

DAY 1

Scientific Tracks & Abstracts



4th World Congress on

Polycystic Ovarian Syndrome

June 07-08, 2018 | London, UK

DAY 1

June 07, 2018

Sessions

PCOS and Pregnancy | Prevention and Management of PCOS | Effects of PCOS on Women's Health | Long-Term Effects of PCOS | PCOS and Obesity

Session Chair

George B. Kudolo

UT Health San Antonio, USA

Session Co-Chair

M A Hasanat

Bangabandhu Sheikh Mujib Medical University (BSMMU), Bangladesh

Session Introduction

Title: Effect of exposure to second-hand smoke from husbands on sex hormones, metabolic profiles, clinical phenotypes and pregnancy outcomes in women with polycystic ovary syndrome undergoing ovulation induction

Ronald Wang, The Chinese University of Hong Kong, Hong Kong

Title: Relationship between variants of menstrual disturbance and insulin resistance in patients with polycystic ovary syndrome in Bangladesh

Naresh Parajuli, Bangabandhu Sheikh Mujib Medical University (BSMMU), Bangladesh

Title: Management for women with PCOS prior to desiring pregnancy

Nobuhiko Suganuma, Kyoto University Graduate School of Medicine, Japan

Title: Prepregnancy phenotype and physiological characteristics in PCOS

Tendai M. Chiware, University of Vermont Larner College of Medicine, USA

Title: Insulin resistance and metabolic syndrome among different phenotypes of women with polycystic ovary syndrome

Hurjahan Banu, Bangabandhu Sheikh Mujib Medical University (BSMMU), Bangladesh

Title: The critical role of p66shc oxidative stress pathway in hyperandrogen-induced ovarian fibrosis

Yong Wang, Nanjing University, China

Title: Ratio of total testosterone to dihydrotestosterone as a marker of adverse metabolic parameters in polycystic ovary syndrome

Sukanti Shah, Bangabandhu Sheikh Mujib Medical University (BSMMU), Bangladesh

Polycystic Ovarian Syndrome

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Ronald Wang et al., J Clin Mol Endocrinol 2018, Volume 3
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EFFECT OF EXPOSURE TO SECOND-HAND SMOKE FROM HUSBANDS ON SEX HORMONES, METABOLIC PROFILES, CLINICAL PHENOTYPES AND PREGNANCY OUTCOMES IN WOMEN WITH POLYCYSTIC OVARY SYNDROME UNDERGOING OVULATION INDUCTION

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Smoking in women impairs fecundity at some stages of reproductive process including folliculogenesis, embryo transport, endometrial angiogenesis, and uterine blood flow. Yet little is known about the hazards of second-hand smoke (SHS) exposure in women with PCOS. This is a secondary analysis of the Polycystic Ovary Syndrome Acupuncture and Clomiphene Trial (PCOSAct), a large randomized controlled trial conducted at 27 hospitals from 2012 to 2015 in mainland China. Out of 1,000 women with PCOS, SHS exposure status were available in 500 women, of whom 271 women were non-exposed, and 229 exposed to cigarette smoke (170≤10 cigarettes per day as low-SHS exposed and 59>10 cigarettes per day as high-SHS exposed). We compared circulating sex steroids, glucose and lipid metabolism, metabolic syndrome and phenotypes, fertility and obstetric outcomes between non-exposed and exposed women. Women exposed to SHS, compared to non-exposed women, had a higher serum total testosterone (1.7 vs 1.5 nmol/L, P=0.01), free androgen index (5.7 vs 4.0, P=0.001) and lower sex hormone binding globulin (30.1 vs 35.6 nmol/L, P=0.03). Metabolic syndrome, but not other phenotypes, was more frequent in exposed women as compared to non-exposed women (21.8% vs 13.3%, adjusted OR=1.66; 95% CI, 1.02–2.71, P=0.04). Ovulation rates between exposed and non-exposed groups were not significantly different (76.9% vs 82.9%, adjusted OR=0.72; 95% CI, 0.45–1.15, P=0.17). Conception rates were significantly

lower in exposed group (26.6% vs 36.9%; adjusted OR=0.61; 95% CI, 0.41–0.91; P=0.01), while clinical pregnancy and live birth rates showed a similar trend that was not significantly different. Gestational age, birth weight and other obstetric outcomes were not affected by SHS exposure. In conclusion, SHS exposure is associated with worsened biochemical hyperandrogenism, higher incidence of metabolic syndrome and reduced conception rates in women with PCOS. These data suggest that smoking partners of infertile women with PCOS who seek treatment should be advised to quit smoking.

Biography

Ronald Wang is currently Professor at the Department of Obstetrics & Gynaecology, Deputy Director, Prenatal Genetics Diagnosis Centre; Laboratory-in-charge, Department of Obstetrics & Gynaecology; Professor (by courtesy), School of Biomedical Sciences; and Principal Investigator, Li Ka Shing Institute of Health Sciences, The Chinese University of Hong Kong. His major research interests are in clinical and basic research in reproductive medicine, and he has been recently involved in a RCT on PCOS. With a wide range of experience in clinical diagnosis, medical research and teaching, he was appointed to the Editorial Boards and Review Panels of many important research funding agents and journals. He has worked on many research projects, received a total of 60 million research grants and owns two patents. He has published over 150 ISI articles in many acclaimed journals.

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RELATIONSHIP BETWEEN VARIANTS OF MENSTRUAL DISTURBANCE AND INSULIN RESISTANCE IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME IN BANGLADESH

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Background: Menstrual disturbance in polycystic ovary syndrome (PCOS) may be a predictor for grade of insulin resistance (IR).

Objectives: To observe relation of variants of menstrual disturbances with IR and metabolic syndrome in PCOS.

Methods: This cross sectional study included 100 PCOS women [age: 22.34±4.40 years; body mass index (BMI) 25.96±4.87 kg/m²; mean±SD], diagnosed by Rotterdam criterion and 60 age matched controls (age: 22.98±4.64 years, BMI 21.15±3.91 kg/m²; mean±SD). The subgroups were classified according to menstrual cycle length as: gr-I (<26 days; polymenorrhoeic), gr-II (26–34 days; eumenorrhoeic), gr-III (35–45days; mild oligomenorrhoeic), gr-IV (6 weeks to three months; severe oligomenorrhoeic) and gr-V (>3 months; amenorrhoeic). Insulin and glucose were measured to determine glycemic status and IR.

Results: Oligomenorrhoea was more among the age group of 16–30 (~60%), whereas one third of age group of 31–35 was amenorrhoeic. BMI and waist circumference (WC) were significantly higher in all subgroups of PCOS than control (gr-I: 30±4.49, gr-II: 24.75±3.85, gr-III: 26.08±5.37, gr-IV: 26.02±4.68, gr-V: 83.58±14.51, control: 21.14±3.90 kg/m²; p<0.001; WC: 92.00±0.00, 81.28±9.75, 85.56±11.57, 81.22±10.61, 83.58±14.51 and 72.02±7.44, respectively; p<0.001). PCOS

and control also showed statistically significant differences for IR (100% vs. 27.3% vs. 51.4% vs. 53.8% vs. 61.5% vs. 3.3%, respectively; p<0.001) and metabolic syndrome (50% vs. 11.1% vs. 31.3% vs. 22.25% vs. 41.7% vs. 3.3%; p=0.002) and prediabetes (50% vs. 22.25% vs. 29% vs. 27.8% vs. 33.3% vs. 1.6%; p=0.002). Each subgroup had statistically significant values of fasting glucose, 2-h glucose, fasting insulin, FG/FI, HOMA-IR, total cholesterol, triglycerides, HDL, LDL than that of control (p<0.05 for all). Multiple regression analysis revealed that cycle length of menstruation (p=0.014), WC (p=0.050) and Ferriman-Gallwey score (p=0.0108) were independent predictors of homeostatic model assessment (HOMA-IR) in PCOS.

Conclusions: Prevalence of IR and metabolic abnormalities are higher in PCOS. Subgroups with amenorrhoea and oligomenorrhoea have adverse metabolic profile and IR.

Biography

N Parajuli is a Resident Doctor studying MD in the Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University (BSMMU) Dhaka, Bangladesh. His research interests are in PCOS, Infertility, Diabetes and obesity. He has attended and presented posters in reputed National and International conferences. He is also working as a member in PCOS Study Group at BSMMU, Bangladesh.

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MANAGEMENT FOR WOMEN WITH PCOS PRIOR TO DESIRING PREGNANCY

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As the management for women with polycystic ovary syndrome (PCOS), Japan Society of Obstetrics and Gynecology recommends a treatment using oral contraceptive (OC) or progestin, prior to desiring pregnancy because PCOS is a progressive disease. However, in Japan, OC-users for contraception are only 3%, which means that OC is not a familiar treatment amongst Japanese people. Recently, a medicine consisting of low-dose estrogen-progestin (LEP) became available for the treatment of dysmenorrhea, covered with National Health Insurance. Moreover, a tablet containing much lower hormone doses (Lunabell ULD: ethinyl-estradiol 0.02mg/norethisterone 1mg, Nobelpharma Co.) is widely used. For the management of PCOS women, the effects of OC, LEP, and conventional Kaufmann therapy (conjugated estrogens/progestin) were evaluated from the viewpoints of improvement of gonadotropins (luteinizing hormone (LH) and follicle-stimulating hormone (FSH)) and androgen secretion. The side-effects such as irregular genital bleeding, digestive symptoms, and liver function were compared among those medicines. By indicating our results, we can discuss a better way to prepare the future childbearing among PCOS women.

Biography

Nobuhiko Suganuma—MD, PhD—is a Professor in the Department of Human Health Sciences, Kyoto University Graduate School of Medicine in Japan. He is the Director of Japan Societies of Fertilization and Implantation, Maternal Health, Reproductive Psychology, and Sexual Science. He is also the Councilor of Japan Society of Reproductive Medicine, and Japan Endocrine Society. Recently, he became the President of Japan Society for Uterus Transplantation (JSUTx), and a Vice President of International Society of Uterus Transplantation (ISUTx), specializing in Uterine Factor Infertility Treatment. As a Reproductive Endocrinologist, he demonstrated that the PCOS occurrence could be connected with LH gene variation using molecular biological technologies. Based on this work, he received the Research Award from the Japan Endocrine Society in 1996. Based on the clinical aspects, his group could succeed the first childbirth in Japan in 1994 using TESE-ICSI method. He has established a Center for Advanced Reproductive Medicine in Kyoto University Hospital in 2013, and is performing cryopreservation of oocytes or ovarian tissues as oncofertility management.

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PREPREGNANCY PHENOTYPE AND PHYSIOLOGICAL CHARACTERISTICS IN PCOS

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Introduction: Polycystic ovarian syndrome (PCOS) affects 5 to 10% of women of reproductive age resulting in menstrual abnormalities, hyperandrogenism, infertility, metabolic disturbances and cardiovascular risk. We aimed to examine the subclinical metabolic and cardiovascular features in young women with PCOS.

Methods: 118 young women were recruited, with 15 self-reporting a diagnosis of PCOS. Body composition was evaluated by DEXA scan and physical fitness by VO2 max testing. Women were assessed for blood pressure, response to volume challenge, aortic-femoral pulse wave velocity, flow mediated vasodilation, adrenergic response to Valsalva, as well as uterine, renal and cardiac hemodynamics. Complete blood counts, metabolic and lipid profiles were assessed. Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) was calculated as an index of insulin resistance. All studies were conducted during the follicular phase of the menstrual cycle, or following a withdrawal bleed (mean 9.4±3.5 days).

Results: There was no difference in age between groups. We identified differences in BMI, total fat and fat distribution, all showing statistically significant increases in PCOS. Renal and cardiac volumetrics, as well as laboratory markers also differed in PCOS (Tables 1). We saw no differences between healthy and PCOS subjects in adrenergic response, plasma volume, blood pressure, vessel compliance in response to volume challenge, uterine blood flow, pulse wave velocity and lipid profile. Angiotensin II, urine sodium and creatinine statistically differed between the two groups. Fasting glucose, insulin and HOMA-IR trended higher in PCOS, although not all significantly.

Conclusions: Although our sample size is small, our results suggest that physiology of women with PCOS differs from that of healthy women. These differences may help explain clinical trajectories, both pregnancy related, as well as long term health risks associated with PCOS.

Table 1: Demographics of renal and cardiac volumetric, and laboratory markers

	Healthy	PCOS	P value
N	103	15	N/A
Age (years)	31.2	30.1	0.4
Parous (%)	30	70	0.033
Cycle Day (days)	9.3	9.8	0.6
BMI (kg/m ²)	24.8	30.1	0.003
Android Fat (g)	1919	2902	0.008
Lean Body Mass (kg)	47.7	43.3	0.3
Cardiac Output (L/min)	4.5	5.2	0.23
Uterine Blood Flow (mL/min)	45.3	40.8	0.3
Uterine Index (% Uterine Blood Flow per Cardiac Output)	1.0	0.8	0.01
Small Vessel Renal System Resistance Index	0.07	0.06	0.28
Small Vessel Renal System Resistance Index	0.11	0.08	0.04
Hemoglobin (g/dL)	12.5	13.1	0.007
Hematocrit (%)	35.4	37.7	0.009
Uric Acid (mg/dL)	4.3	5.3	0.01
Creatinine Clearance (mL/min)	125.3	146.1	0.017
Fasting Blood Glucose (mmol/L)	6.28	6.29	0.03
Insulin (mU/mL)	4.8	7.9	0.06
HOMA-IR	1.22	1.64	0.1

Biography

Tendai M Chiware is a Reproductive Endocrinology and Infertility Fellow in Vermont, USA. She attended medical school at the University of Birmingham in the UK. She was a Trainee in the UK and a member of the Royal College of Obstetricians and Gynaecologists. She completed her Residency in Michigan, USA and is board certified with the American Board of Obstetrics and Gynecology. She worked at the Department of Reproductive Health and Research of the World Health Organization in Geneva, Switzerland. Her interests include PCOS, Diminished Ovarian Reserve, Fertility Preservation, Minimally Invasive Surgery, Reproductive Surgery and Global Health. She has presented her work at national and international meetings including, the Society for Reproductive Investigation, and she will be speaking at the European Society of Human Reproduction and Embryology's annual meeting.

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INSULIN RESISTANCE AND METABOLIC SYNDROME AMONG DIFFERENT PHENOTYPES OF WOMEN WITH POLYCYSTIC OVARY SYNDROME

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Background: Polycystic ovary syndrome (PCOS) is a heterogeneous disorder of uncertain etiology.

Objectives: To see the phenotypes and frequencies of insulin resistance and metabolic syndrome in PCOS.

Materials & Methods: This study included 100 PCOS women (age, mean±SD: 23±5 years; body mass index, BMI: 27.6±4.6 kg/m²), recruited on the basis of Rotterdam criteria and 25 healthy controls (age, mean±SD: 24±5 years; BMI: 24.2±4.9 kg/m²). Hormonal analysis was done using chemiluminescent immunoassay. PCOS phenotypes were defined as: A (oligo-anovulation + hyperandrogenism + PCO), B (oligo-anovulation + hyperandrogenism), C (hyperandrogenism + PCO) and D (oligo-anovulation + PCO).

Results: Frequency of PCOS phenotypes were highest for A (57%), followed by D (16%), B (14%) and C (13%). BMI, waist circumference (WC), waist/hip ratio and Ferriman-Gallwey (FG) score showed statistically significant difference when control group was included, but not among the PCOS phenotypes. Highest value of fasting insulin was observed in A followed by D, B and C, and all were higher than control. Frequencies for pre-diabetes, insulin resistance and metabolic syndrome were significantly higher in PCOS. Phenotypes (A vs. B vs. C vs. D) also showed difference for total testosterone (85.82±28.44

vs. 82.84±22.7 vs. 76.09±27.5 vs. 34.35±5.17 ng/dl; p<0.001); testosterone was higher in A, B, C but all had significantly higher level than D (p<0.001 for all). Homeostatic model assessment (HOMA-IR) significantly correlated with BMI, fasting blood glucose, 2-h glucose, total cholesterol and triglyceride in PCOS. Logistic regression showed that age > 25 years, WC > 80 cm, BMI > 25 kg/m², and FG score were risk factors for metabolic syndrome. Using IR as a dependent variable, A and C was associated with 17-fold, 13-fold and 11-fold increased risk of developing insulin resistance, while phenotype D with 9-fold compared to control.

Conclusions: Phenotype A is the most common, followed by others, while A and B have adverse metabolic outcome.

Biography

Hurjahan Banu is presently working in the PCOS Study Group and holds an FCPS Degree in Endocrinology. She is currently a Post-graduate Fellow and a permanent Staff Researcher in the Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. Her research interests are in PCOS, Infertility, Obesity, Diabetes and Thyroid Disorders. She has already published few articles in national and international journals.

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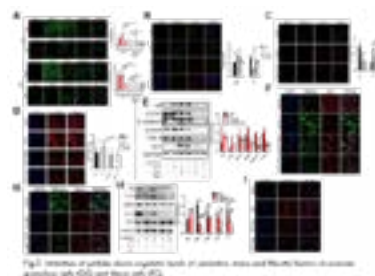
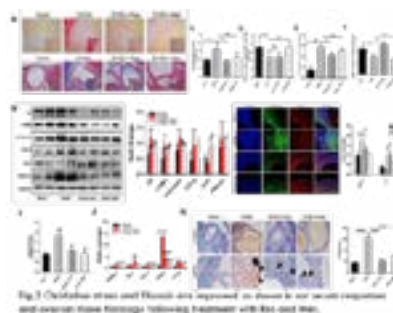
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THE CRITICAL ROLE OF P66SHC OXIDATIVE STRESS PATHWAY IN HYPERANDROGEN-INDUCED OVARIAN FIBROSIS

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Androgen excess is generally considered as one of the major characteristics of polycystic ovarian syndrome (PCOS). Evidence from clinical research has revealed increased levels of oxidative stress (OS) in PCOS patients. Recent research showed that androgen induced PCOS rat existed over fibrosis, which may have influence on ovary function. Our study aimed to investigate the possible inhibition of hyperandrogenic ovarian fibrosis by preventing p66shc-induced oxidative stress. Our data demonstrated that inhibiting the expression of p66shc could suppress ovarian oxidative stress, thereby restraining further fibrosis. In ovarian tissues, reduced fibrosis was observed in resveratrol- and metformin-treated rats. Down-regulation of fibrogenic factors including collagens, TGF- β , CTGF, β -catenin and α -SMA as a result of the inhibition of p66shc was confirmed by western blot, Q-PCR, immunofluorescence and immunohistochemistry. We also observed that p66shc was mainly expressed in the nuclei of granulosa cells (GC) and theca cells (TC). Knockdown of p66shc resulted in dramatic down-regulation of ROS and fibrogenic factors such as TGF- β , CTGF, β -catenin and α -SMA in ovarian granulosa cells and theca cells. Furthermore, inhibition of fibrosis was accompanied with markedly improved ovarian morphology, increased luteal cell number and lowered levels of androgen. These findings suggest that p66shc may be a direct target of SIRT1 for inducing ROS and thus promoting fibrosis. We believe that further exploration of the mechanisms of p66shc in both fibrosis and oxidative stress may provide therapeutic strategies in improving PCOS symptoms and reproductive function.



Biography

Yong Wang is a Professor at Medical School, Nanjing University, China whose research interest focuses on Polycystic Ovary Syndrome. He is dedicated to the teaching of Histology and Embryology.

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RATIO OF TOTAL TESTOSTERONE TO DIHYDROTESTOSTERONE AS A MARKER OF ADVERSE METABOLIC PARAMETERS IN POLYCYSTIC OVARY SYNDROME

Sukanti Shah, Hurjahan Banu, Sharmin Jahan and M A Hasanat

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Background: Polycystic ovary syndrome (PCOS) is a heterogeneous disorder encompassing hyperandrogenism and metabolic disturbances. Androgen excess may correlate with metabolic risk; a lack of clarity persists regarding the specific androgen to be measured.

Aims & Objectives: To determine the association of total testosterone (TT) to dihydrotestosterone (DHT) ratio in assessing the adverse metabolic parameters in PCOS.

Material and method: This study included 44 PCOS women (age, mean±SD: 23.1±4.86 years; body mass index, BMI: 25.78±4.38 kg/m²), recruited on basis of Rotterdam criteria and 44 healthy age matched controls (age, mean±SD: 23.02±4.28 years; BMI: 20.80±3.33 kg/m²). After taking the history, physical examination and anthropometric data in all participants, TT, sex hormone binding globulin (SHBG) and insulin were measured by chemiluminescent immunoassay while DHT by ELISA. TT/DHT ratio, free androgen index (FAI) (TT/SHBG*100) and insulin resistance (homeostatic model assessment (HOMA-IR)) were calculated.

Results: PCOS patients showed significantly higher levels of TT (70.46±27.54 vs. 31.31±13.84 ng/dl; p<0.001), and

FAI (11.24±9.00 vs. 3.03±2.30; p<0.001), and a low SHBG (35.00±31.99 vs. 47.07±23.86 nmol/l; p=0.048) compared to healthy controls. The TT/DHT ratio was significantly higher in PCOS patients (3.62±2.53 vs. 2.06±1.19; p<0.001), no significant difference were found for DHT (p=0.282). In PCOS patients, TT/DHT ratio was significant for impaired glucose tolerance (IGT) (P=0.038) but not for metabolic syndrome (p=0.931), obesity (p=0.094) and insulin resistance (p=0.886). Furthermore, the TT/DHT ratio was found to be high for obese (p=0.004), insulin resistant (p=0.026) and high waist circumference (WC, p=0.002) subjects, irrespective of any group.

Conclusion: TT/DHT ratio may be a useful surrogate marker for adverse metabolic parameters in PCOS..

Biography

Sukanti Shah is a Resident Doctor studying MD in the Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. She has attended and presented posters in reputed national and international conferences. She is also working as a member in PCOS Study Group. Her research interests are in PCOS, Infertility and Obesity.

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DAY 1

Video Presentation



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POLYCYSTIC OVARIAN SYNDROME (PCOS): IT'S NOT JUST ABOUT FERTILITY

Mark P Trolice

Fertility CARE: The IVF Center, Orlando, FL, USA

Polycystic ovarian syndrome (PCOS) is the most prevalent endocrinopathy during the reproductive years, affecting 5%–10% of women, and has been classically associated with ovulatory dysfunction and hyperandrogenism. In 2003, an expert conference was organized in Rotterdam, resulting in revised criteria for making the diagnosis of PCOS using two of the following three features: 1) oligo- or anovulation; 2) signs of hyperandrogenism; and 3) ultrasound evidence of polycystic ovaries. PCOS has a genetic multifactorial inheritance and is associated with a high risk of insulin resistance. Women with PCOS are at increased risk for reproductive and medical complications, including infertility as well as the metabolic syndrome, a ubiquitous pathologic constellation of diseases that place patients at a risk of significant morbidity and mortality. The metabolic syndrome includes abdominal obesity, dyslipidemia, hypertension and pre-diabetes, and occurs at an increased overall prevalence rate of 43%–47% in women with PCOS. The National Cholesterol Education Program–Adult Treatment Panel defines the metabolic syndrome based upon three of the five following factors: waist circumference, fasting serum glucose, fasting serum triglycerides, serum HDL-cholesterol and blood pressure. Further, PCOS patients are significantly predisposed to prediabetes and type 2 diabetes. Metformin is an oral biguanide insulin-sensitizing agent, commonly used to maintain blood glucose control in diabetes and also has a role in menstrual regulation, pregnancy and ameliorating the metabolic syndrome.

In this seminar, the association between the metabolic syndrome and PCOS will be reviewed, as well as evidence based medical therapies and non-pharmacologic therapies to reduce medical complications and improve well-being will be outlined.

Biography

Mark P Trolice, M.D., FACOG, FACS, FACE is the Director of Fertility CARE (Center of Assisted Reproduction & Endocrinology) as well as Clinical Associate Professor in the Department of Obstetrics & Gynecology (OB/GYN) at the University of Central Florida College of Medicine in Orlando. He is the past President of the Florida Society of Reproductive Endocrinology & Infertility (REI) and Central Florida OB/GYN Society as well as past Division Director of (REI) at Winnie Palmer Hospital, part of Orlando Health. He is double Board-certified in REI and OB/GYN and has been awarded the American Medical Association's "Physicians' Recognition Award" annually. He was honored as one among the top 5% of doctors in the U.S. He has authored research studies with publications in many leading medical journals and textbooks. He has lectured at numerous physician conferences and patient seminars around the country. In addition he participated in TV news/talk shows, radio, webcasts and newspapers. He is on the Editorial Boards of The Female Patient and OBG Management, and former Advisory Board of Conceive Magazine and Medical Advisory Council of The American Fertility Association. His current book entitled, "Get Pregnant! Science-based strategies to help you finally overcome infertility and have your baby" is due for release in the Fall of 2019.

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