metabolic screening at time of diagnosis, there is no guidance for ongoing screening. Our data suggest that women with mood disorders warrant ongoing metabolic screening and further studies are needed to evaluate frequency of screening.

(No funding was used for this study.)

Abstract ID #159

Abstract Title: SOCIAL DEPRIVATION INDEX AND RISK OF METABOLIC SYNDROME AMONG PATIENTS WITH POLYCYSTIC OVARY SYNDROME

Lee IT [1], Rees J [2], King S [2], Kim AE [1], Cherlin T [2], Mumford S [1, 3], Dokras A [1]

[1] Department of Obstetrics and Gynecology, University of Pennsylvania, Philadelphia, PA, USA;

[2] Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA;

[3] Department of Biostatistics, Epidemiology and Informatics, University of Pennsylvania, Philadelphia, PA, USA

Abstract: Objectives: PCOS is associated with a high risk of metabolic syndrome (MetSyn), an important predictor of cardiovascular disease (CVD). Social determinants of health (SDoH) such as economic stability and neighborhood environment have been increasingly recognized as modifiable contributors to CVD in the general population. However, the role of SDoH in CVD risk has not been studied in PCOS. This study aimed to determine the association between the social deprivation index (SDI) and risk of MetSyn in women with PCOS.

Methods: This was a longitudinal study of 321 patients with hyperandrogenic PCOS by Rotterdam criteria and at least two visits for MetSyn three years apart between 2008-2022. The primary exposure was SDI, a composite measure of seven demographic characteristics as a proxy for SDoH. SDI ranges from 1 to 100, with higher scores indicating greater social deprivation. The primary outcome was risk of developing MetSyn, defined by the Adult Treatment Panel III. Cox regression was performed to estimate the hazard ratio (HR) for developing MetSyn adjusting for age, race, and ethnicity. Interaction analysis was performed to assess for effect modification by race. Differences in prevalence of MetSyn and fulfilment of individual MetSyn criteria at the first visit were compared between the highest (4th) versus lower 3 SDI quartiles using modified Poisson regression adjusting for the above confounders.

Results: Median duration of follow-up was 7 years (IQR 4-9) and median age at first visit was 28 years (IQR 23-31), with no differences between the 4th and lower 3 SDI quartiles. Number of visits and interval between visits was similar between groups. BMI was higher in the 4th quartile (38.6 vs 31.7 kg/m2, p<0.001), and a larger proportion self-identified as Black race (70.1 vs 13.1%, p<0.001). Adjusted prevalence of MetSyn at the first visit was higher in the 4th quartile compared to the lower 3 (55.5 versus 35.0%, p=0.01). Adjusting for confounders, fulfilment of the glucose criterion was higher in the 4th quartile (56.9 versus 27.0%, p<0.001), with no differences in the other criteria. There was no significant association between SDI and risk of developing new onset MetSyn (adjusted HR 0.79 in 4th quartile compared to lower 3, 95% CI 0.43-1.45, p=0.45), with similar results across all race groups.

Conclusions: This is the first study to show a high prevalence of MetSyn in women with PCOS and high SDI residing in the US. Further studies are needed to identify patient and health system related modifiable factors in patients with high SDI scores. In our cohort seeking follow-up care, high SDI did not increase risk of developing MetSyn during the study period. This lack of association may be due to ongoing metabolic screening and engagement with the healthcare system.

(No funding was used for this study.)

Abstract ID #160

Abstract Title: DIAGNOSTIC ACCURACY OF OVARIAN MORPHOLOGY FOR THE DIAGNOSIS OF POLYCYSTIC OVARY SYNDROME (PCOS) AMONG ADOLESCENTS

Christ JP (1), Vanden Brink H (2), Hoeger K (3), Cedars MI (1), Shinkai K (4), Lujan ME (5), Huddleston HG (1)

(1) Department of Obstetrics and Gynecology, University of California San Francisco, San Francisco, CA USA;

(2) Department of Nutrition, Texas A&M University, College Station, TX USA;

(3) Department of Obstetrics and Gynecology, University of Rochester, Rochester, NY USA;

(4) Department of Dermatology, University of California San Francisco, San Francisco, CA USA;

(5) Division of Nutritional Sciences, Cornell University, Ithaca, NY USA

Abstract: OBJECTIVE: Current international consensus guidelines do not recommend the inclusion of pelvic ultrasonography for the diagnosis of PCOS among adolescents as data assessing diagnostic accuracy of ultrasonography in this population are limited. We sought to evaluate the diagnostic accuracy of pelvic ultrasonography, using a primarily transvaginal approach, for the diagnosis of PCOS among adolescents.

METHODS: A secondary analysis of two prospective cohorts was completed. Adolescents were eligible for inclusion if they were <9 years from menarche or <21 years of age if age of menarche was not available. In the first cohort (n=100), assessment of follicle number per ovary (FNPO) and ovarian volume (OV) was completed using real-time transvaginal ultrasound (n=74), or if not tolerated, transabdominal (n=19, in which case FNPO was omitted) or transrectal approach (n=3), 4 were missing data on imaging method. In the second cohort (n=30) transvaginal ultrasound was utilized to assess ovarian morphology and offline assessment of FNPO and OV was completed post-hoc. All participants underwent standardized anthropometric, hormonal, and metabolic evaluations. PCOS was defined by the presence of hyperandrogenism (HA, modified Ferriman-Gallwey score ≥8 and/or elevated biochemical androgens) and oligo-amenorrhea (OA, using gynecologic age standards). Baseline features were compared between PCOS and non-PCOS using Student's T-tests. Ovarian morphology was adjusted for assessment method (real-time vs offline) in all analyses. ANCOVA models were used to produce assessment method adjusted means for FNPO and OV. ROC curves adjusting for assessment method were utilized to assess diagnostic accuracy of ovarian morphology.

RESULTS: In total, 111 participants met PCOS criteria (OA and HA) and 19 were non-PCOS (neither OA nor HA). Participants with PCOS compared to non-PCOS had similar age at assessment 19±3 vs 20±1 years, age of menarche 13±2 vs 13±1 years, and BMI 29.1±7.5 vs 25.6±4.7 kg/m2, p>0.05. After adjustment for ultrasound method, FNPO and OV were higher in PCOS versus non-PCOS [Mean (95% CI), FNPO: 35 (31-38) vs 24 (16-32) follicles, p=0.02; OV 11.0 (10-12) vs 7.7 (5-10) mL, p=0.009]. Controlling for assessment method, diagnostic accuracy for the prediction of PCOS diagnosis by area under the ROC curve (AUC) was 0.87 for FNPO and 0.85 for OV.

CONCLUSIONS: FNPO and OV have excellent discriminatory power to differentiate adolescents with PCOS versus non-PCOS in a well-defined hyperandrogenic population. Given need to control for assessment method, threshold values to define PCOM in adolescents could not be produced from ROC curves in the current analyses and therefore warrants method-specific diagnostic criteria. These findings should be validated in a larger sample but suggest ovarian morphology may have clinical relevance in the assessment of adolescents with PCOS.

Abstract ID #161

Abstract Title: ASSOCIATION BETWEEN LH LEVELS AND METABOLIC PARAMETERS IN HEALTHY POPULATION AND PCOS WOMEN: SYSTEMATIC REVIEW AND META-ANALYSIS

Cheliadinova U (1), Vasilyeva D (1), Ievleva K (1), Atabiekov I (1), Novikova E (1), Kuo T (1), Gumerova A (1), Barak O (1), Korkmaz F (1), Gimenez Roig J (1), Frolinger T (1), Pevnev G (1), Sims S (1), Sultana F (1), Kannangara H (1), Temple M (1), Kramskiy N (1), Wizman S (1), Orloff M (1), Igel L (1), Liu A (1), Pallapati A (1), Ryu V (1), Rojekar S (1), Moldavski O (1), Yuen T (1), Zaidi M (1), Lizneva D (1)

(1) Icahn School of Medicine at Mount Sinai, New York, NY, USA.

Abstract: OBJECTIVE: Results of studies demonstrating the relationship between gonadotropin levels and metabolic parameters, including body mass index (BMI) and markers of Insulin resistance in normally cycling and PCOS women have conflicted. In some studies, luteinizing hormone (LH) levels did not differ between lean and obese women, whereas in other studies, they differed significantly. The purpose of this meta-analysis was to provide a polled and subgroup estimate of the association between LH and different metabolic parameters, including BMI in healthy reproductive aged and menopausal women, as well as in women with PCOS.

METHODS: This study was conducted in accordance with PRISMA guidelines. We performed PubMed, EMBASE and Cochrane library searches including all available publications not limited by year of publication. Data were extracted using a web-based, piloted form and combined for meta-analysis. Case-control, cohort, and cross-sectional studies were included in the systematic review. The studies included diverse groups of participants varying by age (adolescents, reproductive population, elderly), state of health (healthy, patients with PCOS, metabolic syndrome), body weight (lean, overweight, obese). Study eligibility was assessed by two reviewers independently via the abstract screening software Rayyan (https://rayyan.qcri.org). Data was extracted by two reviewers. 55505 publications were found in the initial search. After duplicates were resolved 5139 papers were excluded due to irrelevant outcomes, study design, population, or publication type or due to the lack of statistical information. In subgroup analysis, we attempted to take into account the effects of PCOS disorder status, LH levels, age, and BMI. Forty-nine potentially relevant full-text articles were assessed, and 24 studies were included in the analysis, totaling 6888 participants. Pooled estimates of standardized mean difference were consequently documented, and I2 statistics as a measure of heterogeneity across all included studies.

RESULTS: We have shown that LH levels are negatively associated with BMI and its levels differ significantly between all obese and non-obese women –2.03 [-3.08, -0.98], lean and obese PCOS –1.78 [-3.57, 0.02], healthy non-obese and obese volunteers of reproductive age –1.93 [-2.80, -1.06], moreover a stronger association was evidenced in menopausal women –7.51 [-11.27, -3.75]. I2 varied between 75% and 98%.

CONCLUSIONS: We can conclude that LH levels are negatively associated with BMI, and the association is stronger for healthy menopausal women. Although our data is associated with high heterogeneity, which should be further evaluated.

Abstract ID #162

Abstract Title: ESTIMATING THE INTANGIBLE BURDEN OF PCOS USING THE EQ-5D-5L: A PATIENT ADVOCACY ORGANIZATION STUDY

Thai L (1), Ottey S (1), Delau O (2), Surabhi Y (2), Buyalos RP (3), Patterson W (1), Azziz R (4,5,6)

(1) PCOS Challenge: The National Polycystic Ovary Syndrome, Atlanta, GA 30308, USA

(2) Dept. of Biostatistics, School of Global Public Health, New York University, New York, NY 10003, USA

(3) Dept. of Ob/Gyn, David Geffen School of Medicine, UCLA, Los Angeles, CA 90095, USA

(4) Dept. of Health Policy, Management, and Behavior, School of Public Health, University at Albany, SUNY, Rensselaer, NY 12144, USA

(5) Depts. of Obstetrics & Gynecology, Medicine, Heersink School of Medicine, University of Alabama at Birmingham, Birmingham, AL 35294, USA

(6) Dept. Healthcare Organization & Policy, School of Public Health, University of Alabama at Birmingham, Birmingham, AL 35294, USA

Abstract: BACKGROUND: Polycystic Ovary Syndrome (PCOS) is clinically evident in 8%-15% of reproductive-aged women globally, and is associated with reproductive, cardio-metabolic, dermatologic, obstetrical, and mental health morbidities, and an estimated healthcare-associated economic burden >$15 billion/yr. for the U.S. alone. The extent of PCOS-related intangible costs (due to pain and suffering and reduced quality of life [QOL]) are unknown.

OBJECTIVE: Determine the intangible burden of PCOS using the European QOL 5-Dimensions, 5-Levels (EQ-5D-5L).

METHODS: A prospective survey was performed among members of an international patient advocacy organization using the European QOL 5-Dimensions, 5-Levels (EQ-5D-5L).

RESULTS: A total of 460 people with PCOS responded to all questions in the survey. Survey responses indicated that 51.1% experienced moderate to extreme anxiety/depression, 11.7% moderate to extreme mobility issues, 37.2% moderate to extreme pain/discomfort, 4.4% moderate to severe problems with self-care, and 22.5% moderate to extreme problems with their usual activities (e.g., work, study, housework, family, or leisure activities). When assessing how good or bad their health was on the day of the survey, using a Visual Analogue Scale (VAS), 38.9% reported best/near best health, 51.5% moderate health, and 9.6% worse/near worse health. Assuming one full year of life, we calculated the QALY (Quality Adjusted Life Year) scores using Model 1: cTTO (Pickard et al. Value Health. 2019;22:931-41), which ranges from 1 (perfect health) to 0 (dead). In our population the QALY estimated using all 5 dimensions of the EQ-5D-5L was 0.681±0.240 and using the VAS health scale it was 0.593±0.191. These values indicate that our PCOS population, on average, experienced about 60% of 'perfect health', i.e., fair to poor health (Craig & Rand, Med Care. 2018;56:529-36).

CONCLUSIONS: Regarding intangible burden, >50% of PCOS subjects studied reported significant anxiety/depression and >20% moderate to significant difficulty in their usual activities; ~10% reported their health as the worse/near worse they could imagine. On average, these women reported fair to poor health. Overall, the total economic burden of PCOS far exceeds just its direct medical costs, and intangible costs need to be considered.

SUPPORT: Supported, in part, by PCOS Challenge: The National Polycystic Ovary Syndrome Association and the Foundation for Research and Education Excellence.

Abstract ID #163

Abstract Title: Increased Prevalence of Cardiometabolic Risk Factors and Cardiovascular Disease in a Canadian Population Cohort

Wang T (1), Bakal J(1), Ghosh M (2), Vine D (3)

(1) Alberta Health Services

(2) Division Endocrinology and Metabolism, Faculty Medicine and Dentistry, U of Alberta

(3) Metabolic and Cardiovascular Disease Laboratory, U of Alberta

Abstract: Objective: Polycystic Ovary Syndrome (PCOS) is the most common metabolic-endocrine-reproductive disorder impacting 10-15% of women across their lifespan. Large epidemiological studies across the globe have found PCOS is associated with increased cardiometabolic risk factors, type 2-diabetes (T2D) and cardiovascular cisease (CVD). In Canada we currently have limited data on the prevalence of cardiometabolic risk factors, T2D and CVD in those afflicted with PCOS. The aim of this study was to determine the prevalence of cardiometabolic risk factors and CVD in PCOS compared to age matched controls in a Canadian population.

Methods: A retrospective observational case-control study in those diagnosed with PCOS and age-matched controls was undertaken using the Alberta Health Services Health Analytics administrative database from 2002-2022 in Alberta, Canada. International Classification of Diseases (ICD-9 and 10) were used to identify health outcomes for exposed (PCOS) and unexposed (non-PCOS) controls.

Results: The prevalence of overweight-obesity, hypertension, dyslipidemia, non-alcoholic liver fatty disease, T1D and T2D were increased 2-3 fold in PCOS, (n=16531) compared to the control population (n=49335, p<0.0001). CVD, peripheral vascular disease (PVD) and cerebrovascular disease (CEVD) had a 1.5, 2.0 and 1.7 fold higher prevalence, respectively, in those with PCOS (p<0.0001), and occurred on average 3 yrs earlier in young females with PCOS (35 yrs vs 38 yrs for PVD, 37 and 40 yrs for CEVD). The prevalence of a myocardial infarction was 40% higher in those with PCOS with a median age of 43 vs 47 yrs in controls.

Conclusion: These findings in a Canadian population are consistent with increased premature CVD risk in young individuals with PCOS. This evidence-based data provides impetus for the need to improve education of patients and clinicians on premature CVD risk and to improve preventative health care in this high-risk population.

Abstract ID #164

Abstract Title: ATHEROSCLEROTIC VASCULAR DISEASE IS ASSOCIATED APO-B LIPOPROTEINS IN YOUNG HIGH-RISK WOMEN WITH AND WITHOUT PCOS

Wu X (1), Wilke M (1), Ghosh M (2), Raggi P (3), Harald H (3), Vine D (1)

(1) Metabolic and Cardiovascular Disease Laboratory, U of Alberta;(2) Division Endocrinology and Metabolism, U of Alberta Hospital;(3) Division Cardiology, Mazankowski Alberta Heart Institute, U of Alberta Hospital

Abstract: OBJECTIVE: Polycystic Ovary Syndrome (PCOS) is associated with increased cardiometabolic risk factors and incidence of cardiovascular disease (CVD). Currently, early screening of dyslipidemia, atherosclerotic CVD (ACVD) and cardiac function are not routine in the primary care of high-risk young females with and without PCOS. The aim of this study was to provide evidence-based research to aid the development of assessment guidelines for early detection of dyslipidaemia, cardiac dysfunction and ACVD in high-risk young women with and without PCOS.

METHODS: A case-control study in high-cardiometabolic risk (body mass index (BMI>25) females aged 25-45 years with and without PCOS, matched for age-BMI, and healthy weight controls was conducted. Outcome measures included blood lipids, apoB-lipoproteins, carotid intima media thickness (cIMT), carotid plaque height and cardiac function using ultrasound and 2D/3D echocardiography.

RESULTS: High-risk females with (n=45) and without PCOS (n=20) had 25% lower HDL-cholesterol (C), 25% higher total apolipoprotein (apo)-B, 30% higher apo-B48, 30% higher non-HDL-C, >50% higher triglycerides (TG) and remnant-C in the fasted state compared to healthy-weight controls (n=10). The PCOS group had an additional 25% higher TG and remnant-C in the fasted and non-fasted state compared to non-PCOS controls. cIMT was increased by 15% in those with and without PCOS, and carotid plaque height was increased 30% (0.40 mm) in PCOS compared non-PCOS and healthy-weight controls (0.25mm). Age, diastolic blood pressure and total ApoB were highly associated with cIMT, and total apoB predicted 12% and 14% of the variability in cIMT and carotid plaque height, respectively. The PCOS and non-PCOS control groups had a 20% increase in systolic and diastolic blood pressure and left ventricular (LV) hypertrophic indices including mass index and posterior wall thickness, and a 5% lower LV global longitudinal strain, compared to healthy-weight controls. The PCOS group had higher re-stratification of scores for 10yr-CVD and Atherosclerotic risk compared to non-PCOS and healthy-weight control groups.

CONCLUSION: High-risk PCOS and non-PCOS controls have impairment in atherogenic apoB-TG lipoprotein and remnant-C metabolism, and these are exacerbated in those with PCOS. Apo-B dyslipidemia was positively associated with ACVD indices. Early screening for apoB-dyslipidemia, ACVD and cardiac hypertrophy may be warranted and could be used to develop a risk re-stratification model to inform prevention and intervention guidelines in high-risk young females with and without PCOS.

Abstract ID #166

Abstract Title: CHALLENGES IN DIAGNOSIS AND HEALTH CARE IN POLYCYSTIC OVARY SYNDROME IN CANADA: A PATIENT PERSPECTIVE TO IMPROVE HEALTH CARE ACROSS THE LIFESPAN

Sydora B (1), Wilke M (1), McPherson M (1), Chambers S (1), Ghosh M (2), Vine D (1)

(1) Metabolic and Cardiovascular Disease Laboratory, U of Alberta; (2) Division Endocrinology and Metabolism, Faculty Medicine and Dentistry, U of Alberta Hospital

Abstract: OBJECTIVE: Polycystic Ovary Syndrome (PCOS) affects 1 in 10 women yet remains understudied despite being the most common endocrine-metabolic disorder in women affecting health and quality of life across the lifespan. To date we do not have a good understanding of the scale of the problem, in terms of its clinical diagnosis, symptom severity, societal impact, health across the lifespan and health care management in Canada. The aim of this study was to assess the perceptions of health status, health care experience and lifestyle management support of women with PCOS in Canada.

METHODS: An online questionnaire was conducted in individuals self-reporting a diagnosis of PCOS. The questionnaire included demographics, PCOS symptoms and diagnosis, follow-up care, health concerns, and information resources. Descriptive statistics of frequency and percentage were used and thematic analyses were applied to open-response questions.

RESULTS: Responses from 194 women living in Canada (93% in Alberta) were included. The average age was 34±8 years and BMI was 35±9. Menstrual irregularity was identified in 84% of respondents as the first symptom noticed and the primary reason for seeking a medical consultation. PCOS diagnosis occurred on average 4.3 years following awareness of first symptoms and included consultation with more than one family clinician or health professional for 57% of respondents. Half (53%) of respondents reported not receiving a referral to specialists, particularly for mental health, for follow-up care, and 70% were not informed about long-term health complications associated with PCOS such as diabetes or cardiovascular disease. Most respondents (82%) did their own research about PCOS using on-line sources, social media, books, and academic literature and sought advice from peer support groups and other health care providers. Themes from open questions about suggested health care improvement included more resources and support, increased and reliable information, better education and training for clinicians, timely diagnosis, prompt referrals to specialists, and generally more compassion and empathy regarding symptoms and challenges in management of their disease.

CONCLUSION: Our findings highlight the challenges in health care for women with PCOS in Canada. A timely diagnosis, continuous disease management support and multidisciplinary care are currently not adequately provided. We aim to translate these findings to improve the health care and experience of women with PCOS in the health care system.

Abstract ID #168

Abstract Title: CHALLENGES IN DIAGNOSIS AND HEALTH CARE IN POLYCYSTIC OVARY SYNDROME IN CANADA: A PATIENT PERSPECTIVE TO IMPROVE HEALTH CARE ACROSS THE LIFESPAN

Sydora B (1), Wilke M (1), McPherson M (1), Chambers S (1), Ghosh M (2), Vine D (1)

(1) Metabolic and Cardiovascular Disease Laboratory, U of Alberta; (2) Division Endocrinology and Metabolism, Faculty Medicine and Dentistry, U of Alberta Hospital

Abstract: OBJECTIVE: Polycystic Ovary Syndrome (PCOS) affects 1 in 10 women yet remains understudied despite being the most common endocrine-metabolic disorder in women affecting health and quality of life across the lifespan. To date we do not have a good understanding of the scale of the problem, in terms of its clinical diagnosis, symptom severity, societal impact, health across the lifespan and health care management in Canada. The aim of this study was to assess the perceptions of health status, health care experience and lifestyle management support of women with PCOS in Canada.

METHODS: An online questionnaire was conducted in individuals self-reporting a

diagnosis of PCOS. The questionnaire included demographics, PCOS symptoms and diagnosis, follow-up care, health concerns, and information resources. Descriptive statistics of frequency and percentage were used and thematic analyses were applied to open-response questions.

RESULTS: Responses from 194 women living in Canada (93% in Alberta) were included. The average age was 34±8 years and BMI was 35±9. Menstrual irregularity was identified in 84% of respondents as the first symptom noticed and the primary reason for seeking a medical consultation. PCOS diagnosis occurred on average 4.3 years following awareness of first symptoms and included consultation with more than one family clinician or health professional for 57% of respondents. Half (53%) of respondents reported not receiving a referral to specialists, particularly for mental health, for follow-up care, and 70% were not informed about long-term health complications associated with PCOS such as diabetes or cardiovascular disease. Most respondents (82%) did their own research about PCOS using on-line sources, social media, books, and academic literature and sought advice from peer support groups and other health care providers. Themes from open questions about suggested health care improvement included more resources and support, increased and reliable information, better education and training for clinicians, timely diagnosis, prompt referrals to specialists, and generally more compassion and empathy regarding symptoms and challenges in management of their disease.

CONCLUSION: Our findings highlight the challenges in health care for women with PCOS in Canada. A timely diagnosis, continuous disease management support and multidisciplinary care are currently not adequately provided. We aim to translate these findings to improve the health care and experience of women with PCOS in the health care system.

Abstract ID #169

Abstract Title: ADDRESSING WEIGHT BIAS IN PCOS TREATMENT: A REVIEW OF CURRENT GUIDELINES

Ottey S (1), McKittrick M (2), Grassi A (3), Abbott S (4), Sherif K (5)

(1) PCOS Challenge: The National Polycystic Ovary Syndrome Association, Atlanta, GA, USA;

(2) Martha McKittrick Nutrition, New York, NY, USA;

(3) PCOS Nutrition Center, LLC, Malvern, PA, USA;

(4) PCOS Nutrition Co., Charlotte, NC, USA;

(5) Dept. of Medicine, Thomas Jefferson University, Philadelphia, PA, USA

Abstract: OBJECTIVE: This abstract aims to critically evaluate the weight bias in healthcare, particularly in the context of Polycystic Ovary Syndrome (PCOS) treatment, and to explore the potential application of Health At Every Size® (HAES®) principles in PCOS management. HAES® is a public health initiative to improve health equity. It also seeks to identify potential improvements for size inclusiveness in healthcare settings.

METHODS: A comprehensive review of the 2018 and draft of the 2023 International Evidence-based Guideline for the Assessment and Management of PCOS was conducted, focusing on the language used about weight and lifestyle. The review also examined the recommendations for preconception and infertility, assessing the extent of weight-centric language and the use of BMI as a guiding factor. The principles of HAES® were studied in-depth to understand their potential application in PCOS treatment.

RESULTS: The review revealed a significant weight bias in healthcare, often manifesting as stigmatizing language such as "overweight," "obese," and "obesity." This bias was particularly evident in PCOS treatment, with a disproportionate focus on weight and Body Mass Index (BMI), including preconception and infertility recommendations. Weight bias can have a significant detrimental impact on the physical and mental health of those with PCOS. Weight bias can lead to the avoidance of seeking medical treatment, poorer treatment adherence, and less trust in the healthcare team. It can also lead to eating and mood disorders. The application of HAES® principles, which emphasize health-promoting behaviors over weight control, was found to be limited in current PCOS management. Size inclusiveness in healthcare settings was also found to be lacking, with many facilities lacking size-inclusive furniture, gowns, blood pressure cuffs, and other accommodations.

CONCLUSIONS: The review underscores the need for a paradigm shift in PCOS treatment, moving away from a weight-centric approach towards a focus on health-promoting behaviors. The application of HAES® principles could provide a more inclusive and less stigmatizing approach to PCOS management. Furthermore, improvements in size inclusiveness in healthcare settings could help to reduce weight bias and improve patient outcomes. The findings highlight the importance of addressing weight bias and promoting size inclusiveness in healthcare, particularly in the context of PCOS treatment.

FUNDING: NONE

Abstract ID #170

Abstract Title: INDIRECT ECONOMIC BURDEN OF PCOS: A PATIENT ADVOCACY ORGANIZATION STUDY

Thai L (1), Ottey S (1), Delau O (1,2), Buyalos RP (3), Patterson W (1), Azziz R (4,5,6)

(1) PCOS Challenge: The National Polycystic Ovary Syndrome, Atlanta, GA 30308, USA; (2) Dept. of Biostatistics, School of Global Public Health, New York University, New York, NY 10003, USA; (3) Dept. of Ob/Gyn, David Geffen School of Medicine, UCLA, Los Angeles, CA 90095, USA; (4) Dept. of Health Policy, Management, and Behavior, School of Public Health, University at Albany, SUNY, Rensselaer, NY 12144, USA; (5) Depts. of Obstetrics & Gynecology and Medicine, Heersink School of Medicine, University of Alabama at Birmingham, Birmingham, AL 35294, USA; (6) Dept. of Healthcare Organization & Policy, School of Public Health, University of Alabama at Birmingham, Birmingham, AL 35294, USA

Abstract: BACKGROUND: Polycystic Ovary Syndrome (PCOS) is a complex genetic trait and the most common endocrine disorder of women, clinically evident in 8% to 15% of all reproductive-aged women globally. However, the disorder persists beyond reproductive years. PCOS is associated with reproductive, cardio-metabolic, dermatologic, maternal health, and mental health morbidities, with an estimated healthcare-associated economic burden exceeding $15 billion yearly for the U.S. alone (2021 USD). However, the extent of indirect costs of PCOS is unknown. Indirect costs are lost wages due to disability or death related to the disease or impaired work productivity related to the disease.

OBJECTIVE: Determine the extent of the indirect economic burden of PCOS.

METHODS: A prospective survey was performed among international patient advocacy organization members using the Work Productivity and Activity Impairment Questionnaire: General Health v2.0 (WPAI:GH).

RESULTS: A total of 510 people with PCOS responded to the study. The WPAI:GH indicated that 80% (408/510) were employed and had worked in the past 7 days, with 69.9% working ≥ 31 hrs. Of those who worked, 36.2% reported impairment while working due to health, and 8.1% had health problems that significantly affected work productivity. Health problems were deemed significant when respondents chose Likert scores 8-10 for how much health affected productivity while working. Of the total hours worked in the prior 7 days, 12.2% (1726.5/14098.8) were reported missed due to health, with 22.2% of respondents missing ≥ 6 hrs. in 7 days. Using the respondent's reported annual income range, the mean indirect economic burden per study participant ranged from $511 to $716 per participant in the prior 7 days. Considering there are at least 6 million people with PCOS in the US and that 80% are employed and work full time (52 weeks), the total indirect costs in this population range from $128 to $178 billion (in 2023 USD).

CONCLUSIONS: Regarding the indirect burden of PCOS, 80% of respondents reported being employed, with more than one-fifth of respondents missing ≥6 hrs. in the 7 days prior to the survey. The yearly indirect cost due to missed work or reduced work productivity was estimated to range from $128 to $178 billion (in 2023 USD) in the U.S. alone. It is important to note that these costs do not reflect the quality of work done, which may be further impacted. Overall, the indirect economic burden of PCOS far exceeds its direct medical costs.

(SUPPORT: Supported, in part, by PCOS Challenge: The National Polycystic Ovary Syndrome Association and the Foundation for Research and Education Excellence.)

Abstract ID #172

Abstract Title: UNLOCKING THE VALUE OF HEALTH: A WILLINGNESS-TO-PAY STUDY OF PCOS IN A PATIENT ADVOCACY ORGANIZATION

Thai L (1); Delau O (1,2); Buyalos RP (3); Ottey S (1); Patterson W (1); Azziz R (4,5,6)

AFFILIATIONS: (1) PCOS Challenge: The National Polycystic Ovary Syndrome, Atlanta, GA 30308, USA; (2) Dept. of Biostatistics, School of Global Public Health, New York University, New York, NY 10003, USA; (3) Dept. of Ob/Gyn, David Geffen School of Medicine, UCLA, Los Angeles, CA 90095, USA; (4) Dept. of Health Policy, Management, and Behavior, School of Public Health, University at Albany, SUNY, Rensselaer, NY 12144, USA; (5) Depts. of Obstetrics & Gynecology, Medicine, Heersink School of Medicine, University of Alabama at Birmingham, Birmingham, AL 35294, USA; (6) Dept. Healthcare Organization & Policy, School of Public Health, University of Alabama at Birmingham, Birmingham, AL 35294, USA

Abstract: BACKGROUND: Polycystic Ovary Syndrome (PCOS) is clinically evident in 8-15% of women and is associated with significant morbidities, with an estimated healthcare-associated economic burden of >$15 billion/yr. (2021 USD) for the U.S. alone. In addition to direct healthcare costs, the economic burden of a disorder also includes indirect (impact on work wages or productivity) and intangible (impact on quality of life) costs. One method of assessing intangible costs is the self-reported willingness-to-pay (WTP) within one's financial means approach. The WTP is used to assess the perceived value that affected individuals are willing to expend for a cure or control of their condition.

OBJECTIVE: Conduct a WTP analysis for PCOS.

METHODS: A prospective survey among members of an international patient advocacy organization using the following question: “Within your economic means, please specify (in US Dollars, no cents) the maximum amount you would pay as a one-time payment to be cured of PCOS.”

RESULTS: A total of 496 people with PCOS responded to this question. Forty-seven (9.5%) results were removed due to invalid data, including: a) when the reported WTP amount exceeded participants’ economic means (>100% of their reported income) or b) when participants reported a low WTP amount due to their belief that a cure was impossible. The average WTP for a one-time payment to cure themselves of PCOS was $9,052 ± $19,310 (N = 449), with values ranging from $0 to $200,000. When grouped in categories, 21.8%, 17.8%, 29.2%, 24.3%, and 6.9% reported a WTP $0-$500, $501-$1000, $1001-$5000, $5001-$25,000, and >$25,000, respectively, to cure themselves of PCOS. As a comparison, the WTP to avoid breast cancer ranged from $11,757 - $23,033 (Franic et al. J Clin Epidemiol 2005;58:291-303). Reported WTP amounts did not correlate with income level.

CONCLUSIONS: In conclusion, the study demonstrates that one-quarter of individuals with PCOS are willing to pay substantial amounts ($5001 to $25,000) relative to their incomes for a potential cure, with ~7% of participants willing to pay even higher amounts (>$25,000). These findings highlight the considerable value placed on improving the health status of those with PCOS and can be used to estimate the mean WTP per quality-adjusted- life-year (QALY).

SUPPORT: Supported, in part, by PCOS Challenge: The National Polycystic Ovary Syndrome Association and the Foundation for Research and Education Excellence.

Abstract ID #173

Abstract Title: WEIGHT MANAGEMENT IN PCOS: PROMISING OUTCOMES FROM DIGITAL THERAPEUTICS LIFESTYLE MANAGEMENT PROGRAM

Lathia T (1), Selvan C (2), Nair V (3), Munje A (4), Joshi S (5), Tanna S (6), Kalra S (7), Tiwaskar M (8), Samudra K (9), Singal A (1

(1) Apollo Hospital, Navi Mumbai, India;

(2) M S Ramaiah Memorial Hospital, Bangalore, India;

(3) Fitterfly Health Tech Pvt Ltd, Navi Mumbai, India;

(4) Fitterfly Health Tech Pvt Ltd, Navi Mumbai, India;

(5) Fitterfly Health Tech Pvt Ltd, Navi Mumbai, India;

(6) Jupiter Hospital, Thane West, Thane, India;

(7) Bharti Research Institute of Diabetes & Endocrinology, Haryana, India,;

(8) Shilpa Medical Research Center, Mumbai India;

(9) Diabetes Care Clinic, Navi Mumbai, India;

(10) Fitterfly Health Tech Pvt Ltd, Navi Mumbai, India;

Abstract: OBJECTIVE: PCOS independently raises cardiovascular disease (CVD) risk, while high BMI and obesity prevalence (80%) in Indian women with PCOS also elevate risks of diabetes, hypertension, and CVD. Approximately 57% of Indian females with PCOS reported difficulty in losing weight due to a lack of dietary knowledge and behavior advice. Implementing lifestyle interventions, that include dietary changes based on personal inputs and motivating individuals to perform adequate exercise, holds promise in mitigating insulin resistance contributing to PCOS. The study aimed to assess the weight change in Indian females with medically diagnosed PCOS via a digital weight loss program.

METHODS: The study analyzed de-identified data from 99 females (mean age-32 years ± 8.1) diagnosed with PCOS, who participated in Fitterfly's weight loss program. The program provided access to wellness application, remote coaching, and multidisciplinary expert care involving nutritionists, physiotherapists, and psychologists for 90 days. Personalized diet plans were given based on their inputs covering all the daily requirements for macro and micronutrients. Digital logging of meals and physical activity and access to in-house nutrition databases consisting of dietary information for each meal item logged were provided. Psychologists used principles of intensive behavioral therapy (IBT) to coach subjects to adhere to lifestyle interventions. The data were collected at the beginning and end of the program. Data are presented as mean (lower & upper 95% CI), with paired data being analyzed using Wilcoxon signed rank test.

RESULTS: The weight loss program helped reduce weight/BMI, waist, and hip circumference in 89.9%, and 76.7% of participants respectively. A reduction in weight by -3.3 (-3.8, -2.8) kg and BMI by -1.2 (-1.5, -1.0) kg/m2 (p-<0.0001, for both) was evident from a baseline of 80.9(77.9,83.9) kg and 31.77(30.7,32.9) kg/m2 respectively. Waist and hip circumferences were reduced by -4.7(-6.4, -2.9) cm and -3.5(-5.3, -1.6) cm (p-<0.0001, for both) from a baseline of 100.3(97.5,103.2) cm and 111.6(108.7,114.4) cm respectively.

CONCLUSION: The digital weight loss program offered by Fitterfly resulted in significant weight reduction, as well as reductions in waist and hip circumferences in females with PCOS. These positive outcomes highlight the potential of lifestyle management to help reduce weight in females with PCOS.

Abstract ID #174

Abstract Title: MEN AND WOMEN HAVE DIFFERENT OPINIONS ABOUT PCOS: A BIG-DATA INFODEMIOLOGY STUDY ANALYSING 85,872 YOUTUBE® COMMENTS OVER 12 YEARS.

Arshad A (1), Ali A (1), Broughton SE (1), Khan S (2), Malhotra K (3,4), Kempegowda P (2,4)

(1) Birmingham Medical School, University of Birmingham, Birmingham, UK;

(2) Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK;

(3) Department of Medicine, Dayanand Medical College, Ludhiana, Punjab, India;

(4) Institute of Applied Health Research, University of Birmingham, Birmingham, UK;

Abstract: OBJECTIVE: Polycystic ovary syndrome (PCOS) is the most common endocrinopathy in women. While attempts have been made to understand the themes and sentiments of the public regarding PCOS at the local and regional level, there are no studies exploring the global views mainly due to financial and logistical limitations. Several researchers have explored the views on social media as a surrogate for global views. We analysed the comments of all videos related to PCOS published on YouTube® from May 2011 to April 2023 and identified the trends over time of these comments, their context, associated themes, gender-based differences, and underlying sentiments as a surrogate to understand the public's perceptions.

METHODS: After extracting all the comments using the YouTube® application programming interface, we contextually studied the keywords and analysed for gender differences employing the Benjamini-Hochberg procedure. We applied a multidimensional approach to analysing the content via association mining using Mozdeh®. We performed network analysis to study associated themes using the Fruchterman-Reingold algorithm and then manually screened the comments for content analysis. The sentiments associated with YouTube® comments were analysed using Sentistrength®.

RESULTS: Of the 85,872 comments extracted, we identified specific gender for 13,106 comments (88.5% female). Keywords including diagnosing PCOS, symptoms of PCOS, pills for PCOS (medication), and pregnancy were significantly associated with female users. Keywords such as herbal treatment, natural treatment, curing PCOS, and online searches were significantly associated with male users. The key themes associated with female users were symptoms of PCOS, positive personal experiences (such as helpful and love), negative personal experiences (such as fatigue and pain), motherhood (such as infertility and trying to conceive), self-diagnosis and usage of professional terminology detailing their journey. The key themes associated with male users were misinformation regarding the "cure" for PCOS, using natural and herbal remedies to cure PCOS, fake testimonies from spammers selling their courses and consultations, finding treatment for PCOS, and sharing perspectives of female members. The overall average positive sentiment was 1.6651 (CI: 1.6593, 1.6709) and the average negative sentiment was 1.4742 (CI: 1.4683, 1.4802) with a net positive difference of 0.1909.

CONCLUSIONS: There is a disparity in views on PCOS between women and men with the latter associated with non-evidence-based approaches and misinformation. The improving sentiment noticed in YouTube® comments may reflect better healthcare services. Prioritising and promoting evidence-based care, and formulation of pragmatic online coverage spread is warranted to continue improving public sentiment trends and limit misinformation.

(Funding: None)

Abstract ID #175

Abstract Title: THE INFLUENCE OF BODY IMAGE ON HEALTH AND WELLBEING IN WOMEN AND INDIVIDUALS WITH POLYCYSTIC OVARY SYNDROME (PCOS): A MIXED METHODS STUDY.

Broughton SE (1), Ali A (1), Arshad A (1), Blendis E (1), Khan S (1), Kempegowda P (2,3)

(1) Medical School, University of Birmingham, Birmingham, UK

(2) Institute of Applied Health Research, University of Birmingham, Birmingham, UK

(3) Queen Elizabeth Hospital Birmingham, University Hospitals Birmingham NHS Foundation Trust, UK

Abstract: OBJECTIVE: Emerging evidence suggests Polycystic Ovary Syndrome (PCOS) negatively impacts body image. We investigated the influence of body image on quality of life, depression, anxiety, acne and hirsutism in individuals with PCOS.

METHODS: This UK-based mixed-methods online questionnaire- and interview-based study on adults with PCOS assessed body image via the body image concern inventory (BICI), Multidimensional Body-Self Relations Questionnaire Appearance Subscale (MBSRQ-AS), Body Esteem Scale for Adolescents and Adults (BESAA) and Beliefs About Obese Persons Scale (BAOP). Outcome measures of emotional wellbeing, acne and hirsutism were administered via the PCOS Quality of Life scale (PCOSQ), Hospital Anxiety and Depression Scale (HADS), SCOFF tool for eating disorder screening, and modified Ferriman-Gallwey (mFG) questionnaire. Sociodemographic information including deprivation as calculated by Townsend deprivation index was collected. Statistical analysis was performed with SPSS 28.0.

RESULTS: 25 participants completed the survey in July 2023, 18 of white ethnicity, 6 of Asian ethnicity and 1 of other ethnic group. One participant did not have PCOS and one participant chose not to answer body image questions. Body image scores for appearance evaluation, appearance orientation and body areas satisfaction subscales of MBSRQ-AS were lower than sex-matched norms ($n=23$)($p<0.001$). In multiple linear regression models accounting for age, ethnicity and deprivation, the weight subscale of PCOSQ was significantly associated with appearance evaluation, body areas satisfaction, overweight preoccupation and self-classified weight subscales of MBSRQ-AS ($p<0.01$). Both HADS depression and HADS anxiety scores were significantly associated with MBSRQ-AS appearance evaluation, body areas satisfaction and overweight preoccupation ($n=21$)($p<0.05$). Of the 22 participants who completed the SCOFF questionnaire, 50% scored positive for potential presence of eating disorders. Of the 18 participants with acne and/or hirsutism, there were no associations with MBSRQ-AS.

CONCLUSIONS: Adults with PCOS have increased body image distress which is associated with higher levels of depression and anxiety, and increased weight concerns. Screening and management of body image distress in PCOS should be considered and may improve levels of depression and anxiety as well as factors of quality of life.

(Funding: Miss SE Broughton was awarded the Sir Arthur Thomson Trust Vacation Studentship by University of Birmingham to conduct this research.)

Abstract ID #176

Abstract Title: INCREASING TRENDS IN ONLINE INFORMATION-SEEKING FOR POLYCYSTIC OVARY SYNDROME AND DECREASING TRENDS FOR FUNDING ITS RESEARCH: DATA FROM 1980 TO 2022

Malhotra K (1,2), Kempegowda P (2,3)

Department of Medicine, Dayanand Medical College, Ludhiana, Punjab, India

Institute of Applied Health Research, University of Birmingham, Birmingham, UK

Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK

Abstract: OBJECTIVE: The internet has become the primary source for health-related information, and online health information-seeking behaviour has been used as a reliable surrogate of public awareness. However, there is a paucity of research to understand the trends of PCOS information-seeking behaviour and funding provided for PCOS articles. We studied the trends of search interest in PCOS over time and whether funding for PCOS research corresponded with the changes in search interest. We also studied the geographic reach of PCOS interest and whether PCOS awareness month (September) is an effective strategy to increase PCOS interest.

METHODS: We performed joinpoint regression on relative search volume (RSV) data for PCOS using Google Trends from 2004 to 2022 comparing weekly, monthly and yearly trends. RSV indicates the popularity of a keyword and is calculated by dividing the sampled search data points by the total number of searches done in the specific region and time, after which the resulting value is scaled from 0 to 100. A minimum of zero and a maximum of three joinpoints were set for the model to capture an increase in RSV during the public health campaign, a decline in RSV afterwards, and a return to the pre-campaign RSV level after the campaign. We did a Mann-Whitney U test analysis comparing the mean RSV during the PCOS awareness month versus the rest of the weeks on a yearly basis. We retrieved the PCOS-related articles from 1980-2022 to study trends in funded and unfunded literature.

RESULTS: Three joinpoints were seen at months 70, 196, and 199 months which were statistically significant when compared to the null hypothesis of zero joinpoint ($p=.0002$) one joinpoint ($p=.0002$), and two joinpoints ($p=.0395$) respectively. The highest slope of increase in search interest was seen during 196-199 months with a monthly per cent change (MPC) of 4.2 (95% CI: -16.8, 30.5; $P=0.720$) followed by increasing interest from 199-228 months with MPC of 0.6 (95% CI: 0.3, 0.9; $P<0.001$). The search interest of "Polycystic ovary syndrome" was seen in 195 regions globally. The mean RSV in September, corresponding to PCOS awareness month, was higher compared to other months in all years from 2013 to 2022. Of the 41,292 journal articles analysed, there was a positive trend in funded PCOS research from the 2000s until the onset of the COVID-19 pandemic.

Conclusions: An increasing PCOS search interest is probably driven by major legislative and scientific events suggesting the importance of such events. PCOS awareness month appears to be an effective international awareness initiative to increase online PCOS information-seeking behaviour. The declining trend in funding is a concern as it mismatches with the continued increase in online information-seeking behaviour globally.

(Funding: None)

Abstract ID #177

Abstract Title: A comprehensive transethnic metabolomic analysis in women with PCOS in the Born in Bradford (BiB) study.

Harshal Deshmukh Thozhukat Sathyapalan

University of Hull, UK. Hull University teaching hospitals NHS trust UK

Abstract: Introduction: Polycystic ovary syndrome (PCOS) is the most prevalent endocrine and metabolic disorder of women of reproductive age. Comprehensive metabolic profiling of women with PCOS across different ethnicities will help in understanding the pathophysiology of this condition.

Methods: The Born in Bradford (BiB) study is a UK longitudinal birth cohort. Profiling of circulating lipids, fatty acids, and metabolites was done by a high-throughput targeted NMR platform (Nightingale Health© (Helsinki, Finland) providing quantitative information on 227 metabolic traits. We obtained the PCOS case-control status using the ctv3 codes available as part of the dataset. We used the Mann-Whitney U-test to compare the metabolomics in the PCOS and control population.

Results: The study consisted of 10608 women in the Born in Bradford study with a median age of 28 (25-31) years. The predominant ethnic groups included 3979 participants (37%) with English, Welsh, Scottish, Northern Irish, or British ethnicity, 4250 Pakistani (40%), 405 Indian (3%), and 133 African ethnicities (1%). The study consisted of 276 women with PCOS and 10332 control. The metabolomics analysis showed that several metabolites in the pathways inflammation (Glycoprotein acetyls $P<0.0001$), Glycolysis related metabolites (Glycerol and Citrate $P<0.0001$), amino acids (Phenylalanine, Leucine, Isoleucine, $P=0.0003$), and Lipid pathways (Triglycerides in medium VLDL and Cholesterol esters in medium VLDL $P=0.0003$) were differentially expressed in cases with PCOS as compared to controls. Analysis restricted to women with south-Asian and white populations showed similar results.

Conclusion

The study identified differential expression of metabolites involved in inflammation, glycolysis, amino acid metabolism, and lipid pathways in women with PCOS with a similar association in the South Asian and white populations. These findings contribute to our understanding of PCOS pathophysiology and highlight potential targets for further investigation and therapeutic interventions.

Abstract ID #178

Abstract Title: CONTINUOUS VERSUS CYCLICAL ORAL CONTRACEPTIVE PILL USE IN POLYCYSTIC OVARY SYNDROME (PCOS)- A PILOT RANDOMIZED CONTROL TRIAL

Christ JP (1), Morris J (1), Mody A (2), Corley J (1), Shinkai (3), Cedars MI (1), Huddleston HG (1)

1) Department of Obstetrics and Gynecology, University of California San Francisco, San Francisco, CA USA

2) Department of Pediatrics, University of California Davis, Sacramento, CA USA

3) Department of Dermatology, University of California San Francisco, San Francisco, CA USA

Abstract: BACKGROUND: Combined oral contraception pills (OCPs) are the recommended first line treatment for patients with PCOS. Historically, OCPs were prescribed cyclically with 21 days of active hormonal pills and 7 days of inactive pills, however continuous schedules, skipping the hormone free interval, have become increasingly accepted primarily for patient convenience. Whether continuous schedules lead to improved treatment outcomes in PCOS is not known. We hypothesized a continuous schedule of OCPs would lead to greater hormonal suppression compared to cyclical.

METHODS: A single center, randomized, open-label clinical trial comparing two schedules for an OCP (3mg drospirenone/30 mcg ethinyl estradiol) was completed. Participants were randomized in a 1:1 fashion to daily OCP use (continuous group) vs cyclical use (21 days of active hormone and 7 days of inactive pills; cyclical group). Inclusion criteria were age 15-40 years, PCOS diagnosis using AEPCOS criteria (biochemical or clinical hyperandrogenism and oligo-amenorrhea and/or polycystic ovarian morphology), and >2 years from menarche. Exclusion criteria included current use of hormonal contraception or spironolactone or contraindications to OCPs. Primary outcomes were change in serum androgen levels and secondary outcomes were change in metabolic measures. Mean change between baseline and follow up time points (1, 3 and 6-months) were compared between groups using Student's T-tests and Mann–Whitney U tests.

RESULTS: 51 participants were randomized, with 26 assigned to continuous and 25 to cyclical. At baseline, there were no differences in any measure including age between continuous and cyclical groups (Mean (S.D.), 26 (4) vs 25 (8) years). Compared to cyclical use, the continuous group had a greater decline in androstenedione (-1.7 (0.7) vs -0.6 (1.5) ng/mL) and follicle stimulating hormone (FSH) (-3.4 (2.2) vs 0.6 (2.5) IU/mL) at 1-month, dehydroepiandrosterone sulfate (-88.1 (65.7) vs-37.9 (69) ug/mL) and FSH (-3.5 (2.0) vs 0.3 (3.1) IU/mL) at 3-months, and FSH (-3.7 (2.4) vs -0.03 (2.35) IU/mL) at 6-months, p<0.05 for all. Change in total testosterone did not differ between groups at any time point. For metabolic measures, the continuous group exhibited a greater decrease in LDL and total cholesterol at 3 months and in fasting glucose and LDL at 6 months compared to the cyclical group, p<0.05.

CONCLUSIONS: OCP's are considered a first line treatment for PCOS, however the relative benefits of continuous versus cyclical schedules have not previously been established. In this study we demonstrated that continuous OCPs result in a greater reduction in androgens and gonadotropins and more favorable changes in cholesterol and fasting glucose. These results indicate continuous OCP schedules may provide optimal endocrine and metabolic benefits in women with PCOS.

Abstract ID #179

Abstract Title: OBSTRUCTIVE SLEEP APNEA (OSA) RISK MAY MEDIATE NEUROPSYCHOLOGIC DEFICITS SEEN AMONG SOME PATIENTS WITH POLYCYSTIC OVARY SYNDROME (PCOS).

Christ JC (1), Pasch L (1), Rasgon N (2), Huddleston HG (1)

1) Department of Obstetrics and Gynecology, University of California San Francisco, San Francisco, CA USA

2) Maternal & Child Health Research Institute, Stanford University, Palo Alto, CA UA

Abstract: OBJECTIVE: Altered cognitive abilities have been noted among patients with PCOS, but the cause of these changes is unknown. Given increased risk of OSA among PCOS patients and a link between OSA and cognitive deficits we sought to investigate the relevance of OSA risk on cognitive functioning among patients with PCOS.

METHODS: A secondary analysis of a single center prospective cohort study was completed. Inclusion criteria included age 18-44 years, Rotterdam criteria for PCOS, and fluency in English. Exclusion criteria included history of insulin-dependent diabetes, untreated hypothyroidism, and neuropsychologic disorders that may affect psychometric test results. Those that completed the Berlin Questionnaire (BQ) for sleep apnea risk were eligible for secondary analysis. Participants underwent standardized anthropometric, ultrasound, endocrine, and metabolic phenotyping. Cognitive function was assessed using the Wechsler Adult Intelligence Scale (WAIS) IV indexes for processing speed (Symbol Search and Coding Subtests), vocabulary (Vocabulary Subtest), perceptual reasoning (Matrix Reasoning Subtest), working memory (Digit Span Subtest), as well as the California Verbal Learning Test (CVLT) for memory, Wechsler Memory Scale Symbol Span Test for working memory, and Delis-Kaplan Executive Function System for cognitive control and generativity. Sample-based z-scores were calculated for cognitive outcomes and compared between those with and without a high risk BQ using Student's T-test or Mann–Whitney U test. Associations between OSA risk and cognitive outcomes controlling for age and education were assessed using multivariable linear regression analyses.

RESULTS: In total, 46 participants were included, of which 21 (44%) had a high risk BQ. Those with a high risk BQ had higher body mass index (mean (S.D.)) (38.1 (10.4) vs 26.8 (5.2) kg/m2, p<0.001) and age (33 (6) vs 29 (5) years, p=0.032). Years of education (16 (2) vs 17 (2) years), percentage non-white (8 (47%) vs 9 (53%)), and percentage making > $75,000 a year (9 (41%) vs 13 (59%)) were not significantly different between those with and without a high risk BQ, respectively. Those with a high risk BQ had lower WAIS symbol search subtest z-scores (-0.3 (1.0) vs 0.3 (0.8), p=0.028) and WAIS coding subtest z-scores (-0.39 1.0) vs 0.4 (0.7), p=0.005). All other cognitive function assessments did not differ between groups. In multivariable modeling OSA risk predicted WAIS coding subtest z-scores (B=-0.6, S.E.=0.2, p=0.025).

CONCLUSIONS: Patients with PCOS at high risk for OSA showed decreased cognitive performance, particularly in processing speed, compared to those without increased OSA risk. OSA may mediate neuropsychologic deficits seen among some patients with PCOS, especially with regards to processing speed, and may represent an under recognized treatment avenue with broad health benefits including for cognition.

Abstract ID #180

Abstract Title: PREVALENCE OF INSULIN RESISTANCE, PREDIABETES AND TYPE 2 DIABETES AMONG OVERWEIGHT AND OBESE INFERTILE WOMEN WITH AND WITHOUT POLYCYSTIC OVARY SYNDROME.

Reyes-Muñoz E (1), Mancebo-Salazar ET (1), Elizarraraz-Cendejas JL (2), Valdes-Zuñiga CLT (3), Aguayo-González P (4), Morales-Hernández FV (5).

(1) Department of Gynecological and Perinatal Endocrinology, Instituto Nacional de Perinatologia Isidro Espinosa de los Reyes, Mexico City, Mexico.

(2) Direction of Assisted Reproduction Center, CERH Clinic. Irapuato, Mexico.

(3) Department of Obstetrics and Gynecology, Hospital General Universitario Joaquin del Valle Sánchez, Universidad Autonoma de Coahuila, Coahuila, Mexico.

(4) Department of Human Reproduccion, Instituto Nacional de Perinatologia Isidro Espinosa de los Reyes, Mexico City, Mexico.

Abstract: OBJECTIVE: Overweight and obesity affect almost 80% of women with polycystic ovary syndrome (PCOS). This study aimed to compare the prevalence of insulin resistance (IR), prediabetes, and type 2 diabetes mellitus (T2DM) among infertile Mexican women with and without PCOS according to body mass index (BMI).

METHODS: A cross-sectional study. Two groups were integrated: Group 1, women with PCOS, and Group 2, women without PCOS. Each group was subdivided according to BMI into normal weight, overweight, or obesity. Women who attended the infertility clinic in Mexico City between 2017 and 2020 were included. Women with incomplete clinical records, insulin sensitizers, or contraceptive intake three months before admission to the infertility clinic, pregnant women, a history of clinical hypothyroidism, or type 1 or 2 diabetes were excluded. The prevalence of IR, prediabetes, T2DM, and clinical-biochemical characteristics were compared between the two groups according to BMI.

RESULTS: 1061 women were analyzed; group 1 PCOS women (n=449); normal-weight n=62, overweight n=205, obesity n=182 and group 2 non-PCOS women (n=612)); normal weight n=210, overweight n=253, obesity n=117 were analyzed. There was a significantly higher prevalence of IR, and prediabetes, in group 1 vs. group 2, 73.1 vs. 50.2% and 21.6 vs. 13.1% (p= 0.0001). The prevalence of IR in PCOS vs. non-PCOS women grouped by normal weight, overweight, and obesity were 41.9% vs. 25.7% (p=0.01), 72.2% vs. 53.8% (p=0.0001) and 84.6% vs. 79.1% (p=0.19), respectively. Prevalence of prediabetes in women with PCOS vs. non-PCOS women grouped by normal weight, overweight, and obesity were 4.8% vs. 9.5% (p= 0.24), 18 vs. 13.8% (p=0.21) and 31.3% vs. 16.9% (p=0.003), respectively. The prevalence of T2DM in PCOS vs. non-PCOS women grouped by normal weight, overweight, and obesity were 3.2% vs. 1% (p= 0.19), 2% vs. 2% (p=0.99) and 7.1% vs. 5.4% (p=0.52), respectively.

CONCLUSIONS: IR and prediabetes were significantly higher in women with PCOS than those with non-PCOS. There was a significant increase in the prevalence of IR in normal-weight and overweight with PCOS vs. non-PCOS women; however, there were no significant differences in IR between obese women with and without PCOS. Prediabetes was significantly higher in obese PCOS than in non-PCOS women.

Abstract ID #181

Abstract Title: GUT MICROBIOME AND METABOLITES ARE ALTERED AND ASSOCIATED WITH DIET IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

Silva TR (1,2), Marchesan LB (1,2), Rampelotto PH (3,4), Longo L (4,5), Oliveira TF (6), Landberg R (7), Mello V (8) and Spritzer PM (1,2,9)

(1) Postgraduate Program in Endocrinology and Metabolism, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, Brazil;

(2) Gynecological Endocrinology Unit, Division of Endocrinology, Hospital de Clínicas de Porto Alegre (HCPA), Porto Alegre, Brazil;

(3) Postgraduate Program in Genetics and Molecular Biology, Universidade Federal do Rio Grande do Sul, Porto Alegre, Rio Grande do Sul, Brazil;

(4) Experimental Laboratory of Hepatology and Gastroenterology, Center for Experimental Research, Hospital de Clínicas de Porto Alegre, Porto Alegre, Rio Grande do Sul, Brazil;

(5) Postgraduate Program in Gastroenterology and Hepatology, Universidade Federal do Rio Grande do Sul, Porto Alegre, Rio Grande do Sul, Brazil;

(6) Department of Diagnostic Methods, Universidade Federal de Ciências Médicas de Porto Alegre (UFCSPA), Porto Alegre, Brazil;

(7) Department of Life Sciences, Division of Food and Nutrition Science, Chalmers University of Technology, 412 96 Gothenburg, Sweden;

(8) Department of Clinical Nutrition, Institute of Public Health and Clinical Nutrition, University of Eastern Finland, Kuopio, Finland;

(9) Department of Physiology, Laboratory of Molecular Endocrinology, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, Brazil.

Abstract: Objective: To investigate associations between gut microbiome, metabolites (short-chain fatty acids, SCFA and indole-3-propionic acid, IPA) generated by gut, and diet in women with PCOS and compare these findings with those observed in age-matched healthy control women.

Methods: 24 women with PCOS (BMI 31.1±4.2 kg/m2) and 14 controls (BMI 26.7±4.6kg/m2) were evaluated. Main outcome measures were as follows, gut microbiome, analyzed by sequencing the V4 region of the 16S rRNA gene; IPA concentration in fasting serum samples, measured by liquid chromatography/triple-quadrupole mass spectrometry (LC-QqQ-MS); and fecal and plasma SCFA concentration, measured by LC-MS/MS.

Results: Alpha diversity was significantly lower in women with PCOS, and beta diversity analysis showed a clustering differentiation between the PCOS and control groups. PCOS was associated with altered gut microbiome composition, specifically in two operational taxonomic units (OTUs), Otu0003 (Agathobacter) and Otu0051 (Lachnoclostridium). Lower IPA, higher fecal propionic acid, and higher plasma acetic, propionic, and formic acid concentrations were significantly associated with PCOS diagnosis, independently of BMI. Propionic acid in feces and dietary glycemic load (GL) intake were significantly associated with microbiome variation in PCOS participants.

Conclusion: Gut microbial diversity and composition, as well as IPA and SCFA concentrations, differed between women with PCOS and healthy controls. Fecal propionic acid and dietary GL intake are associated with the overall gut microbial composition in women with PCOS and need to be considered in future studies.

Abstract ID #182

Abstract Title: THE PHENOTYPE AND EPIDEMIOLOGY OF POLYCYSTIC OVARY SYNDROME IN COLOMBIA (COLOMBIA-PEP) STUDY: PRELIMINARY RESULTS.

Giraldo JL (1), Osorio WE (1), Posada MN (1), Salazar S (1), Duitama JP (2), Abad V (3), Bedoya D (4), Tamayo S (1), Cano JF (1), Azziz R (5-7)

(1) Instituto Antioqueño de Reproducción – Inser, Medellin, Colombia; (2) Dept. of Obstetrics & Gynecology, Clínica El Rosario, Medellin, Colombia; (3) ABAD Laboratorios, Medellin, Colombia; (4) Colmédicos IPS S.A.S, Medellín, Colombia; (5) Dept. of Health Policy, Management, and Behavior, School of Public Health, University at Albany, SUNY, Rensselaer, NY, USA; (7) Depts. of Obstetrics & Gynecology and Medicine, Heersink School of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA; (7) Dept. of Healthcare Organization & Policy, School of Public Health, University of Alabama at Birmingham, Birmingham, AL, USA

Abstract: BACKGROUND: PCOS is a common life-long endocrinopathy, clinically evident in 8-15% of women of reproductive age. There is a paucity of high-quality epidemiologic studies in many parts of the world, including Latin America.

OBJECTIVE: To determine the prevalence of PCOS among reproductive age women in a medically unselected population in Colombia.

MATERIALS AND METHODS: Participants were women (18-45 yrs.) from Medellín, Colombia and surrounding metro area, scheduled for a routine pre-employment exam. Participants provided a blood sample and a history and physical exam (H&P), including a transvaginal ultrasound (TV-U/S). The modified Ferriman-Gallwey (mF-G) score was used to indicate clinical hyperandrogenism (CH), and the specific cut-off score was determined by cluster analysis of the entire population studied. Menstrual dysfunction (MD) was defined as menstrual cycle lengths >35 or <21 days, or < 8 cycles per year. Polycystic ovarian morphology (PCOM) was defined as antral follicle count of ≥20 and/or ovarian vol. ≥ 10 cm3 in at least one ovary. 'Possible PCOS' was established when CH, MD, or PCOM were present. All 'possible PCOS' subjects were assayed for TSH, prolactin (PRL), and 17-hydroxyprogesterone (17-HP) and scheduled for a 2-hr. oral glucose tolerance test and androgen measures. PCOS was defined according to the 2018 international evidence-based guidelines.

RESULTS: Of 626 participants recruited, 594 (95%) completed their H&P and were included (589 also had a TV-U/S). Their mean (SD) age was 29.1 (6.6) yrs., body mass index (BMI) was 25.06 (1.94) kg/m2, waist circumference was 80.5 (2.8) cm, and waist-to-hip-ratio (WHR) was 0.82 (0.10). K2-cluster analysis indicated that a mFG score ≥5 indicated CH. Overall, 51 (8.6%) had CH, 135 (22.7%) had MD, and 164 (27.8%) had PCOM. Of 210 subjects (35.4%) with 'Possible PCOS'), 41 had either high PRL (>25 ng/ml), TSH (>4.7 ng/ml), and/or 17-HP (>2 ng/ml) levels. Pending hormonal reevaluation and androgen measures, 130 patients (21.9%) had PCOS: 20 (15.4%) had CH+MD+PCOM, consistent with PCOS Phenotype A; 26 (20.0%) had CH+MD or Phenotype B; 27 (20.8%) had CH+PCOM or Phenotype C; and 57 (43.8%) had MD+PCOM or Phenotype D.

CONCLUSIONS: These data suggest that at a minimum, the prevalence of PCOS in an unselected population of reproductive-age women from Colombia is 21.9%. Phenotype D appeared to be the most common (~40%) followed by Phenotypes B and C (~20% each), then A. Further analyses are ongoing.

Abstract ID #183

Abstract Title: ADOLESCENTS' VIEWS ON CHANGING THE NAME OF POLYCYSTIC OVARY SYNDROME

Luu Y (1), Teede H (2), Gibson M (2,3), Peña AS (1,4)

(1) Discipline of Paediatrics, Robinson Research Institute, University of Adelaide, Adelaide, South Australia, Australia;

(2) Monash Centre for Health Research and Implementation (MCHRI), School of Public Health and Preventive Medicine, Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Victoria, Australia;

(3) Te Tātai Hauora o Hine – National Centre for Women's Health Research Aotearoa, Faculty of Health, Victoria University of Wellington, New Zealand;

(4) Department of Endocrinology and Diabetes, Women's and Children's Hospital, North Adelaide, South Australia, Australia;

Abstract: OBJECTIVE: Women with polycystic ovary syndrome (PCOS) report that the name of the condition is confusing and it should be changed to reflect the broader clinical syndrome, however, no studies have investigated adolescents' views. This study aimed to investigate adolescents' perspectives of the name 'PCOS' and whether they believe it should be changed.

METHODS: This cross-sectional study included adolescent girls aged between 13-19 years who had been diagnosed with PCOS by a medical practitioner. Participants were recruited consecutively from paediatric outpatient hospital clinics in South Australia (n=34) and online PCOS support organisations in Australia and the United Kingdom (n=47). A validated questionnaire was used to investigate adolescents' views on the name 'PCOS' and the importance of the name to different stakeholders. Adolescents indicated on a 5-point Likert scale (strongly disagree to strongly agree) whether the name was confusing, should be kept, should be changed to reflect the broader clinical picture; and the value of increased education about PCOS.

RESULTS: Eighty-one adolescent girls with PCOS participated in the study (mean [SD] age 16.7 [1.8] years, menarche 12.2 [1.5] years, 57 Caucasian, 11 Asian, 7 Aboriginal, 5 Middle Eastern, 1 Hispanic). All but one completed all questions. The majority of adolescents were diagnosed with PCOS within 2 years of completing the questionnaire (n=61, 75%). Sixty-six (82%) adolescents agreed/strongly agreed that increased education about PCOS would be more effective than a name change, whilst 14 (18%) neither agreed/disagreed nor disagreed. There was a diverse opinion among adolescents on whether the name can be confusing (30 [37%] disagreed/strongly disagreed, 21 [27%] were neutral and 29 [36%] agreed/strongly agreed). Half of adolescents (n=41, 51%) agreed/strongly agreed that the name should stay the same, whilst 26 (33%) neither disagreed nor agreed and 13 (16%) disagreed/strongly disagreed. The most common preference by adolescents was neutral that the name 'PCOS' should be changed to reflect the range of symptoms (n=33, 41%), yet almost half felt that increased education about PCOS and a name change are both needed (n=37, 46%). Over half of adolescent girls with PCOS (n=50, 62%) felt the name is important for women and adolescents with PCOS, and is less important for family and friends of those affected with PCOS, medical doctors, health professionals, researchers, support awareness and advocacy organisations; and the general community.

CONCLUSIONS: The majority of adolescent girls with PCOS placed a higher value on increased education about PCOS than a name change, but recognise that the name of the condition is more important to people with PCOS than other stakeholders.

Funding: National Health and Medical Research Council Centre of Research Excellence Project Support Grant, MS McLeod Departmental Research Grant

Abstract ID #184

Abstract Title: SUSTAINABILITY OF EXERCISE TRAINING FOLLOWING A STRUCTURED EXERCISE INTERVENTION IN POLYCYSTIC OVARY SYNDROME

Benham JL (1), Booth JE (2), Friedenreich CM (3), Rabi DM (4), Sigal RJ (5)

(1) Departments of Medicine and Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada;

(2) Department of Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada;

(3) Departments of Community Health Sciences and Oncology, and Faculty of Kinesiology, Cumming School of Medicine University of Calgary and Department of Cancer Epidemiology and Prevention Research, CancerControl Alberta, Alberta Health Services, Calgary, AB, Canada;

(4) Departments of Medicine, Community Health Sciences and Cardiac Sciences, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

(5) Departments of Medicine, Community Health Sciences and Cardiac Sciences, and Faculty of Kinesiology, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

Abstract: OBJECTIVE: Lifestyle management including regular exercise is the cornerstone of polycystic ovary syndrome (PCOS) treatment, but little is known about the acceptability and sustainability of exercise interventions. Our aims were: 1) to determine if participation in a structured exercise intervention resulted in sustained increases in exercise training levels after three months, and 2) to identify factors that motivate and prevent participation in physical activity.

METHODS: This is a secondary analysis of a six-month randomized controlled trial in women aged 18-40 years with PCOS evaluating the reproductive and cardiometabolic effects of supervised high-intensity interval training (HIIT) and continuous aerobic exercise training (CAET) compared with no-exercise control. Participants completed prescribed exercise training three times weekly. Three months after trial completion, participants were invited to complete a survey assessing their exercise habits, confidence in exercising and factors affecting participation in exercise training. Means and proportions were calculated. Groups were compared using ANOVA.

RESULTS: Of 40 participants who completed the trial, 33 completed the survey at three months (control n=13, HIIT n=10, CAET n=10). Three months after the intervention, mean exercise sessions per week were 1.8 (95%CI 1.3-2.4), 2.3 (95%CI 1.7-2.9), and 1.8 (95%CI 1.3-2.4) for no-exercise control, HIIT, and CAET, respectively with no statistically significant differences between groups. For those who completed exercise training (n=20), 5/20 (25%) maintained their exercise levels while 12/20 (60%) reported a decrease and 3/20 (15%) reported an increase in exercise. The most common types of exercise training were brisk walking (19/33, 58%) and cycling (13/33, 39%). Seven of 10 (70%) participants randomized to CAET, and 5/10 (50%) participants randomized to HIIT continued with the form of training they did during the trial. Following participation in the trial, 11/33 (33%) participants reported an increase in motivation to exercise, 13/33 (39%) reported unchanged motivation, and 8/33 (24%) reported a decrease. The top reasons reported for participating in exercise were health benefits (25/33, 76%), weight control (24/33, 73%), and appearance (20/33, 60%). The main reported barriers to exercise were lack of time (25/33, 76%) and lack of motivation (20/33, 61%). Among control participants, inexperience was a barrier to exercise for 4/13 (31%).

CONCLUSIONS: Participation in a structured supervised exercise intervention consistent with clinical practice guidelines for PCOS did not result in sustained levels of exercise training post-intervention. Further research is needed to evaluate and address barriers to exercise training to facilitate acceptability and sustainability of exercise training and physical activity among individuals with PCOS. (CSM/AHS Clinical Research Fund)

Abstract ID #186

Abstract Title: THE PHENOTYPE OF POLYCYSTIC OVARY SYNDROME (PCOS) IN A REFERRAL POPULATION IN NIGERIA

Makwe CC (1), Olamijulo JA (1), Akinkugbe AO (2), Samuel TA (3), Udenze IC (4), Balogun MR (5), Bril F (6), Buyalos RP (7), Laven J (8), Azziz R (6,9,10,11)

(1) Dept. of Ob/Gyn, College of Medicine, University of Lagos, Lagos, Nigeria;

(2) Dept. of Medicine, College of Medicine, University of Lagos, Lagos, Nigeria;

(3) Dept. of Biochemistry, College of Medicine, University of Lagos, Lagos, Nigeria;

(4) Dept. of Clinical Pathology, College of Medicine, University of Lagos, Lagos, Nigeria;

(5) Dept. of Community Health & Primary Care, College of Medicine, University of Lagos, Lagos, Nigeria;

(6) Dept. of Medicine, Heersink School of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA;

(7) Dept. of Ob/Gyn, David Geffen School of Medicine, UCLA, Los Angeles, CA, USA;

(8) Dept. Ob/Gyn, Erasmus University Medical Center, Rotterdam, Netherlands;

(9) Dept. of Health Policy, Management, and Behavior, School of Public Health, University at Albany, SUNY, Rensselaer, NY, USA;

(10) Dept. of Ob/Gyn, Heersink School of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA;

(11) Dept. Healthcare Organization & Policy, School of Public Health, University of Alabama at Birmingham, Birmingham, AL, USA

Abstract: OBJECTIVE: To determine the phenotypic presentation of PCOS in Nigerian women in a referral setting.

METHODS: We studied 82 consecutive reproductive-aged women (18-45 yrs.) presenting to Lagos University Teaching Hospital, Lagos, Nigeria with features suggestive of PCOS. A history and physical exam was obtained, including assessing for hirsutism using the modified Ferriman-Gallwey (mF-G) score. On days 2-7 of the menstrual cycle (natural or progestin-induced, or randomly for women who had a negative progesterone challenge test, all underwent a 75 gm, 2-hr. oral glucose tolerance test (OGTT) and pelvic ultrasound. Clinical hyperandrogenism (CH) was defined as an mF-G score of ≥6. Menstrual dysfunction (MD) was defined as menstrual cycle lengths >35 or <21 days, or < 8 cycles/yr. Polycystic ovarian morphology (PCOM) was defined as antral follicle count ≥20 and/or ovarian volume ≥10 cm3 in least one ovary. PCOS was defined according to the 2018 international evidence-based guidelines.

RESULTS: Mean (SD) age was 29.0 (2.1) yrs., body mass index (BMI) 26.5 (5.6) kg/m2, and mean waist-to-hip-ratio (WHR) 0.84 (0.06). Four (4.8%) participants were underweight, 32 (39.0%) had normal BMI, 28 (34.2%) were overweight, and 18 (22.0) were obese. Fasting and 2-hr. glucose were 85.4 (10.7) and 108.4 (21.7) mg/dL, respectively. One (1.2%) had diabetes, 2 (2.4%) had impaired glucose tolerance, 6 (7.3%) had impaired fasting glucose, and 73 (89.1%) were euglycemic. Overall, 36 (43.9%) had CH, 56 (68.3%) had MD, and 61 (74.4%) had PCOM. The mean (SD) of baseline total testosterone, SHBG, and FAI were 0.47 (0.36) ng/mL, 52.57 (54.67) nmol/L, and 10.65 (16.87) %nmol/L, respectively. Two (2.4%) participants with only MD had hyperprolactinaemia. Our preliminary results, pending further hormonal analysis, indicate that 27 (32.9%) women had no evidence of PCOS. Of 55 women with PCOS, 25 (45.5%) had HA+MD+PCOM, consistent with PCOS Phenotype A; 3 (5.5%) had HA+MD or Phenotype B; 5 (9.0%) had HA+PCOM or Phenotype C; and 22 (40.0%) had MD+PCOM or Phenotype D.

CONCLUSION: Our preliminary results indicate that in a referral (clinical) population in Nigeria, PCOS was detected in ~70% of women seen with possible PCOS. Of the 55 women with PCOS Phenotypes A and D were the most common (40-50% each). It appears that the phenotypic presentation of PCOS in the clinical setting in Sub-Sahara African mirrors global reports. Further studies are ongoing.

SUPPORT: Supported, in part, by the Foundation for Research and Education Excellence.

Abstract ID #187

Abstract Title: DEVELOPMENT AND THERAPEUTIC POTENTIAL OF LOW-MOLECULAR-WEIGHT AGONIST OF THE LUTEINIZING HORMONE RECEPTOR ORG43553 AS AN ANTI-OBESITY TARGET—SPECIFIC AGENT.

Lizneva D (1), Gumerova A (1), Ievleva K (1), Cheliadinova U (1), Barak O (1), Korkmaz F (1), Vasilyeva D (1), Gimenez Roig J (1), Frolinger T (1), Pevnev G (1), Sultana F (1), Kramskiy N (1), Wizman S (1), Orloff M (1), Pallapati AR (1), Ryu V (1), Rojekar S (1), Moldavski O (1), Yuen T (1), Zaidi M (1).

(1) Center for Translational Medicine and Pharmacology, Icahn School of Medicine at Mount Sinai, New York, NY, USA.

Abstract: OBJECTIVE: Epidemiologic data suggests a negative relationship between LH levels and BMI in healthy reproductive age and postmenopausal volunteers, as well as women with PCOS. Moreover, central adiposity in women is associated with loss of ovulatory function, including the amplitude and frequency of LH surge. We previously reported the presence of Lhcgr transcripts in white adipose tissue in C57BL/6mice.We have also demonstrated that LH agonists injected into animals fed a high fat diet can prevent diet induced obesity. Here we are for the first time we are testing therapeutic potential of Org 43553 for the prevention and treatment of obesity.

METHODS: Single cell RNA sequencing, molecular dynamics studies, IHC, ELISA, western blotting, 3D cell cultures, oxygen consumption rate (Seahorse Xf96), preventive and therapeutic treatment on high fat diet-induced obesity mouse models, energy expenditure measures, qNMR.

RESULTS: We demonstrated presence of LHCGR in human fat, with a higher expression in female adipose tissue (single cell RNA sequencing, IHC). We modeled the binding of ORG43553 with mouse and human LHCGR. Molecular dynamics studies show that ORG43553 binding to LHCGR induces a kink at P588 in transmembrane domain (TM)6, enhancing the interaction between I577 in TM6 and F630 in TM7. We developed a solution formulation for ORG by incorporating co-solubilizers and surfactants, which demonstrated optimal in vivo and in vitro results. We have shown that ORG43553 induces ERK phosphorylation and acts via ATF3 - a member of the cAMP response element binding family, which activates by cAMP. ORG43553 decrease differentiation, as evident by differentiation markers in monolayer and three-dimensional culture of 3T3-L1 adipocytes and increase oxygen consumption rate at baseline and upon oligomycin exposure, indicating mitochondria proton leak. Moreover, in vivo oxygen consumption and energy expenditure increased acutely in ORG43553–treated mice, with no change in locomotor activity. Injection or oral gavage of ORG43553 into C57BL/6 mice twice per week caused a significant reduction in fat mass (qNMR), with reduced WAT weight in fat depots in both preventive and therapeutic diet-induced obesity animal models. Serum testosterone remained unchanged confirming that the anti–adiposity effect of ORG43553 was independent of sex steroids. Moreover, we observed morphological changes toward smaller adipocyte size in gonadal adipose tissue of ORG43553–treated animals. Inguinal fat depots remained morphologically unchanged. Our findings led us to development the formulation for adipose tissue specific delivery of ORG43553 for human use, encapsulating ORG43553 within liposomes and employ fat-specific ligand that can bind to receptors present in human adipocytes.

CONCLUSIONS: ORG43553 has therapeutic potential for the prevention and treatment of menopausal and PCOS-related obesity.

Abstract ID #188

Abstract Title: MANAGEMENT OF PCOS – PATIENT AND CLINICIAN PERSPECTIVES ON QUALITY OF CLINICAL CARE IN THE UNITED KINGDOM.

Al Wattar BH (1,2) Bhattacharyya S (3), Talaulikar V (3,4), Clarke SA (3,4)

(1)Beginnings Assisted Conception Unit, Epsom and St Helier University Hospitals, London, United Kingdom:

(2)Comprehensive Clinical Trials Unit, Institute for Clinical Trials and Methodology, University College London, London, United Kingdom:

(3) Institute of Women's Health, University College London, London, UK:

(4)Reproductive Medicine Unit, University College London Hospital, London, UK:

Abstract: OBJECTIVE: Polycystic ovarian syndrome (PCOS) is the commonest endocrine condition affecting women of reproductive age, often adversely impacting their quality of life. Delayed diagnosis and poor patient experience are common themes reported by affected women. Several factors contribute to poor clinical care including the lack of specialised multi-disciplinary clinics and poor clinician familiarity with the varied health needs of affected women. We aimed to identify patient priorities, clinician perspectives, and barriers to effective clinical care by surveying both women with PCOS and relevant clinicians in the UK.

METHODS: We conducted two web-based, anonymous quantitative surveys, one aimed at women self-reporting a diagnosis of PCOS and one for clinicians in primary and secondary care settings involved in PCOS care provision. Surveys were disseminated via social media. We reported using natural frequencies and percentages and assessed data distribution using Chi-squared test and one-way ANOVA tests.

RESULTS: We received responses from 47 women with PCOS and 33 clinicians including GPs (n=6, 18.2%), Endocrinologists (n=11, 33.3%), and Gynaecologists (n=15, 45.5%). Most participating women (n=34, 75.6%) reported that conversations regarding psychosocial symptoms never took place despite 53.2% (n=25) self-reporting mental health concerns. When asked which symptoms participating women felt should be covered in greater detail during the consultation, mental health concerns were most frequently chosen (n=25, 54.3%), followed by fertility (n=23, 50%), and weight loss (n=19, 41%). Only 1 (3%) participating clinician agreed that mental health was always covered as part of the consultation. Patient and clinician perspectives on quality of care differed with only 8.5% (n=4) of participating women reporting satisfaction with care in contrast to 75.8% (n=25) of clinicians reporting that patients' priorities were always met in their care. Similarly, only 8.5% (n=4) of participating women felt that clinicians were well informed about PCOS, in contrast to 72.7% of (n=24) clinicians indicating that they were well familiarised with current diagnosis and management guidelines. Clinicians identified several barriers to providing optimal PCOS care including staff shortages (n=21, 65.6%), time constraints in the clinic (n=19, 59.4%), and lack of service availability (n=16, 50%).

CONCLUSION: There is a systematic under-provision and appreciation of the health needs of women with PCOS in the UK. Additionally, patient and clinician perspectives on quality of clinical care differ, highlighting the need for a collaborative approach to optimise care. More clinician education and awareness are needed to optimise PCOS care provision, especially to offer holistic psychosocial and mental health support for affected women.

Abstract ID #191

Abstract Title: EFFECT OF SINGLE NUCLEOTIDE POLYMORPHISM (308 G/A) OF TNF-α ON LEFT VENTRICULAR MYOCARDIAL MASS IN WOMEN WITH PCOS–A SINGLE CENTRE CROSS SECTIONAL STUDY

Soofi AR(1), Hafeez I(2), Zargar MA (3), Masood A (4) ,Makhdoomi M(1), Jahan N(1), Wani I A (1)Nisar S(5), Ganie MA (1)

1) Department of Clinical Research, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, India;

2) Department of Cardiology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, India;

3) Department of Biotechnology, Central University of Kashmir, Ganderbal, India;

4) Department of Biochemistry, University of Kashmir, India;

5) Department of Medicine, Govt Medical College, Srinagar, India;

6) Department of Endocrinology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, India

Abstract: Objective: Polycystic ovary syndrome (PCOS), the commonest endocrinopathy of reproductive-age women, displays a clustering of metabolic derangements such as obesity, insulin resistance (IR), abnormal glucose tolerance, dyslipidemia, and hypertension, including elevated cardiovascular (CV) risk. Echocardiographic parameters of left ventricular (LV) deformation and velocity have been used to detect preclinical alterations of LV structure and function in various diseases and can be of prognostic significance. Among women with PCOS, data on cardiac structure and function are limited and are at best inconclusive. Although there is some indication of inflammation being related to causation of LV function abnormalities among women with PCOS, there is no data-evaluating role of genetic polymorphism of pro-inflammatory markers on LV mass index (LVMI) among these women.

Methods: A total of 260 drug-naive women qualifying the Rotterdam 2003 criteria for diagnosis of PCOS and 250 apparently healthy women matched for age and body mass index (BMI) as controls. Clinical, biochemical, hormonal and inflammatory marker assessment was followed by estimation of LVM and LVMI by 2-dimensional echocardiography.DNA was isolated by phenol-chloroform method and single nucleotide polymorphism (SNP) in TNF-α 308 G/A was analyzed by RFLP-PCR.

Results: Mean ages (28.08 ±4.18 vs. 29.44 ±6.33 years) and BMI (24.43 ±4.15 vs. 23.92 ± 4.21 kg/m2) of cases vs. controls were comparable, as was blood pressure and plasma glucose 1 hour. Women with PCOS had fewer menstrual cycles per year and higher Ferriman-Gallwey scores, plasma insulin, homeostasis model assessment of IR, total testosterone, plasma glucose (fasting and 2 hours after OGTT), and tumor necrosis factor- α than the controls (P<.001). The genotypic distribution and allele frequency of TNF-α 308 G/A was similar between cases and controls (p = 0.43).The difference in the serum TNF-α concentrations in PCOS women with TNF-α 308 G/ G and G/ A genotypes also remained insignificant (34.11±2.62 vs. 30.78±2.84pg/ml).Moreover, we found that TNF-α 308 G/ G and G/A genotype was not associated with LVM/LVMI among women with PCOS (p=0.30).

Conclusion: Our data did not show any association of TNF-α 308 G/ G and G/A genotype with LVM/LVMI among women with PCOS. Although, the results remain inconclusive, this is the first attempt among a large cohort of Indian women with PCOS to study an association between TNF-α gene polymorphism and LVMI.

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Abstract ID #192

Abstract Title: PHYSICAL AND MENTAL HEALTH IN A COMMUNITY SAMPLE OF INDIVIDUALS LIVING WITH PCOS

Williams, SL (1), Thai L (2); Delau O (2,3); Soucie K (4); Buyalos RP (5); Ottey S (2); Patterson W (2); Azziz R (6,7,8)

(1) Dept. of Psychology, East Tennessee State University, Johnson City, TN, USA 37614; (2) PCOS Challenge: The National Polycystic Ovary Syndrome, Atlanta, GA 30308, USA; (3) Dept. of Biostatistics, School of Global Public Health, New York University, New York, NY 10003, USA; (4) Dept. of Psychology, University of Windsor, Windsor, ON, Canada N9B 3P4; (5) Dept. of Ob/Gyn, David Geffen School of Medicine, UCLA, Los Angeles, CA 90095, USA; (6) Dept. of Health Policy, Management, and Behavior, School of Public Health, University at Albany, SUNY, Rensselaer, NY 12144, USA; (7) Depts. of Ob/Gyn and Medicine, Heersink School of Medicine, University of Alabama at Birmingham, Birmingham, AL 35294, USA; (8) Dept. of Healthcare Organization & Policy, School of Public Health, University of Alabama at Birmingham, Birmingham, AL 35294, USA

Abstract: BACKGROUND: Polycystic Ovary Syndrome (PCOS) is clinically evident in 8-15% of women. PCOS women consistently evidence poorer physical and mental health than unaffected individuals. However, these findings come primarily from medical-based clinics that may not reflect the general population of individuals living with PCOS. This study explores the physical and mental health status of women with PCOS members of a patient advocacy organization.

OBJECTIVE: Determine the health status of individuals living with PCOS using the RAND Short Form 36-Item Health Survey (SF-36; Ware & Sherbourne, Medical Care 1992;30:473-483).

METHODS: We undertook a prospective study among members of an international PCOS patient advocacy organization using the SF-36. The SF-36 assesses 8 health dimensions: physical functioning, bodily pain, role limitations due to physical health, energy/fatigue, role limitations due to emotional concerns, emotional well-being, social functioning, and general perceived health. Individual items were recoded (RAND, 2023) and averaged to form 8 subscale scores. Scores closer to zero indicate the most disability, whereas scores closer to 100 indicate an absence of disability, with a score of 50 at approximately a norm mean score.

RESULTS: A total of 459 individuals with PCOS responded to the survey. The scores were approximately at the mid-point for emotional well-being (M = 49.67, SD = 19.70), social functioning (M = 51.31, SD = 24.86), and pain (M = 56.48, SD = 23.13), but were below the mid-point on most other health indicators: role limitations due to physical concerns (M = 36.98, SD = 38.86), role limitations due to emotional concerns (M = 28.54, SD = 37.66), fatigue (M = 24.25, SD = 17.55), and general perceptions of health (M = 40.49, SD = 19.70). Alternatively, respondents scored above the mid-point on physical functioning (M = 71.49, SD = 22.70).

CONCLUSIONS: While many studies have documented poorer health and quality of life among PCOS patients in medical facilities, this study examined the health status of those with PCOS in a non-medical sample. Findings from this study indicate relatively higher levels of physical concerns and fatigue, and lower levels of role function and general perceptions of health among women living with PCOS.

SUPPORT: Supported by PCOS Challenge: The National Polycystic Ovary Syndrome Association and the Foundation for Research and Education Excellence.

Abstract ID #193

Abstract Title: EXPLORING THE TRENDS OF ASSESSMENTS IN LINE WITH INTERNATIONAL PCOS GUIDELINES AT INITIAL CONSULTATIONS ACROSS DIFFERENT ETHNICITIES SINCE THE COVID-19 PANDEMIC

Khan S (1), Ali A (2), Arshad A (2), Kempegowda P (1,3)

1. Queen Elizabeth Hospital Birmingham, University Hospitals Birmingham NHS Foundation Trust, UK

2. Birmingham Medical School, University of Birmingham, Birmingham, UK

3. Institute of Applied Health Research, University of Birmingham, Birmingham, UK

Abstract: OBJECTIVES:

To explore the trends of various assessments recommended by the International PCOS guidelines at first consultation.

METHODS:

This retrospective study was done in a tertiary care centre in Birmingham, UK in July 2023. All women seen for first consultations in a dedicated PCOS clinic from July 2020 to June 2023 were included. Those undergoing follow-up or without PCOS were excluded. Data on sociodemographics and assessments (Diagnosis based on guidelines, Cardiometabolic risk, Dermatology, Emotional wellbeing, Long term risk education, Lifestyle management, Reproductive screening) were collected. Patients were divided into three groups based on their first consultation date: A (July 2020 to June 2021), B (July 2021 and June 2022) and C (July

2022 to June 2023). Descriptive statistics were assessed by ethnicity using SPSS 28.0.

RESULTS:

A total 111 women were included in the study(A (n=42), B (n=32) and C (n=37)). The median age of the cohort was 31.0 years (A (n=26.5), B (n=30.0) and C (n=29.0)). The most common reasons for referral were excess and unwanted hair growth in A (47.6%) and C (59.5%) and irregular ovulation in B (50.0%). The most common assessment was for dermatological concerns in A and B and cardiometabolic screening in C. There was a shift in the frequency of various assessments over the years (A vs B vs C (%): Diagnosis based on guidelines: 28.6 vs 46.9 vs 40.5, Cardiometabolic: 83.3 vs 71.9 vs 75.7, Dermatology- 88.1 vs 96.9 vs 70.3, Emotional wellbeing: 28.6 vs 28.1 vs 37.8, Long term risk education: 28.6 vs 21.9 vs 21.6, Lifestyle management: 47.6 vs 43.8 vs 43.2, Reproductive screening: 54.8 vs 34.4 vs 51.4).

27.9% were White, 12.6% Asian, 12.6% Black, mixed or other groups and 46.8% preferred not to disclose their ethnicity. The most common assessment was for dermatological concerns across all ethnicities. There was a variation in the frequency of various assessments by ethnicity (White vs Asian vs Black, mixed or other (%): Diagnosis based on guidelines: 25.8 vs 35.7 vs 35.7, Cardiometabolic: 83.9 vs 64.3 vs 71.4, Dermatology: 90.3 vs 100.0 vs 92.9, Emotional wellbeing: 29.0 vs 42.9 vs 35.7, Long term risk education: 22.6 vs 35.7 vs 7.1, Lifestyle management: 29.0 vs 50.0 vs 57.1, Reproductive screening: 54.8 vs 57.1 vs 42.9.)

CONCLUSION:

Dermatological assessment was the most addressed over the years and across ethnicities. Long term risk management was the least addressed over the years. Assessments varied by ethnicities. Developing a standardised approach to assess during PCOS consultations may minimise variation in care.

(Funding: None)

Abstract ID #194

Abstract Title: THE EFFECTS OF MATERNAL PCOS ON THE CARDIOMETABOLIC RISK AND LIVER STEATOSIS IN DAUGHTERS AND SONS

Ng Noel YH (1), Tsang Atta YT (1), Cheung Jamie (1), Cheung Lai Ping (2), Ng Karen (2), Chung Jacqueline PW (2), Chan Michael Ho Ming (3), Chan Juliana CN (1,4,5), Kong Alice PS (1,2,3), Luk Andrea OY (1,4,5), Wang Chi Chiu (2,5), Tam Wing Hung (2), Ma Ronald CW (1,4,5)

(1) Department of Medicine and Therapeutics, The Chinese University of Hong Kong, HKSAR, P. R. China,

(2) Department of Obstetrics and Gynaecology, The Chinese University of Hong Kong, HKSAR, P.R. of China,

(3) Department of Chemical Pathology, The Chinese University of Hong Kong, Prince of Wales Hospital, HKSAR, PR of China,

(4) Hong Kong Institute of Diabetes and Obesity, The Chinese University of Hong Kong, HKSAR, P. R. China,

(5) Li Ka Shing Institute of Health Sciences, The Chinese University of Hong Kong, HKSAR, P. R. China,

Abstract: OBJECTIVE: We established a cohort of women with PCOS and matched controls along with their offspring to evaluate the effects of maternal PCOS on the cardiometabolic risk and liver steatosis in offspring, as well as any differential impact between boys and girls.

METHODS: We invited Chinese women diagnosed PCOS based on 2003 Rotterdam diagnostic criteria from our registry, who have children to participate in this study. The mothers and their sons (PCOSs) and daughters (PCOSd) were evaluated. For controls, we recruited women from another study, who did not have PCOS, together with their sons (Cs) and daughters (Cd), for comparison. All offspring aged 15-25 years were included in the current analysis, and all have undergone anthropometric assessment, biochemical tests and a standardized 75g OGTT. Controlled attenuation parameter (CAP) value was obtained by FibroScan® in order to evaluate their liver steatosis. Differences between groups were evaluated using independent sample t-test or Mann-Whitney U test for continuous variables, while Chi-square test were used for categorical variables. All analyses were adjusted for the age differences.

RESULTS: A total of 33 PCOSs and 29 PCOSd (mean age 19.67 ± 4.53 and 18.52 ± 2.59) as well as 95 Cs and 128 Cd (mean age 17.28 ± 0.72 and 17.40 ± 0.80), were recruited to date respectively. PCOSd had more elevated androgen levels (46.4% vs 23.0%, p=0.013), were more centrally obese (31.0% vs 5.5%, p<0.001); and had higher prevalence of dyslipidemia (24.1% vs 0.8%, p<0.001) and glucose abnormality (20.7% vs 6.3%, p=0.014) than Cd. The prevalence of severe liver steatosis (CAP ≥ 280 dB/m) was higher in PCOSd in comparison with Cd (17.2% vs 5.2%, p=0.029); and such high rate of severe liver steatosis in PCOSd (17.2%) is comparable with that in Cs (20%). Higher log-transformed alanine aminotransferase (ALT) levels were found in PCOSd compared with Cd (PCOSd: 17.00 (13.00-29.00) vs Cd: 14.00 (12.00-20.00), p=0.015), which is consistent with the higher rates of steatosis. Yet, no significant difference was observed in log-transformed ALT and the rate of liver steatosis between PCOSs and Cs. Multivariate logistic regression analyses for the association between the maternal history of PCOS and the risk of moderate to severe liver steatosis stratified by offspring sex suggested that maternal history of PCOS is significantly associated with the moderate to severe liver steatosis in female offspring (adjusted OR 5.745; 95% CI 1.153-28.612); yet, such association rendered non-significant after adjusting for z-score of offspring WHR.

CONCLUSIONS: Difference in cardiometabolic traits were observed between PCOSd and Cd but not between PCOSs and Cs. The prevalence of severe liver steatosis in PCOSd was similar to that in Cs. Maternal history of PCOS is significantly associated with the moderate to severe liver steatosis in female offspring.

Abstract ID #195

Abstract Title: ESTIMATED AVERAGE GLUCOSE AND OTHER BIOMARKERS OF DYSGLYCEMIA PREDICTION BY ANTHROPOMETRIC, LIPID, AND ENDOCRINE ABNORMALITIES IN WOMEN WITH DIFFERENT PHENOTYPES OF PCOS

de Medeiros SF1,2; Yamamoto AKLW2,3; de Medeiros MAS2; Carvalho ABS2; Yamamoto MMW2; Junior JMS4; Baracat EC4

Department of Gynecology and Obstetrics, Medical School, Federal University of Mato Grosso, Cuiabá, MT, Brazil1; Tropical Institute of Reproductive Medicine, Cuiabá, MT, Brazil2; University of Cuiabá, Cuiabá, MT, Brazil3; Disciplina de Ginecologia, University of São Paulo, São Paulo, Brazil4.

Abstract: Objective. To compare the efficacy of estimated average glucose with other biomarkers of dysglycemia to predict anthropometric, metabolic, and endocrine abnormalities in women with different phenotypes of polycystic ovary syndrome (PCOS).

Methods. This cross-sectional study included 648 women with PCOS and 330 controls. A single protocol of investigation was applied for all subjects. PCOS women were divided by phenotypes according to the Rotterdam criteria. Biomarkers of dysglycemia were considered dependent variables and were examined as predictors of anthropometric, lipid, and hormone alterations using univariate and multivariate logistic regressions.

Results. PCOS patients were two years younger than non-PCOS controls (p<0.001). Univariate logistic regression analysis, controlled for age and BMI, showed that many biomarkers of dysglycemia could predict abnormalities in several independent variables. Multivariated logistic models showed that in non-PCOS women, eAG predicted lower TSH levels (OR=0.3; p=0.045), and fasting glucose predicted increased T (OR=2.3; p=0.039). For PCOS, phenotype A, eAG predicted decreased HDL-C (OR=0.17, p=0.023) and high levels of free estradiol (OR=7.1, p<0.001). Otherwise, in PCOS, phenotype D, eAG predicted higher levels of HDL-C.

Conclusions. The current study demonstrated that eAG without adding significant benefits in predicting anthropometric, lipid and hormone alterations was comparable with other established markers of dysglycemia in women with different PCOS phenotypes.

Key words. Polycystic ovary syndrome, biomarkers, insulin resistance, androgens, dyslipidemia.

Abstract ID #196

Abstract Title: EXPLORING THE ASSESSMENT AND MANAGEMENT OF DERMATOLOGICAL MANIFESTATIONS ASSOCIATED WITH POLYCYSTIC OVARY SYNDROME (PCOS) SINCE THE COVID-19 PANDEMIC

Ali A (1), Arshad A (1), Khan S (2), Kempegowda P (2,3)

(1) Birmingham Medical School, University of Birmingham, Birmingham, UK

(2) Queen Elizabeth Hospital Birmingham, University Hospitals Birmingham NHS Foundation Trust, UK

(3) Institute of Applied Health Research, University of Birmingham, Birmingham, UK

Abstract: OBJECTIVE: We investigated the assessment and management of dermatological manifestations with PCOS since the pandemic and further studied the differences based on ethnicity.

METHODS: This retrospective study was done in a large tertiary care centre in Birmingham, UK in July 2023. All women>18 years consulted for PCOS from 1st July 2020 to 30th June 2023 were included in the study. Those who did not have a formal diagnosis of PCOS were excluded. Data at first consultation including reasons for referral, dermatological manifestations, treatment before and after consultation were collected. Women were divided into three groups based on the first consultation date: A (July 2020 to June 2021), B (July 2021 and June 2022) and C (July 2022 to June 2023). Descriptive statistics were performed with SPSS 28.0. The data was also analysed by ethnicity.

RESULTS: There were 186 women during the study period, of which 111 had a first consultation (A (n=42), B (n=32) and C (n=37)). The most common reasons for referral were excess hair growth in A (47.6%) and C (59.5%) and irregular ovulation in B (50.0%). The proportion of referrals due to dermatological complications increased yearly (A: 59.5%, B: 62.5% and C: 67.6%). 101 were diagnosed with a form of dermatological manifestation of PCOS. Among these, hirsutism was the most common symptom (A: 91.7%, B: 96.6% and C: 94.4%) followed by acne (A: 38.9%, B: 51.7% and C: 36.1%) and androgenic alopecia (A: 36.1%, B: 20.7% and C: 19.4%). Before the first consultation, shaving was the most popular treatment for hirsutism across all groups: A (30.6%), B (27.6%) and C (26.3%). Following assessment, 46 women were commenced on pharmacological treatment. The most common drug prescribed was metformin in A (45.5%), followed by spironolactone in B (56.3%) and C (50.0%). 27.9% were White, 12.6% Asian, 12.6% Black, mixed or other and 46.8% preferred not to disclose their ethnicity. 58.1% (White), 57.1% (Asian) and 71.4% (Black, mixed or other) were referred due to a form of dermatological manifestation of PCOS. Hirsutism was more common in the Asian group (85.7%) compared to White (80.6%) and Black, mixed or other (78.6%). Prior to first consultation, shaving was most tried for hirsutism in White (25.8%) and Asians (21.4%), whereas plucking was more common in Black, mixed or other (35.7%). After first consultation, the most prescribed drug was spironolactone for White (22.6%) and Black, mixed or other (28.6%), and the oral contraceptive pill for Asians (14.3%).

CONCLUSIONS: There is an increasing number of women referred due to dermatological concerns with PCOS. Developing a standardised approach to assess and treat these concerns may minimise variation in care.

Abstract ID #197

Abstract Title: DIETARY INTAKE WITHIN THE FIRST YEAR OF MENARCHE IS ASSOCIATED WITH SYMPTOMS OF PCOS 6-12 MONTHS LATER

Vanden Brink H*(1), Ha S (2), Bertomo A (3), Spinola G (3), Sfeir J (1), Burgert TS (4), Barral R (5)

(1) Department of Nutrition, Texas A&M University, College Station, TX, USA;

(2) Department of Statistics, Texas A&M University, College Station, TX, USA;

(3) Division of Nutritional Sciences, Cornell University, Ithaca, NY, USA;

(4) Division of Endocrinology, Children's Mercy Hospital, Kansas City, MO, USA;

(5) Adolescent Medicine, Children's Mercy Hospital, Kansas City, MO, USA;

*Corresponding and presenting author

Abstract: OBJECTIVE: Differences in dietary intake have been described among people living with PCOS. However, we do not know whether differences in dietary intake precede a PCOS diagnosis, or the degree to which dietary intake contributes to or exacerbates the progression of PCOS. To begin to address this knowledge gap, we conducted an ancillary study alongside a longitudinal cohort study of early post-menarcheal adolescents to determine whether dietary intake was prospectively associated with the development of PCOS symptoms in the early post-menarcheal years.

METHODS: Dietary intake was evaluated via two 24-hour diet recalls in n=26 adolescents participating in a prospective cohort study at 6-10 months and again at 12 months post-menarche (12m PM). At approximately 6-10, 12-, 18-, and 24-months post-menarche, a fasting blood draw, anthropometry, and hirsutism score were also conducted. Menstrual diaries were maintained by participants during the study. Dietary data from 6-10- and 12-months post-menarche were transcribed into a nutritional analysis software and then patterned for adherence to a Mediterranean-style Diet, Healthy-Eating Index, and their respective individual dietary components. The degree to which dietary intake at predicted symptoms of PCOS and/or evidence of reproductive dysfunction at the end of the study (n=4 at 18 months, n=22 at 24 months) was determined using generalized mixed models, adjusting for race, household income, total caloric intake, and baseline BMI. For continuous variables, random effects of study site were included.

RESULTS: Added sugars (total and sugar-sweetened beverages) and ultra-processed food intake at 12 months post-menarche were positively associated with AMH concentrations at the end of the study (p=0.01, 0.01, and 0.03, respectively). Red meat intake (g/1000kcal/day) at 12 months post-menarche tended to predict menstrual irregularity at the end of the study (p=0.05), whereas red meat intake at 6-10 months post-menarche was associated with free androgen index (p=0.05). Higher hirsutism scores were associated with lower intakes of legumes (p=0.02), vegetables (p=0.04), and whole grains (p=0.02) at 6-10 months post-menarche. Overall dietary patterns and other dietary components were not significant predictors of reproductive symptoms in these analyses.

CONCLUSION: Dietary intake within the first post-menarcheal year may be associated with evidence of reproductive dysfunction consistent with a trajectory towards PCOS. Research is underway to model dietary intake over time through 2 years post-menarche and to replicate these findings in a larger cohort.

(National Institutes of Health (R21-HD095372), Canadian Institutes of Health Research (Postdoctoral Fellowship #171268).

Abstract ID #198

Abstract Title: EMERGENCE OF PHENOTYPIC DIFFERENCES IN ADOLESCENTS WHO DEVELOP PCOS IN THE EARLY POST-MENARCHEAL YEARS

Vanden Brink H (1), Gadiraju M (2), Burgert TS (3), Barral R (4), Johnson L (5), Lujan ME (6)

(1) Department of Nutrition, Texas A&M University, College Station, TX, USA;

(2) School of Medicine, University of Missouri Kansas City, Kansas City, MO, USA

(3) Division of Endocrinology, Children's Mercy Hospital, Kansas City, MO, USA;

(4) Adolescent Medicine, Children's Mercy Hospital, Kansas City, MO, USA;

(5) Department of Statistics, Cornell University, Ithaca, NY, USA;

(6) Division of Nutritional Sciences, Cornell University, Ithaca, NY, USA;

Abstract: OBJECTIVE: Diagnosis of PCOS during adolescence is often delayed owing to a lack of data describing the emergence of PCOS in the early post-menarcheal years which could yield robust diagnostic markers of early reproductive axis miscalibration. In this preliminary analysis of a prospective cohort, we define the emerging clinical features of early post-menarcheal adolescents who went on to meet criteria for PCOS.

METHODS: Adolescents within one year of menarche participated in a prospective cohort study completing study visits at 6-10 (n=33), 12 (n=35), 18 (n=34), and 24 (n=31) months post-menarche (PM). At each timepoint, participants underwent a fasting blood draw to measure reproductive and metabolic hormones, an evaluation of hirsutism and acne, anthropometry, and transabdominal ultrasonography of the ovaries to obtain follicle number per ovary (FNPO 4-9mm) and ovarian area (OA). At study completion, participants were categorized as PCOS (menstrual irregularity and clinical and/or biochemical hyperandrogenism), at risk for PCOS (menstrual irregularity or hyperandrogenism alone), or regular (no evidence of PCOS) per the 2018 International PCOS Guideline criteria for adolescents. Differences in reproductive and metabolic endpoints were contrasted using Kruskal-Wallis tests at each study timepoint to determine the emergence clinical features in adolescents who ultimately met criteria for PCOS. Post-hoc analyses were conducted using Steel-Dwass analyses.

RESULTS: 31 participants completed the study through 24 months PM and 3 completed through 18 months PM. At the end of study participation, 8 participants met criteria for PCOS, 16 were considered at-risk for PCOS, and 10 had regular menstrual cycles and no evidence of androgen excess. Free androgen index tended to be higher at 6-10 months PM and was subsequently persistently elevated in those who ultimately met criteria for PCOS (P6-10mo = 0.06, P12mo =0.007, P18mo = 0.01, P24mo = 0.006). Likewise, hirsutism was persistently elevated beginning at 18 months PM (P18mo = 0.048, P24mo = 0.036). BMI tended to be elevated at 6-10 months (P6-10mo = 0.06), and OA (P18mo = 0.08) and total testosterone (P18mo = 0.07) tended to be higher at 18 months. Ovarian morphology, AMH, insulin, LH, waist-to-hip ratio, and fasting glucose did not differ across time points for any cohort.

CONCLUSION: Early differences in hyperandrogenism emerged among adolescents who met criteria for PCOS between 18 and 24 months PM. Given that the majority of adolescents remained at-risk for PCOS at the end of the study period, a longer follow-up period may be needed to resolve early morphological and metabolic markers of PCOS during adolescence.

(National Institutes of Health (R21-HD095372), Canadian Institutes of Health Research (Postdoctoral Fellowship #171268).

Abstract ID #199

Abstract Title: LONGITUDINAL ANALYSIS OF OVARIAN MORPHOLOGY IN EARLY POST-MENARCHEAL ADOLESCENTS

Vanden Brink H (1), Burgert TS (2), Barral R (3), Rahman E (4), Zhang A (4), Gadiraju M (5), Johnson L (6), Lujan ME

(1) Department of Nutrition, Texas A&M University, College Station, TX, USA;

(2) Division of Endocrinology, Children's Mercy Hospital, Kansas City, MO, USA;

(3) Adolescent Medicine, Children's Mercy Hospital, Kansas City, MO, USA;

(4) Division of Nutritional Sciences, Cornell University, Ithaca, NY, USA;

(5) School of Medicine, University of Missouri Kansas City, Kansas City, MO, USA

(6) Department of Statistics, Cornell University, Ithaca, NY, USA.

Abstract: OBJECTIVE: Biological and technical factors are hypothesized to confound the utility of ovarian morphology in the diagnosis of PCOS in adolescence. Biological factors include the notion that enlarged, polycystic ovaries are physiological and not specific to PCOS during the early post-menarcheal years. Technical factors include the reduced image quality of transabdominal ultrasonography (TAUS), which may be exacerbated by type of equipment and obesity. To address these concerns, we quantified the effects of time, image quality, and body mass index (BMI) on follicle number and ovarian size obtained with TAUS during the early post-menarcheal years.

METHODS: Adolescents (n=30) were followed prospectively at 6-10, 12-, 18-, and 24-months post-menarche as part of a multi-site prospective cohort study. At each timepoint, participants underwent anthropometry and TAUS of the ovaries. Right and left ovarian images were graded for image quality (IQ) and analyzed offline to obtain follicle number per ovary (FNPO 2-9mm, 4-9mm) and ovarian area (OA). Linear mixed models were used to quantify any impact of biological and technical factors on changes in ovarian morphology over time.

RESULTS: FNPO 2-9mm tended to differ over time (21 ± 2, 17 ± 2, 21 ± 2, 17 ± 2 follicles across timepoints, Ptime = 0.07) and was higher in participants where the right ovary was deemed to have Excellent versus Partially Visible IQ (23 ± 2 vs 16 ± 2 follicles respectively, PRO IQ = 0.006). BMI or left ovary IQ did not explain differences in FNPO. Likewise, no unexplained variance in FNPO 2-9mm was attributed to study site (proxy for different ultrasonographic equipment). FNPO 4-9mm differed over time (15 ± 2, 10 ± 2, 13 ± 2, 10 ± 2 follicles across timepoints, Ptime = 0.008), driven by a reduction in follicle counts from 6-10 to 12 months post-menarche (Pposthoc = 0.014), and 6-10 to 24 months post-menarche (Pposthoc = 0.030). IQ and BMI were not associated with differences in FNPO 4-9mm, and 4% of the remaining unexplained variance was attributed to study site. In contrast, OA increased over time (4.6 ± 1.0, 4.1 ± 1.0, 5.6 ± 1.0, 5.3 ± 1.0 cm2 across timepoints, POA = 0.020), explained by an increase in OA from 12 to 18 months post-menarche (Pposthoc = 0.017). OA negatively associated with BMI (PBMI = 0.019), but not IQ, and 40% of the remaining unexplained variance was attributed to study site.

CONCLUSION: Ovarian morphology is dynamic in the early post-menarcheal years. FNPO 4-9mm may represent a preferred marker over FNPO 2-9mm and OA using TAUS as variance in their estimation is less impacted by equipment, IQ or BMI. Analyses are underway to determine whether divergences in reproductive maturation (towards PCOS or eumenorrhea) align with ovarian morphology during this developmental window.

(National Institutes of Health (R21HD095372), Canadian Institutes of Health Research (Postdoctoral Fellowship #171268)

Abstract ID #200

Abstract Title: THE PREVALENCE OF POLYCYSTIC OVARY SYNDROME IN THE MULTIETHNIC FEMALE POPULATION: A CROSS-SECTIONAL EASTERN SIBERIA PCOS EPIDEMIOLOGY & PHENOTYPE (ESPEP) STUDY.

Suturina L(1), Lizneva D(2), Lazareva L(1), Danusevich I(1), Nadeliaeva I(1), Belenkaya L(1), Atalyan A(1), Sholokhov L(1), Rashidova M(1), Sharifulin E(1), Kuzmin M(1), Igumnov I(1), Babaeva N(1), Tyumentseva D(1), Egorova I(1), Salimova M(1), Stanczyk FZ(3), Legro RS(4), Yildiz BO(5), and Azziz R(6)

(1) Scientific Center for Family Health and Human Reproduction Problems, Irkutsk, Russian Federation

(2) Icahn School of Medicine at Mount Sinai, New York, NY, USA

(3) Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

(4) Hershey Medical Center, Penn State College of Medicine, Penn State University, Hershey, PA, USA

(5) Hacettepe University School of Medicine, Hacettepe, Ankara, Turkey

(6) School of Medicine, the University of Alabama at Birmingham, Birmingham, AL, USA

Abstract: OBJECTIVES: Previous studies have demonstrated that prevalence of polycystic ovary syndrome (PCOS) may vary according to ethnicity, but data were still insufficient. The present study aimed to determine the prevalence of PCOS and phenotypes under the Rotterdam (2003) criteria in unselected (medically unbiased) premenopausal women from the Eastern Siberia region.

DESIGN AND METHODS: We performed the multicenter, institution-based, cross-sectional Eastern Siberia PCOS Epidemiology & Phenotype (ESPEP) study from March 2016 to December 2019 (Study protocol ID: NCT05194384, ClinicalTrials.gov). Initially, 1552 premenopausal women were eligible, of those 418 were not included. Finally, the study included 1134 women aged 18 to 44 yrs., of Caucasians, Asians (Buryats), and mixed ethnicity, who were undergoing an obligatory annual employment medical assessment. Methods included a questionnaire survey, anthropometry and mF-G scoring, gynecological examination and pelvic U/S. Serum samples were analyzed for total testosterone (TT) using LC-MS/MS, for DHEAS, sex hormone-binding globulin (SHBG), prolactin, TSH, LH, FSH, AMH, and 17-OHP by ELISA and Free Androgen Index (FAI). PCOS was defined by the Rotterdam 2003 criteria as a presence of two of three features, including oligo- or anovulation (OA), clinical and/or biochemical signs of hyperandrogenism (HA), and polycystic ovarian morphology (PCOM), after exclusion of related disorders (uncompensated thyroid dysfunction, hyperprolactinemia, 21-hydroxylase deficient non-classic congenital adrenal hyperplasia (NC-CAH), premature ovarian failure (POF).

RESULTS: The total prevalence of PCOS was estimated as 14.6% (165/1134), with the following distribution of PCOS phenotypes: 27.9% (A), 15.8% (B), 24.8% (C), and 31.5% (D). There was no significant difference in PCOS prevalence between Caucasians and Asians (14.9% vs 10.9%, pχ2=0.08), whereas in women of Mixed ethnicity PCOS observed more frequent (22.4%) vs Caucasians and Asians (pχ2=0.049 and 0.003, respectively). PCOS phenotypes A and B were found in a comparable number of PCOS women of different ethnicity. PCOS women of mixed ethnicity demonstrated the highest prevalence of phenotype C, whereas phenotype D was more prevalent in Caucasians.

CONCLUSIONS: The study results demonstrated a 14.6% total prevalence of PCOS, and highlighted ethnicity-dependent difference in the frequency and clinical manifestation of PCOS in the population of Siberian premenopausal women of Caucasian, Asian and Mixed ethnicity living in similar geographic and socio-economic conditions.

Abstract ID #201

Abstract Title: TOWARDS A MORE OBJECTIVE DIAGNOSIS OF HIRSUTISM: THE QUANTIFICATION OF TERMINAL HAIR BY DIGITAL MICROSCOPY

de Kroon RWPM (1,2), den Heijer M (2), Haarman SJ (1), Verdaasdonk RM (3), Heijboer AC (1)

1) Endocrine Laboratory, Dept. of Laboratory Medicine, Amsterdam UMC location University of Amsterdam, Amsterdam, The Netherlands

2) Dept. of Internal Medicine, Amsterdam UMC location Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

3) Dept. of Biomedical Photonics & Imaging, University of Twente, Enschede, The Netherlands

Abstract: OBJECTIVE: The modified Ferriman-Gallwey (mFG) score, used to clinically evaluate and quantify hirsutism, has limitations because of the subjective nature of the assessment. This could possibly be improved by making use of a digital microscope camera to quantify terminal hair. In this study we aimed to validate a digital microscope camera by quantifying terminal hairs in men and women and to determine the inter-observer variability. Furthermore, we aim to investigate whether the visible light or UV light function of the camera is preferred.

METHODS: This cross-sectional study included 20 healthy men, 15 healthy women and 1 patient with hirsutism. A handheld digital microscope camera was used by two independent researchers to obtain visible light and UV light photos of the upper lip and chin in men and women. A hair thickness greater than 60 µm indicated the presence of a terminal hair. The facial mFG-score, hair thickness (when > 60 µm), number of terminal hairs and hair color were determined to indicate mean differences between men and women by an independent t-test. Additionally, Pearson correlation coefficients (r) were determined to assess the inter-observer variability. In one participant, visible light and UV light photos were taken under 4 ambient light conditions to test the stability in output of both types of light.

RESULTS: Terminal hairs were quantified and mean (± standard deviation) number of terminal hairs varied between men (27 (SD 15)) and women (0 (SD 1)) on the upper lip, as well as on the chin (29 (SD 18) and 0 (SD 0), with mean differences (95% confidence interval) of respectively 27 (95% CI 19-34) and 28 (95% CI 19-39) terminal hairs between men and women. Eight terminal hairs per view (approximately 1 cm2) with a mean hair thickness of 66 µm (SD 7.5) were observed on the chin of the hirsutism patient. The hair parameters showed a strong positive correlation (all analyses: r > 0.89) between two independent researchers. The number of terminal hairs on visible light photos were strongly correlated to those on UV light photos of the upper lip (r = 0.897) and chin (r = 0.971), yet the output of the UV light function seemed to be subject to variable ambient light conditions.

CONCLUSIONS: Digital microscopy with visible light could contribute to a more objective method for the diagnosis of hirsutism by the quantification of terminal hair, even directly after shaving and in a darker skin color. This method is associated with a minimal inter-observer variability. Future studies should focus on the applicability of this new method in patients with hirsutism and to investigate whether the analyses could be automatized.

Abstract ID #202

Abstract Title: EPIDEMIOLOGIC STUDIES OF PCOS: DEVELOPMENT AND VALIDATION OF A NOVEL QUALITY ASSESSMENT TOOL

Hatoum S (1), Amiri M (2), Buyalos RP (3), Azziz R (4,5,6)

(1) Foundation for Research and Education Excellence, Vestavia, AL 35243, USA;

(2) Reproductive Endocrinology Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran;

(3) Dept. of Obstetrics & Gynecology, David Geffen School of Medicine, UCLA, Los Angeles, CA, USA;

(4) Depts. of Obstetrics & Gynecology, and Medicine, Heersink School of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA;

(5) Dept. of Healthcare Organization & Policy, School of Public Health, University of Alabama at Birmingham, Birmingham, AL, USA;

(6) Dept. of Health Policy, Management, and Behavior, School of Public Health, University at Albany, SUNY, Rensselaer, NY, USA.

Abstract: OBJECTIVE: There is a lack of high-quality epidemiologic studies of polycystic ovary syndrome (PCOS). We aimed to develop and validate a novel tool specifically designed for assessing the quality of epidemiologic studies of PCOS, the PCOS Epidemiology and Phenotype (PEP) scoring method, comparing it with two other existing quality assessment tools, the Newcastle-Ottawa Scale (NOS) and the Joanna Briggs Institute 2017 Checklist (JBI), using data from a study assessing the link between the prevalences of obesity and PCOS in medically unbiased populations.

METHODS: We developed the PEP scoring tool based on the recommendations for epidemiologic and phenotypic research in PCOS by the Androgen Excess & PCOS Society (Azziz et al, Hum Reprod. 2019; 34:2254–65). The test dataset was identified through a systematic review conducted on PubMed and Embase databases. We used linear regression models to test the association between BMI/obesity and PCOS prevalence.

RESULTS: We retrieved 6,645 studies and found 57 eligible for inclusion (total sample=73,197). Considering all studies, regardless of quality, we found no association between obesity and PCOS for any diagnostic criteria (NIH, Rotterdam, or AE-PCOS). However, when we restricted our analyses to high-quality studies as defined by the PEP tool we found an association between mean population BMI and the prevalence of PCOS by the Rotterdam (r=0.5; P=0.011), but not the NIH or AE-PCOS criteria, and an association between obesity and PCOS prevalences with the Rotterdam (r= 0.661; P=0.001) and the AE-PCOS (r= 0.667; P= 0.050) criteria. When we used the NOS to select high-quality studies, we found only an association between obesity and PCOS prevalences based on the NIH (r= 0.4; P= 0.047), but not the Rotterdam or AE-PCOS criteria. When using the JBI tool to select high quality studies we did not observe any significant associations for any of the diagnostic criteria.

CONCLUSIONS: Our findings highlight the critical need to identify and use high-quality studies when analyzing PCOS epidemiologic data. Further, our data supports the use of a novel quality assessment tool, the PEP scoring method, over other more general quality assessment tools (NOS and JBI). Finally, this study also provides important insights into the relationship between obesity and PCOS prevalence. These results have important implications for epidemiologic research in PCOS.

Keywords: Obesity; Polycystic Ovary Syndrome; Prevalence; Quality assessment

(SUPPORT: Supported by the Foundation for Research and Education Excellence.)

Abstract ID #203

Abstract Title: GEOGRAPHIC VARIATIONS IN POLYCYSTIC OVARIAN MORPHOLOGY IN INDIA AND UNITED STATES-BASED WOMEN WITH POLYCYSTIC OVARY SYNDROME

Lujan ME (1), Zhang H (1), Pea J (1), Carter FE (1), Rahman E (1), Hoeger K (2), Kar S (3).

(1) Division of Nutritional Sciences, Cornell University, Ithaca, New York, United States.

(2) Department of Obstetrics and Gynecology, University of Rochester, Rochester, New York, United States.

(3) Department of Obstetrics and Gynaecology, Kar Clinic and Hospital, Bhubaneswar, Odisha, India.

Abstract: OBJECTIVE: Ethnic and racial variations in the clinical presentation of PCOS have been reported suggesting that screening and diagnosis of PCOS may require consideration of regional differences in reproductive symptomology. Given that limited data exist on the potential for geographic variations in polycystic ovarian morphology (PCOM), we determined whether ovarian features differ between women with PCOS from two distinct regions of the globe.

METHODS: A retrospective, cross-sectional analysis of de-identified research and medical records was completed for 331 women with PCOS based in India (N=119) or United States (US, N=212) for which both an archived ultrasound scan of the ovaries and clinical data were available to corroborate a PCOS diagnosis. Two-sample t-tests, chi-square or Fisher's exact tests were used to assess differences across groups. Bivariate Pearson correlation analysis was used to determine associations between markers of ovarian morphology and PCOS symptoms.

RESULTS: Nearly all participants in both groups met the criteria for PCOM (99%) with the India-based group demonstrating a higher prevalence of follicle excess compared to the US-based group (94% vs. 86%, p = 0.039). Prevalence of ovarian enlargement was similar across groups (India 71% vs. United States 70%, p=0.900). Further, follicle number per ovary (35 ± 13 vs. 39 ± 20 follicles), follicle number per single cross-section (9 ± 3 vs. 10 ± 4), and ovarian volume (9.0 ± 3.9 vs. 8.8 ± 4.4mL) did not differ between India- and US-based groups (p>0.05). Of the non-conventional ovarian features assessed, stromal area (4.3 ± 1.4 vs. 4.2 ± 1.4cm2) and stromal to ovarian area ratio (0.8 ± 0.1 vs. 0.8 ± 0.1) did not differ between groups – albeit ovarian area was slightly larger in women with PCOS from India (6.3 ± 1.7 vs. 6.0 ± 1.8cm2, p=0.030). Collectively, a vast majority of participants from India met the criteria for Frank PCOS (95%) whereas US-based participants had a more heterogeneous phenotypic presentation. Subgroup analyses of women meeting the criteria for Frank PCOS (India N=113; US N=73) confirmed little to no variation in ovarian size and stromal characteristics across the India- and US-based groups. Last, associations between ovarian morphology markers and menstrual cycle length (ρ=0.16 – 0.25), Ferriman-Gallwey hirsutism scores (ρ = 0.16 – 0.26), and/or total testosterone (ρ=0.24 – 0.34) were noted in both the U.S.- and India-based group on both the full and subgroup analysis (p<0.05).

CONCLUSIONS: Geographic differences exist in the clinical presentation of PCOS. However, variations in ovarian morphology may not be sufficient to warrant regional definitions of PCOM. Ovarian dysmorphology served as a biomarker of the severity of reproductive symptomology in both regions consistent with the ovary being a central component of the pathophysiology of PCOS across populations.

Abstract ID #204

Abstract Title: THE INFLUENCE OF RACE ON MOOD DISORDERS IN PATIENTS WITH PCOS

Jacob Christ

Rachel Blank

Alex Milani

Heather Huddleston

UCSF (Huddleston, Christ)

Allara (Blank and Christ)

Abstract: OBJECTIVE: Patients with PCOS have a 3 to 5-fold increased rate of depression and anxiety. While race/ethnicity are known to influence the prevalence of mood disorders in the general population, less is known about their impact among patients with PCOS. We sought to evaluate the influence of race/ethnicity on mood disorders among a multi-ethnic population-based cohort of patients with PCOS living in the United States.

METHODS: A cross-sectional survey was administered to a community-based sample of women identified via advertisements on social media and virtual care waitlist emails. Inclusion for these analyses required self-report of a PCOS diagnosis by a healthcare provider. Surveys interrogated socio-demographic variables, medical history and PCOS symptoms including history of or current depression and anxiety diagnoses as well as whether depression or anxiety were part of their PCOS symptomatology. Depression and anxiety symptoms were also measured with the Patient Health Questionnaire (PHQ)-9 and the Generalized Anxiety Disorder 7-item scale (GAD7). Frequency of PHQ-9 score ≥15, corresponding to moderately severe or greater depressive symptoms, was assessed. Outcomes were compared across race/ethnicity groups using one way ANOVA with post-hoc Tukey statistical tests and Chi-squared test.

RESULTS: In total, 1064 participants were included. Race/ethnicity was self-identified as follows: 602 (56.5%) Caucasian, 76 (7.1%) Asian, 129 (12.1%) Black, 203 (19.1%) Hispanic, 18 (1.7%) mixed ethnicity, and 36 (3.4%) other. Overall, 52.8% reported a prior diagnosis of anxiety and 53.1% reported a prior diagnosis of depression, with no difference by race/ethnicity group. In contrast, the proportion reporting anxiety as part of their PCOS condition differed between groups (Caucasian 12.6%, Asian 18.4%, Black 19.7%, Hispanic 14.3%, mixed ethnicity 27.8%, and other 3.2%, p < 0.05). PHQ-9 scores differed overall with significantly higher scores among Hispanic vs Caucasian participants in post-hoc analysis (Caucasian (mean±SD) 14±7, Asian 14±7, Black 14±7, Hispanic 16±7, mixed ethnicity 13±8, and other 13±6, p<0.05). Given significant differences in PHQ-9 between Caucasian and Hispanic participants these groups were separately compared for proportion without a diagnosis of depression but with a PHQ-9 ≥15 which was more prevalent among Hispanic (58.3%) than Caucasian (45.1%) participants, p<0.05. GAD7 scores did not differ by group.

CONCLUSIONS: History of diagnosed depression and anxiety were highly prevalent in this cohort of participants with PCOS. Although rates of reported diagnoses of depression were similar across groups, PHQ9 scores were higher among Hispanic participants, indicating potential under-recognition of depression in this group. Future work should aim to better clarify the contributors and solutions to mood disturbance in high risk race and ethnicity groups.

Abstract ID #205

Abstract Title: THE POWER OF SOCIAL MEDIA IN TACKLING MISINFORMATION AND RAISING AWARENESS OF PCOS

Elhariry M (1), Malhotra K (2,3) , Goyal K (4), Kempegowda P (3,5)

1. College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK
2. Dayanand Medical College and Hospital, Punjab, India
3. Institute of Applied Health Research, University of Birmingham, Birmingham, UK
4. Delhi Heart Institute and Multispeciality Hospital, Punjab, India
5. Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK

Abstract: OBJECTIVE:

1.to create and disseminate peer-reviewed short videos about PCOS and Thyroid conditions.

2.to explore content creators' experience, video outreach and audience engagement on social media.

METHODS:

This project was run from December 2022 to May 2023 in collaboration with British Thyroid Foundation and PCOS Vitality. Scripts based on the most searched topics in PCOS and thyroid conditions were created and reviewed by experts and patients to ensure scientific accuracy and acceptability. Once finalised, we invited medical students to create videos using the scripts. The videos were reviewed, edited to fit the requirements, and posted on TikTok, Instagram, YouTube, and Twitter.

Video engagement across social media over two months was analysed. Content creators were invited to a semi-structured virtual interview to explore their experiences and motivation to participate. Two independent authors coded the interview transcripts using Nvivo 12.0 to identify themes using thematic inductive analysis.

RESULTS:

Over 2 months, the videos received 718 likes, 120 shares, and 54686 views for 20 videos-19458 on TikTok, 12944 on Instagram, 2606 on YouTube, and 19678 on Twitter. There was an increase in followers across all platforms - from an 89% increase on TikTok to a 5% increase on Twitter. Analysis of participant experience yielded 4 main themes:Views on social media, advice when using social media, reasons for participating in this project, and thoughts on this project. Regarding views on social media, content creators highlighted advantages of social media, including "large outreach"(12 references), "convenience"(10 references), and "accessibility to opportunities" in fields of interest(7 references). The most common themes about advice were awareness of "audience's demographics"(9 references), "sharing on more than one platform"(5 references), and "collaborating with organisations"(3 references). Content creators mentioned that "non-restricting participation criteria", "convenience" (8 references) and "ability to record from home with a pre-written script"(6 references) made it easier to participate.

CONCLUSIONS:

Disseminating peer-reviewed information is a great way of harnessing the power of social media to increase awareness, tackle misinformation, and provide a channel for the public/patients to receive evidence-based information. Medical students have untapped potential to be content creators working with relevant authorities and patient support groups.

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Abstract ID #207

Abstract Title: Disparities in Polycystic Ovary Syndrome diagnosis in Boston Medical Center Cohort

Emily L. Silva (1), Kevin J. Lane (2), Breanna Van Loenen (2), Brent Coull (1, 3), Jaime E. Hart (1, 4), Tamarra James-Todd (1, 5), Shruthi Mahalingaiah (1, 6)

(1) Department of Environmental Health, Harvard T.H. Chan School of Public Health, Boston, MA, USA
(2) Department of Environmental Health, Boston University School of Public Health, Boston, MA, USA
(3) Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, MA, USA
(4) Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA
(5) Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, USA
(6) Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Massachusetts General Hospital, Boston, MA USA

Abstract: OBJECTIVE: Receiving a polycystic ovary syndrome (PCOS) diagnosis allows for earlier intervention, access to treatment, and lower risk of comorbidities including infertility, diabetes, hypertension, obesity, and metabolic syndrome. Here we aim to use electronic health records (EHR) data at Boston Medical Center (BMC) to identify predictors of missed diagnosis, among those who meet criteria for PCOS.

METHODS: Physician-diagnosed cases were identified as females aged 18 to 45 years with an ICD-9 code for PCOS between 2003 and 2015. Algorithm PCOS cases were identified as those with ICD codes for irregular menstruation and at least one of the following: ICD code for hirsutism, elevated testosterone lab, or polycystic ovarian morphology as identified using natural language processing on pelvic ultrasounds. Logistic regression models were used to estimate odds of missed PCOS diagnosis by demographic and socioeconomic factors: age, race/ethnicity, education, and insurance type. Social vulnerability index (SVI) score, calculated using data from the 2010 American Community Survey and assigned by census tract linked to updated residential addresses, was used to evaluate spatial predictors and adjust for residual confounding. Sensitivity analyses further adjusted for body mass index (BMI) among those with complete data.

RESULTS: A total of 1,282 women with PCOS ICD diagnoses and 761 women with algorithm PCOS were identified in the BMC-EHR cohort (mean age ± SD, 27.4 ± 6.7). The cohort was 47% Black, 23% White, 15% Hispanic/Latino, and 63% of women were on Charity or Medicaid insurance. In main models including age, race/ethnicity, education, and insurance type, being Black vs. White was associated with a 45% (95% CI, 13, 88) increase in odds of missed PCOS diagnosis, and having Medicaid or Charity vs. private insurance was associated with an 82% (95% CI, 41, 235) and 64% (27, 213) increase in odds of missed diagnosis, respectively. Effect estimates were robust to adjustment for SVI score. A 10% increase in housing type/ transportation factor vulnerability score (i.e., less stable housing; less transportation access) was associated with an 8% (95% CI, 1, 16) increase in odds of missed diagnosis in fully adjusted models. BMI was missing for 464 (22.7%) women. Among those with complete data, higher BMI was associated with increased probability of receiving a PCOS diagnosis, and adjustment for BMI increased the magnitude of effect estimates for race/ethnicity and insurance type.

CONCLUSIONS: We observed increased probability of missed PCOS diagnosis among Black women and women on Charity or Medicaid insurance in our BMC cohort. Disparities in diagnosis may be partially attributable to disease phenotype or severity, which we were unable to capture in our EHR dataset. Further research should explore reasons behind disparities, such as wealth and healthcare access, to inform areas for intervention.

Abstract ID #208

Abstract Title: THE EFFECT OF 4 MONTHS OF ORAL SEMAGLUTIDE ON WEIGHT, CLINICAL, METABOLIC AND REPRODUCTIVE MEASURES IN ADOLESCENTS WITH OBESITY AND PCOS (TEAL STUDY)

Cree, MG (1,5,6), Morelli, N (1) Lo J (1), Ware, MA (1), Vivas, C (1), Taylor, A (1), Garcia-Reyes, Y (1), Fuller, K (1,2), Faulkner, C (2), Pyle L (3,4)

(1) Division of Pediatric Endocrinology, Department of Pediatrics, University of Colorado Anschutz, Aurora, CO, USA;
(2) Division of Pediatric Nutrition, Department of Pediatrics, University of Colorado Anschutz, Aurora, CO, USA;
(3) Department of Pediatrics, University of Colorado Anschutz, Aurora, CO, USA;
(4) School of Public Health, University of Colorado Anschutz, Aurora, CO, USA;
(5) Childrens Hospital Colorado, Aurora, CO, USA;
(6) Ludeman Center for Women's Health, University of Colorado Anschutz, Aurora, CO, USA

Abstract: BACKGROUND: Polycystic ovary syndrome (PCOS) affects one in ten females, is characterized by elevated testosterone and often includes obesity and obesity related co-morbidities. Treatment with Glucagon Like Peptide-1 receptor agonists (GLP1-RA) improves glycemia and induces weight loss in individuals with obesity. The reproductive and metabolic effects of Semaglutide, a stronger GLP1-RA, have not been measured in adolescents with PCOS and obesity. METHODS: Adolescents with PCOS and obesity were randomized to 4-months of 3mg/7mg of oral Semaglutide (SEMA) or to weekly zoom meetings with a dietician (DIET). Anthropomorphics, clinical symptoms, reproductive and metabolic laboratory measures were performed at baseline and 4 months post medication or diet intervention. Data are expressed as mean ± standard deviation or median (25th,75th percentile).
RESULTS: A total of 60 girls were enrolled, with 50 completing the study (at baseline: SEMA Age 15.7 ± 1.5y, weight 94.3 (82.0, 104.5)kg, BMI 35.1 (31.4,37.3.0)kg/m2, and DIET 14.4 ± 1.7y, 91.0 (80.4, 99.8)kg, 33.7 (29.5, 36.8)kg/m2). There was no discontinuation due to safety concerns. In SEMA, 3 withdrew due to side effects, and 1 in SEMA completed the study with the 3 mg dose due to side-effects. In SEMA, GI side-effects were common (66% nausea, 17% emesis) vs DIET (21% nausea, no emesis). Youth in SEMA lost -4.75 (-8.5, -1.7)kg which was 5.2 ± 5.0% total body weight, whereas DIET lost -2.0(-3.7, 0.25)kg which was 1.6 ± 3.5% total body weight. Within SEMA, 50% lost >5% body weight, 40% lost 0-5% body weight and 10% gained up to 5% body weight. Waist circumference changed in SEMA (-3.6 ± 8.2 cm) vs DIET (-0.7 ± 5.7). HbA1c decreased in SEMA (-0.1 ± 0.2%) and increased in DIET (0.1 ± 0.2). Fasting total cholesterol and triglycerides decreased in both groups, whereas SHBG and Adiponectin increased in SEMA relative to DIET. There were no differences in change for fasting glucose or fasting insulin. In the 4 months prior to the study, the average number of menses was 1.4±1.3 in SEMA and 1.1±0.8 in DIET, and during the study it was 1.9±1.4 in SEMA and 1.6±1.2 in DIET. In SEMA, 48% increased menses frequency and 41% had no change, compared to DIET with 57% increase and 36% no change. Free testosterone decreased in both groups. There was no difference in acne severity or degree of hirsutism changes.
Conclusions: Oral semaglutide induced greater weight loss and HbA1c improvements compared to a very intensive diet intervention in adolescents with obesity and PCOS, supporting its use in this patieint population for weight loss and dysglycemia. Both groups experienced an improved menstrual frequency and decreases in testosterone. Future work needs to include higher doses and longer duration of treatment with GLP1RA therapy to fully understand the metabolic and reproductive effects.
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Abstract ID #209

Abstract Title: HYPEREXPRESSION OF CIRCULATING MIR-21-5P MAY BE RELATED TO INDETERMINATE PHENOTYPES OF POLYCISTIC OVARY SYNDROME: AN EXPLORATORY ANALYSIS

Maffazioli, GD (1,2), Baracat, EC (1,2), Soares-Jr, JM (1), Carvalho, KC (1,2), Maciel, GAR (1,2,3)

(1) Disciplina de Ginecologia, Departamento de Obstetricia e Ginecologia, Hospital das Clínicas HCFMUSP, Faculdade de Medicina da Universidade de Sao Paulo, Rua Dr Eneas de Carvalho Aguiar, 255, 10th floor, Cerqueira Cesar, Sao Paulo, SP, Brazil, 05403-000

(2) Laboratório de Ginecologia Estrutural e Molecular (LIM 58), Disciplina de Ginecologia, Departamento de Obstetricia e Ginecologia, Hospital das Clinicas, Faculdade de Medicina Universidade de Sao Paulo, HCFMUSP, SP, Brazil. Av. Dr Arnaldo 455, room 4125, Cerqueira Cesar, Sao Paulo, SP, Brazil, 05403-010,

(3) Fleury Laboratory, Av General Valdomiro de Lima 588 Sao Paulo, SP, Brazil, 04344-070

Abstract: BACKGROUND: Polycystic Ovary Syndrome (PCOS) is a heterogeneous endocrinopathy whose etiology is not completely understood, but it encompasses a complex genetic trait associated to epigenetic factors. We have previously identified up-regulation of circulating miR-21-5p in PCOS women when compared to normo-cycling healthy controls. Recently, it has been proposed a new classification of PCOS, taking into account genomic background information, in three subtypes: (a) reproductive (higher LH and SHBG levels and relatively low BMI), (b) metabolic (high BMI and insulin levels with lower LH and SHBG levels) and (c) indeterminate (more relatively generic PCOS cases, presenting genetic homogeneity). OBJECTIVE: To explore the differential expression of circulating miR-21-5p across the three subtypes of PCOS. METHODS: Cross-sectional study analyzing 36 PCOS women, diagnosed according Rotterdam consensus. The three subtypes were determined according to the following criteria: (a) Reproductive: BMI < 30 kg/m2 & LH:FSH ratio > 2 & SHBG > 37.5 ng/mL; (b) Metabolic: BMI >30 kg/m2 & LH:FSH ratio <2 & SHBG > 37.5 ng/mL; (c) Indeterminate: not meet other groups criteria. Expression profile of miR-21-5p was determined by RT-PCR using individual Taqman assays (Termo Scientific, Mass, USA) and described as relative expression (2^(-ΔCT)). Statistical analysis was performed using STATA (version 4.0). RESULTS: Five (14%) participants belonged to the reproductive subtype, 4 (11%) to the metabolic subtype, and 27 (75%) the indeterminate subtype, according to the used criteria. Groups were age matched (26.6 ±4.7 vs 29.3±5.7 vs 29.3±4.9 years old, p=0.55, respectively), and did not differ regarding total testosterone (67.6±30.4 vs 48.5±10.7 vs 50.8±25.1 ng/dL, p=0.45), free testosterone levels (23.6±9.0 vs 39.5±12.0 vs 33.4±20.1 ng/dL) and AMH (7.78±4.93 vs 6.21±4.77 vs 7.62±4.08 ng/mL, p=0.27). The metabolic phenotype presented higher HOMA-IR levels (2.1±0.7 vs 14.4±19.7 vs 6.7±4.5, p=0.03) and glucose 2 hours after 75g (77.6±14.9 vs 125.8±10,2 vs 110.0±29.7 mg/dL, p=0.001). Overall expression of circulating mir-21-5p did not differ between groups (0.271±0.232 vs 0.115±0.154 vs 0.354±0.454, p=0.27). However, the indeterminate group presented 4 participants in which mir-21-5p were hyperexpressed (1.298±0.465). When analyzed as distinct subgroup, these participants presented a trend towards a lower SHBG levels (22.6±3.0 vs 44.2±25.2 ng/mL, p=0.08) and a trend towards a high HOMA-IR levels (10.7±6.2 vs 6.4±7.7, p=0.06) compared to other PCOS women. Groups did not differ by age (p=78), BMI (p=0.96), LH:FSH ratio (p=0.80), total and free testosterone (p=0.86 and 0.21) and AMH (p=0.53) levels. CONCLUSION: hyperexpression of miR-21-5p seems to be related to some cases of indeterminate subtypes, especially those related to worse insulin profile. More studies are necessary to confirm theses findings.

Abstract ID #210

Abstract Title: CLINICAL AND BIOCHEMICAL CHARACTERISTICS OF POLYCYSTIC OVARY SYNDROME (PCOS) IN NORTH AFRICA : A PILOT CROSS-SECTIONAL STUDY

Nour El Houda MIMOUNI*(1) Amina Belkbir*(2), Valentine Andreu(1) , Bianca Marlin Jones(1,3,4)

1 Mortimer B. Zuckerman Mind Brain and Behavior Institute, Department of Neuroscience, Columbia University, New York, NY, 10027 USA

2 Obstetrics Gynecology Clinic of Algiers, 16000, Algeria.

3 Department of Psychology, Columbia University, New York, NY, 10032 USA

4 Department of Neuroscience, Columbia University, New York, NY, 10032 USA

* These authors contributed equally

Abstract: PLEASE CONSIDER For POSTER ONLY!

Introduction: Polycystic Ovary Syndrome (PCOS) is a multifaceted endocrine disorder affecting 10-20% of women in their reproductive years. It is a prominent cause of hormonal imbalances, infertility, and has links to chronic metabolic, cardiovascular, and psychological disorders. Both genetic and environmental factors play a role in the negative outcomes associated with PCOS, such as obesity and infertility. Despite extensive efforts to study PCOS in various countries, research specific to North Africa, particularly in Algeria, is lacking. This cross-sectional study aims to investigate the clinical and biochemical characteristics of PCOS in Algerian women, the largest country in Africa. By focusing on this understudied population, the research seeks to contribute the understanding and management of PCOS in the North African context.

Methods and Preliminary results : As of now, the study has successfully recruited 130 women diagnosed with PCOS and 112 control women without the condition, all within the reproductive age range (18-45 years), recruited from both urban and rural areas in Algeria. The PCOS group was defined based on the Rotterdam diagnostic criteria. Participants completed structured questionnaires to provide demographic data, medical history, and information on PCOS-related symptoms. Clinical assessments, including blood pressure measurements and pelvic ultrasounds, were conducted. Blood samples were collected for homonal measurements. The study received approval from the local Ethics Committee, adhered to the principles outlined in the Declaration of Helsinki regarding the use of human blood samples, and obtained informed consent from all participants.

Conclusion : This pilot study could provide unprecedented insights into PCOS characteristics in Algeria, shedding light on potential variations in PCOS phenotypes influenced by diverse genetic backgrounds, environmental factors, and dietary habits in North Africa. This first research provides a crucial foundation for further research in the region, offering a basis for comparative studies across different North African countries where genetic diversity and lifestyle factors may contribute to distinct PCOS patterns, leading to more personalized and effective approaches for managing PCOS.

Keywords: Polycystic Ovary Syndrome, PCOS, North Africa, clinical characteristics, reproductive health, hormonal imbalance.

Abstract ID #211

Abstract Title: IMPLEMENTATION OF DEDICATED REPRODUCTIVE ENDOCRINOLOGY SERVICE FOR WOMEN WITH POLYCYSTIC OVARY SYNDROME - CROSS SECTIONAL AND LONGITUDINAL DATA FROM A TERTIARY CENTRE

McDonnell, Tara(1,2), Madden Doyle, Lauren (1), Cussen, Leanne (1,2), Michael W.O'Reilly (1,2)

1 Department of Endocrinology, Beaumont hospital, Dublin Ireland

2 Academic Department of Endocrinology, Royal College of Surgeons in Ireland (RCSI)

Abstract: Following the establishment of a dedicated Reproductive Endocrinology service in Beaumont hospital in 2019, we carried out a retrospective review of all women who were diagnosed with PCOS and attended clinic in the first 12months. We aimed to profile symptoms at presentation, prevalence of androgen excess,and longitudinal weight change.

We undertook a retrospective chart review. Data was collected on symptom prevalence, metformin prescription and longitudinal weight change in women with a minimum of 12months follow up.

85 women with PCOS attended clinic in the first 12 months. Median age at referral was 26(IQR21-30) years. Symptoms of hyperandrogenism were present in 87.9% (hirsutism 75.3%, acne 60%, androgenic alopecia 22.4%). Oligo/amenorrhea were identified in 76.5% and menorrhagia in 17.7%. 67.1% had biochemical evidence of hyperandrogenism. Median serum testosterone level was 1.6nmol/L(IQR1.2-2.2),DHEAS 9.94umol/L(IQR 6.8-11.5) and SHBG 29.25nmol/l(IQR 22.7-51.35). BMI data was available on 55women. 78.2% of women had overweight/obesity. Median BMI was 32.04kg/m2(IQR 25.35-36.70).43 women had at least 12months of follow up. The median weight change in this cohort was+1.6kg[IQR-3.4-6]in these women. Metformin was prescribed in 61% of patients. There was no significant weight change between women with PCOS who had ever tried metformin(-0.41kg±1.3) compared with those who had not (+2.44kg±1.7, p=0.15).

There was a high prevalence of overweight/obesity in women with PCOS in this specialist clinic,with no significant change in weight observed after 12months of follow up. Prevalence rates of androgen excess and oligomenorrhoea match those reported internationally. These results demonstrate the need for a multi-disciplinary approach to management of PCOS.

Abstract ID #212

Abstract Title: THE ULTRA TRIAL: TRANSVAGINAL ULTRASOUND-GUIDED OVARIAN ABLATION IN WOMEN WITH PCOS-RELATED INFERTILITY: THE ENDOCRINE OUTCOME OF THE FIRST–IN-HUMAN FEASIBILITY CLINICAL TRIAL

Amer S (1), Hansen K (2), Wyns C (3), Autin C (4), Fernandez H (5), Jegaden M (5), Jayaprakasan K (6), Metwally M (7)

(1) Academic Unit of Translational Sciences, University of Nottingham, Derby, UK; (2) Gynecology & Reproductive Medicine, University of Oklahoma Health Sciences Center OUHSC, Oklahoma, U.S.A; (3) Gynaecology & Fertility, Cliniques Universitaire Saint-Luc, Brussel, Belgium;

(4) Gynaecology & Fertility, CHU Saint-Pierre, Brussel, Belgium; (5) Hopital Bicetre - APHP, Gynaecology & Fertility, Paris, France; (6) Gynaecology & Reproductive Medicine, University Hospitals of Derby and Burton NHS Foundation Trust, Derby, UK; (7) Gynaecology & Reproductive Medicine, University of Sheffield and Sheffield Teaching Hospitals, Sheffield, uk.

Abstract: OBJECTIVES: Transvaginal ultrasound (TVUS)-guided ovarian ablation has shown preliminary evidence of effectiveness in inducing ovulation in PCOS women who are resistant to clomiphene citrate (CC) and/or letrozole (LTZ). The aim of this part of the study was to evaluate the effect of the ablation procedure on ovarian hormones and ovarian volume as a possible mechanism of action.

METHODS: This study included two phase-1 feasibility, single-arm clinical trials running in parallel in Europe (UK, France, Belgium) and the US assessing the TVUS-guided ovarian ablation as a second line ovulation induction treatment in PCOS women. Participants were CC/LTZ-resistant PCOS women (aged 18-40 years) diagnosed according to Rotterdam criteria. TVUS-guided ovarian ablation was performed using May Health device. Post-procedure, ovulation was assessed by weekly serum progesterone measurements until confirmation of ovulation or up to 12 weeks. Serum levels of AMH, testosterone and LH as well as ovarian volume were compared at baseline and post-procedure at three and six months using non-parametric tests.

RESULTS: Twenty-five participants (mean±sd age, 31.6±3.3 years; BMI, 29.6±4.9 kg/m2) underwent TVUS-guided ovarian ablation and completed at least three-months FU. Overall spontaneous ovulation rate was 44% at 3-month, increasing to 65% at 6-month FU after restarting CC/LTZ in four participants. After ovarian ablation, the median (IQR) serum AMH concentrations significantly decreased from baseline 72.3 (31.8, 115.3) pmol/l to 54.3 (21.6, 80.2) pmol/l at 3-month (p=0.003) and 33.2 (18.5, 76.4) pmol/l at 6-month (p=0.003) post-procedure. The magnitude of post-ablation decline in serum AMH levels was significantly (p = 0.046) greater in women who ovulated spontaneously (responders) (23.7% (72.2, 10.9)) compared to non-responders (7.3% (25.2, 2.2)). There were no statistically significant changes in other PCOS-related parameters including circulating testosterone, luteinizing hormone, FAI or ovarian volume at 3- or 6-months FU after the procedure.

CONCLUSION: These preliminary data suggest that ovarian ablation seems to significantly reduce the abnormally high circulating AMH in PCOS women, an effect which is sustained up to six months after the procedure. This normalisation of AMH could be the underlying mechanism of ovarian rebalancing with resumption of ovulation in anovulatory PCOS women. This is further supported by the observation that women who ovulated showed a greater reduction in their circulating AMH compared to the non-responders. These data should, however, be interpreted with caution given the small sample size.

(Funding: this trial has been funded by May Health SAS, 9 rue d'Enghien,75010 Paris, FRANCE.)

Abstract ID #213

Abstract Title: THE PCOS EPIDEMIOLOGY AND PHENOTYPE IN TRINIDAD AND TOBAGO (TRINIDAD-PEP) STUDY: PRELIMINARY RESULTS

Mohammed S (1), Sundaram V (2), Cockburn B (3), Ottey S (4), Azziz R (5,6,7)

(1) Dept. of Pre-Clinical Sciences, Faculty of Medical Sciences, The University of the West Indies, St. Augustine, Republic of Trinidad and Tobago; (2) Dept. of Basic Veterinary Sciences, School of Veterinary Medicine, Faculty of Medical Sciences, The University of the West Indies, St. Augustine, Republic of Trinidad and Tobago; (3) Dept. of Life Sciences, Faculty of Science and Technology, The University of the West Indies, St. Augustine, Republic of Trinidad and Tobago; (4) PCOS Challenge: The National Polycystic Ovary Syndrome, Atlanta, GA, USA; (5) Dept. of Health Policy, Management, and Behavior, School of Public Health, University at Albany, SUNY, Rensselaer, NY, USA; (6) Depts. of Obstetrics & Gynecology, Medicine, Heersink School of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA; (7) Dept. of Healthcare Organization & Policy, School of Public Health, University of Alabama at Birmingham, Birmingham, AL, USA

Abstract: BACKGROUND: Polycystic Ovary Syndrome (PCOS) is clinically evident in 8-13 % of women of reproductive age. Assessing the prevalence of the disorder in different countries is essential to determine the impact that lifestyle, environment and race/ethnicity has on the development and phenotype of PCOS. There is a significant paucity of epidemiologic studies regarding PCOS in the Caribbean.

OBJECTIVE: To determine the prevalence of PCOS in the Republic of Trinidad and Tobago in a medically-unbiased population.

METHODS: A community-based, prospective, cross-sectional study of females aged 18-45 years. The study population was randomly chosen across 8 locations in Trinidad reflecting a diversity of ethnicities and social-economic status. A history and physical (H&P) was obtained using a uniform questionnaire and all subjects provided blood samples. Clinical hyperandrogenism (CH) was defined as a modified Ferriman-Gallwey (mF-G) ≥6 and menstrual dysfunction (MD) as <9 menstrual cycles/yr. PCOS was defined according to the NIH 1990 criteria.

RESULTS: So far, the study has included 184 participants (33 Africans, 59 Mixed, 88 East Indians and 4 'other'). Clinically, 12 had CH+MD, 27 MD only and 65 had CH only, representing the subgroup with 'Possible PCOS'. Of the total 28 (15.2%) had a prior PCOS diagnosis and 3 were captured in the 'Possible PCOS' subgroup. We examined the association of infertility and body mass index (BMI) with PCOS, and observed a positive association when considering the entire population (n=184; r=0.644, p<0.01; and r=1.31, p=0.08, resp.). A positive association with prior PCOS diagnosis and infertility and obese (n=28; r=0.644, p<0.001 and n=59; r=0.636; p<0.01 resp.)

CONCLUSIONS: Our preliminary findings indicate that approximately 7% of reproductive-age women in Trinidad and Tobago exhibit possible PCOS. Among the participants who reported being diagnosed with PCOS in this study, there is a notable correlation with BMI and infertility. Our study is ongoing.

SUPPORT: Supported by the Campus Research & Publication Fund, School of Graduate Studies and Research, The University of the West Indies, St. Augustine Campus; The Rotary Clubs of St. Augustine, Central Port of Spain, Felicity/Charlieville; RAMPS Logistics; and the Caribbean Eye Institute.

Abstract ID #214

Abstract Title: Glycated hemoglobin as a screening tool for prediabetes and type 2 diabetes in polycystic ovary syn

Macchione RF (1), Maffazioi GD (1), Soares JM Jr (1), Lopes, CP (1), Pintao MCT (2), Baracat EC (1), Maciel GAR (1,2)

(1) Disciplina de Ginecologia, Departamento de Obstetricia e Ginecologia, Hospital das Clínicas

HCFMUSP, Faculdade de Medicina da Universidade de Sao Paulo, Brazil

(2) Fleury Laboratory, São Paulo, Brazil

Abstract: Polycystic ovary syndrome (PCOS) is one of the most common endocrinopathies in women of reproductive age. It is linked with several metabolic abnormalities, including insulin resistance, impaired glucose tolerance (IGT), and a high risk of developing type 2 diabetes (T2DM). Most guidelines currently recommend active screening for T2DM using oral glucose tolerance tests (OGTT). However, OGTT is relatively expensive, uncomfortable, and time-consuming, which hampers its widespread use, especially in a public health system. Conversely, glycated hemoglobin (HbA1c) is a marker of glucose metabolism that has also been used in primary screening of T2DM, does not demand fasting and its availability is higher. OBJECTIVE: Compare the accuracy of HbA1c in the diagnosis of IGT and T2DM in PCOS and its applicability as a wide population screening in a low-income country with disparities in access to the health system. METHODS: It was an observational study with 100 PCOS women from a tertiary university center and 19.293 control women from a general population database in the same age range (18-40 years old not completed), having OGTT as reference. The analysis of the collected data was carried out using the STATA program. To assess the diagnostic value of testing HbA1c (using the 5.7 and 6.4% cutoffs) against OGTT for the diagnosis of IGT (between 140 and 199 mg/dL) or T2DM (?200mg/dL), global accuracies, sensitivity, specificity were calculated. The analysis of the ROC curve (Receiver operating characteristic curve) was performed to compare the area under the curve of HbA1c. A p-value less than 0.05 was considered significant (*p). The sample size was calculated based on a previous study (Lerchbaum et al., 2013). For a power of 90% and an α (alpha) of 0.05; a sample of 54 participants would be sufficient. RESULTS: The HbA1c values were <5.7%, 5.7-6.4%, and >6.5%, euglycemic, IGT, and T2DM respectively. The median range on PCOS OGTT was 122(100-146) mg/dL and on HbA1c 5.3% (5.1-5.6); with 29% women IGT e 0% T2DM, although HbA1c diagnosed 12% only of those. The HbA1c provided 41% sensitivity, 87% specificity, and 73% accuracy on PCOS. The median range in the control group was OGTT 117 (99-137) mg/dL (p=0.23) and HbA1c 5.0% (4.8-5.3) (p<0.0001); 30% were altered in OGGT (above 140 md/dL), and 3,4% in HbA1c. HbA1c provided 15% sensitivity, 97% specificity, and 78% accuracy in the 5.7% threshold. The receiver operating characteristic analysis (ROC) performed an area under the curve (AUC)=0.58 in PCOS, and AUC=0.62 in the control group. CONCLUSIONS: In our population HbA1c was insensitive and missed most diagnoses presenting as a non-ideal tool for screening T2DM, however, in a country with a public health system, its high specificity can identify women with PCOS who should be closely monitored.

Abstract ID #215

Abstract Title: Clinical Science

Soucie K (1), Thai L (2), Ottey S (2), Williams SL (3), Delau O (4), Buyalos RP (5), Patterson W (3), Partridge T (6), Azziz R (7,8,9)

ESTIMATING THE INTANGIBLE BURDEN OF PCOS: THE QUALITY-ADJUSTED LIFE-YEAR (QALY) VALUE

Abstract: BACKGROUND: The Polycystic Ovary Syndrome (PCOS)-related intangible costs (due to pain and suffering and reduced quality of life [QOL]) are unknown. The quality-adjusted life-year (QALY) is a measure of the value of health outcomes, i.e., the fraction of a perfectly healthy life-year that remains after accounting for the damaging effects of an illness or condition.

OBJECTIVE: Determine the QALY values for PCOS.

METHODS: Members of an international patient advocacy organization were surveyed, and QALY values derived from their responses to the 36-Item Short Form Survey (SF-36). We then estimated SF-6D scores via a standardized algorithm (Brazier et al. J Health Econ. 2002;21: 271–92). The SF-6D is comprised of 6 subscales (Physical Functioning, Role Limitations, Vitality, Mental Health, Social Functioning, and Pain). We then regressed these 6-dimensions onto the EQ-5D total score. A utility index was then calculated using the obtained regression weights to obtain a weighted linear sum of the SF-6D scores. The utility scores were scaled using the worst possible score on the SF-6D (Craig et al., Value Health. 2014;17:846-53).We then converted the utility scores to QALY (Prieto & Sacristán. Health Qual Life Outcomes. 2003;1:80), with values ranging from 0-absolute worst to 1-absolute best. An individual with a QALY of 0.5 would lose 50% of the year to poor QOL, whereas someone in perfect health would have a full quality year.

RESULTS: A total of 460 people with PCOS responded to all questions in the survey. Calculated QALY values ranged from 0.21-1.0, with a mean±SD of 0.63±0.15. Of all respondents, 6 (1.3%) had QALY scores ≤0.20, 24 (5.2%) scores 0.21-0.39, 55 (12.0%) scores 0.40-0.49, 102 (22.2%) scores 0.50-0.59, 129 (28.0%) scores 0.60-0.69, 72 (15.7%) scores 0.70-0.79, 51 (11.1%) scores 0.080-0.89, and 21 (4.6%) scores ≥0.90.

CONCLUSIONS: These data suggests that 40% of women with PCOS reported a loss of up to 50% of quality life years and only ~5% reported near perfect health. The mean QALY of PCOS was slightly worse than that of diabetes, which has a population-based1 norm of 0.70 (van den Berg. Health Econ. 2012;21:1508-12). Overall, these data indicate that PCOS critically impacts QOL in affected women, resulting in significant intangible economic burden.

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1 This is a UK based population value.