THE PCOS SOCIETY INDIA

PANDORA

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...The Newsletter of The PCOS Society, India

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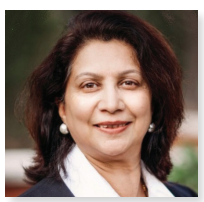
Welcoming....

Our New Patrons



Dr. Madhuri Dixit
Ophthalmologist

Dr. Neha Sardar
Gynaecologist

Dr. Raj Rajeshwari Patil
Gynaecologist

Dr. Rahul Anand Kanakasabapathy
Gynaecologist

Dr. Pragya Gupta
Gynaecologist

Dr. Bharati Karwa
Gynaecologist

Our New Life Members

Dr(Ms.) Sangeeta Sharma	Gynaecologist
Dr. Sudhir Kumar	Physician
Dr. Madhavi Bahulikar	Gynaecologist
Dr. Saubhagya Bhajantri	Gynaecologist
Dr. Sritheja Gurram	Gynaecologist
Dr. Arya Bodhe	Gynaecologist
Dr. Ajay Kushwaha	Gynaecologist
Dr. Varsha Bharti	Gynaecologist
Dr. Imran Kutchi	Gynaecologist
Dr Sandhya Khare	Gynaecologist
Dr. Neena Gupta	Gynaecologist
Dr. D. Senthamaraiselvi	Gynaecologist
Dr. Pallavi Bhatwal	Gynaecologist
Dr. Rohitha Cheluvaraju	Gynaecologist
Dr. Monika Rajput	Gynaecologist
Dr Manjula Pathri	Gynaecologist
Dr. Abhilaasha Macheria	Gynaecologist
Dr. Abhijna Rao	Gynaecologist
Dr. Jyoti Atul Chiddarwar	Gynaecologist
Dr. G. Kirana Selvi	Gynaecologist
Dr. Rajina Muneer	Gynaecologist
Dr. Sandhya Salunkhe	Gynaecologist

Associate Member

Ms. Riddhi Acharya	Gynaecologist

Activity Section

WORD GAME

Find the answers to the below questions in the letter maze.
The answers can be horizontal, vertical, diagonal and backwards.

1 The drug is considered to ameliorate the effects of reactive oxygen species and free radical induced oxidative stress at the mitochondrial level.

2 ---------- helps in increasing the insulin sensitivity, FSH signaling and oocyte maturation.

3 A natural compound found in plants, nuts, red wine and has beneficial effects in PCOS patients.

4 A dopamine agonist used in the treatment of Ovarian Hyperstimulation Syndrome.

5 Aromatase inhibitor used for ovulation induction in PCOS patients.

6 Has proven to be beneficial when used during ovarian stimulation/ has improved the oocyte quality ----------

7 An iatrogenic complication seen more in PCOS patients during IVF.

8 A highly viable and non hormonal treatment option for acne.

A	U	M	L	L	G	S	C	C	A	R	C
N	I	F	Z	C	A	M	S	E	M	T	R
B	S	T	B	A	A	E	L	H	B	W	E
I	S	O	T	R	E	T	I	N	O	I	N
N	E	S	D	N	F	F	H	Z	U	K	I
O	N	L	K	I	O	O	Z	R	L	P	L
S	A	B	B	T	T	R	T	Y	M	O	O
I	I	C	F	I	N	M	M	K	G	V	G
T	K	X	V	N	M	I	S	P	R	L	R
O	G	D	J	E	I	N	F	C	K	J	E
L	O	R	T	A	R	E	V	S	E	R	B
T	M	J	W	H	P	O	N	E	E	A	A
L	E	T	R	O	Z	O	L	E	V	B	C

Created by Dr Nagadeepti Nagarjuna (Youth Brigade)

Solution on page 11

The PCOS WORDLE

Instructions to play

How to play: Point your camera or your QR code scanner to scan the above code.
The aim: Your challenge is to guess a five-letter word in six attempts.

Rules:

- You have to guess the Wordle in six tries or less
- Every word you enter must be in the word list. Once you select your word hit enter.
- A correct letter turns green
- A correct letter in the wrong place turns yellow
- An incorrect letter turns grey
- Letters can be used more than once
- The used letters can be seen on the keyboard below

Created by Dr Riddhi Desai (Youth Brigade)

Editorial

Dr. Duru Shah
MD, FRCOG, FCPS, FICS, FICOG, FICMCH, DGO, DFP
Director, Gynaecworld
The Center for Women's Health & Fertility, Mumbai
Founder President, The PCOS Society, India
Chief Editor, Pandora

Dr. Sabahat Rasool
MRCOG (London), MD, DNB
Diplomate in Advanced Infertility
Fellowship in Reproductive Endocrinology
Assistant Professor & Reproductive Medicine Consultant
Editor, Pandora

Dear Friends,

It is so good to see the shadow of COVID Pandemic finally fading away! We have started our lives afresh, finally stopped calling days of the week as Thisday, Thatday, Otherday, Someday, Yesterday & Today. We lost many, but the band continued to play when the Titanic was sinking!

This is the 20th Edition of Pandora and thanks to the newsletter for keeping us all connected through times good and bad. We are proud to announce that the PCOS Society of India has bought an office space for the Society at Worli, Mumbai, which is till now housed complimentary at Gynaecworld. It has taken a lot of toil and hard work to finally take this big leap!

Truly excited about the **Grand Finale of "PCOS Quizzes"** which will be held during the Annual Conference with our top 3 young colleagues bagging huge cash awards of Rs. 1 lakh, 75,000 and 50,000! So please get started. The 1st Elimination Round will be held on 21st August, 2022 and the 2nd Elimination Round will be held on 28th August, 2022.

The current issue of Pandora will take you through some brilliant academic works, and Society's activities both offline and online. We have been hosting W3 Webinars and Science Live Programs regularly and trying to cover different facets of PCOS through interactive and exhaustive discussions with experts. Our **Annual International Conference** is scheduled to be held between 16th and 18th September at Mumbai and we are looking forward to having you all join us in this academic feast. The details of the Conference are available on pages 6 & 7.

Member of the Society have the privilege of getting certified for the **"Expert Course"** and the **"Basic Course on PCOS"**.

Please visit our website www.pcosindia.org enjoy the wealth of information on it and become life members to enjoy a lovely journey with us!With warm regards,

Dr. Duru Shah
Chief Editor, Pandora
Founder President, The PCOS Society

Dr. Sabahat Rasool
Editor, Pandora

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Debate: Laparoscopic Ovarian Drilling

Dr Kaberi Banerjee
- MBBS, MD (AIIMS), FRCOG (UK), Commonwealth Fellow IVF (UK)
- Medical Director, Advance Fertility and Gynae Centre (AFGC), New Delhi

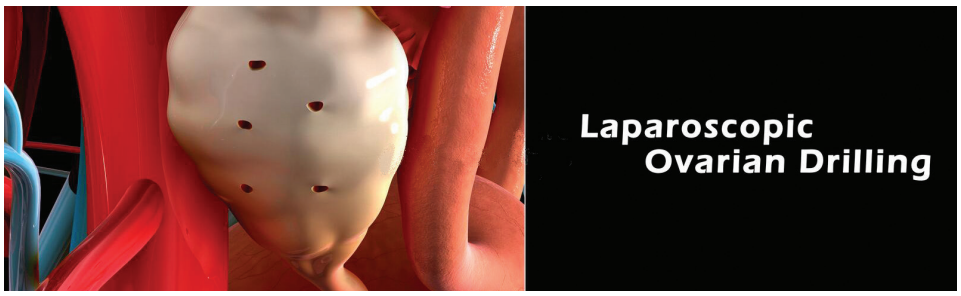
Dr Parikshit Tank
- MD,DNB,FCPS,DGO,MNAMS
- Consultant Ashwini Maternity & Surgical Hospital, Mumbai

LAPAROSCOPIC OVARIAN DRILLING – PRO

Laparoscopic ovarian drilling (LOD) , mediated mainly by thermal effects, produces a series of morphological and biochemical changes. These changes include the formation of artificial holes in the very thick cortical wall, loosening of the dense and hard cortical wall, destruction of ovarian follicles with a subsequently decreased amount of theca and/or granulosa cells, destruction of ovarian stromal tissue.

LOD may increase ovarian blood flow, allowing a high delivery of gonadotrophins, improved insulin sensitivity and post-surgical local growth factors.

The way LOD is performed also decides its efficacy and safety. Four punctures per ovary using a power setting of 30 W applied for 5 s/puncture (i.e., 600 J/ovary) are sufficient to produce optimal response . Reducing the thermal energy (<300 J/ovary) and/or number of punctures (2/ovary) reduces the chances of spontaneous ovulation and conception, while higher thermal doses (>1000 J/ovary) and/or number of punctures (≥7/ovary) causes extensive tissue destruction without additional improvement in outcomes.



The spontaneous ovulation and pregnancy rates after various techniques of LOD, are 30-90% to 13-88% respectively, within 1-year of the procedure. LOD alone is usually effective in about 50% of women. Nada et al in 2020 found the clinical pregnancy rate higher and OHSS rate lower in the group that underwent LOD.LOD may be considered in women with CC-resistant PCOS, particularly when there are other indications for laparoscopy, if there is a high risk of multiple pregnancies or a contra-indication of multiple pregnancies.

A study in 2019 evaluated the long term pregnancy rate of LOD. Pregnancy was obtained in at least 137 (47.4%) women after drilling, and 71 (51.8%) of these pregnancies were spontaneous, 48 (16.6%) women achieved at least two pregnancies after drilling, and 27 (56.3%) of these were spontaneous. It appeared that a second drilling was effective either when the first drilling had been successful (pregnancy achieved after drilling) or when it had failed in cases of high AFC greater than 55. The predictive factors for effectiveness were a normal body mass index (BMI), an infertility period of less than three years, an AFC of less than 50, and an age of less than 35.

Complications like multiple pregnancies, miscarriage, and development of gestational diabetes, pre eclampsia and premature delivery were studied in women who conceived after CC, LOD or Metformin. The highest complication rate was in the CC group (70%), followed by LOD (45%) and

Continued on page 11

LAPAROSCOPIC OVARIAN DRILLING – THE CASE AGAINST

Every surgical procedure, however archaic, can be justified in a small minority of the population that is subjected to it. The utility of the procedure cannot be judged in this narrow, niche context. It should be assessed in the framework of whether it serves a useful purpose in the majority of situations. Keeping these considerations in mind, Laparoscopic Ovarian Drilling (LOD), a popular procedure in treating women with PCOS-related infertility in the 1980s and 90s is something that is best relegated to the archives.

LOD has too many things going against it to be considered as a useful treatment option in modern times. The most important ones are discussed in this portion of the debate article.

For starters, this is a surgical intervention. Even though general anesthesia and laparoscopic surgery are safer today than they have ever been, there is still a tangible risk associated with both these aspects of LOD. It does not come risk-free. The risks of general anesthesia and laparoscopic surgery are well known. They can in rare circumstances even be fatal.

The indications for doing LOD in women with PCOS have narrowed down over time. Surgeons have become more selective in their approach. However, there are no clear guidelines on who represents an ideal candidate. In the absence of such guidelines, decisions are based on an amorphous set of criteria which keep changing with surgeons, populations and care settings with some decisions made quite arbitrarily.

If one looks at the effectiveness of LOD in restoring ovulation and fertility in women with PCOS, it is comparable to gonadotropin based ovarian stimulation combined with intrauterine insemination carried out in 3 to 4 cycles. This is of course, a rough equivalence. The surgical procedure has a lower success rate than what can be expected in a cycle of ART with subsequent thaw transfers.

The negative fallouts of LOD on fertility are only too real to ignore. The drop in ovarian reserve is marked when the procedure is performed in women with PCOS who have a borderline ovarian reserve assessment and also in those over 35 years. This has been curbed to some extent with the standardization of puncture techniques. Yet, every thermal damage to the ovary is an iatrogenic reduction of ovarian reserve, a resource that is irreplaceable. There is also the chance of developing peritubal adhesions after LOD, leading to an altered anatomy and adding another dimension to the couple's fertility issues.

For all these reasons, one should consider LOD as a surgery performed in bygone times and not a useful intervention in PCOS related infertility.

PCOS Diagnosis in Adolescents

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- Executive Director Monash Partners Academic Health Sciences Centre

Dr Anju Joham
- MBBS (Hons), FRACP, PhD
- Endocrinologist, Monash Health, Ausralia

The diagnosis of polycystic ovary syndrome (PCOS) during adolescence is challenging as the diagnostic criteria that have been used in adult women such as irregular menstrual cycles, acne and polycystic ovary morphology (PCOM) on pelvic ultrasound can be normal physiological events occurring during puberty.

Menstrual cycle variability is common during adolescence,[1] but decreases with age, with the majority of adolescents achieving regular menstrual cycles and higher ovulation rates 3-5 years post-menarche, which relates to the physiological maturation of the hypothalamic-pituitary-ovarian axis.[2, 3] One of the criteria required for diagnosis of PCOS during adolescence is the presence of irregular menstrual cycles and ovulatory dysfunction.[4] As menstrual irregularity is common in healthy

adolescents soon after menarche,[1, 2] a clear and detailed definition of what constitutes normal and abnormal irregular menstrual cycles must include menstrual cycle duration and time post-menarche.[4, 5] The most updated definition of irregular menstrual cycles or oligo/amenorrhoea during adolescence includes the following: 1) Part of normal pubertal transition less than 1 year post-menarche; 2) Cycles > 90 days for any one cycle more than 1 year post-menarche; 3) Cycles < 21 or > 45 days between 1 and 3 years post-menarche; and 4) Cycles < 21 or > 35 days (or < 8 cycles per year) > 3 years post-menarche. Additionally, primary amenorrhoea defined as menstrual cycles that have not started by age 15 years or within 3 years post-breast development is a feature of PCOS if associated with hyperandrogenism.[4, 5]

Healthy post-menarcheal girls can have PCOM as increased ovarian volume can be present after menarche[6] and higher number of follicles are also often present in healthy post-menarcheal girls.[7] PCOM is detected in upto 70% of adolescents (using original criteria for PCOM); therefore, **the PCOS evidence- based guideline does not recommend use of PCOM for diagnosis of PCOS in adolescents until eight years post menarche[8] due to the overlap of PCOM in healthy adolescents and adolescents with PCOS, as it may lead to overdiagnosis of PCOS in this cohort.**

Currently, the 2003 Rotterdam criteria is the most widely used diagnostic criteria for PCOS and this is also the definition recommended by the 2018 international PCOS evidence-based guideline to diagnose adult women.[8] Due to the overlap of PCOS diagnostic features with normal pubertal physiology, the application of the Rotterdam criteria in adolescents is likely to over-diagnose adolescents with PCOS with potential detrimental long-term health implications.[9] With a lack of research on an accurate diagnostic approach in adolescents, based on evidence-informed consensus, the new PCOS guideline recommends modified diagnostic criteria in adolescents. **The guideline recommends that the diagnosis of PCOS in adolescents requires menstrual cycle irregularity well defined according to time post menarche and clinical hyperandrogenism (severe acne and/or hirsutism) / biochemical hyperandrogenism as the two essential criteria.[8] It is recommended that PCOM should not be used as a criterion for PCOS diagnosis within eight years of menarche.[8]** Adolescents meeting one of the PCOS diagnostic criterion may be considered "at risk" of PCOS and benefit from follow up, in addition to symptom management.

A recent publication from the Raine Study in Western Australia, which is a community-based prospective cohort study that enrolled and followed-up more than 2900 pregnant women and their subsequent live births from 1989 compared PCOS prevalence in this cohort using two adolescent specific diagnostic criteria. Using the adult Rotterdam criteria (requiring at least two features of oligo/amenorrhoea, hyperandrogenism and PCOM) led to 29% of this adolescent population meeting the criteria for PCOS, however adolescent specific criteria (requiring both oligo/amenorrhoea and hyperandrogenism and not including PCOM) detected a prevalence of 16% which is comparable to the estimated adult prevalence shown in literature[10]. Furthermore, the group of adolescents who fulfilled the adolescent diagnostic criteria demonstrated higher body mass index (BMI) trajectories commencing from pre-pubertal years compared to those without PCOS. In comparison, the adolescents meeting the original adult Rotterdam criteria phenotypes oligo/amenorrhoea and PCOM or hyperandrogenism and PCOM, had similar BMI trajectories to those without PCOS. **Using the adolescent criteria identifies adolescents with PCOS who are at risk of rapid BMI trajectory and weight gain, representing a high risk group that are likely to benefit from early intervention to prevent clinical sequelae of PCOS.**

PCOS diagnosis in adolescents can be

Continued on page 11

Table 1. PCOS diagnostic criteria and phenotypes

	1990 NIH criteria			
	AE-PCOS criteria			
	2003 Rotterdam criteria			
	Phenotype A	Phenotype B	Phenotype C	Phenotype D
Hyperandrogenism	+	+	+	-
Ovulatory dysfunction	+	+	-	+
Polycystic ovary morphology	+	-	+	+

AE-PCOS: Androgen Excess and Polycystic Ovary Syndrome Society; NIH: National Institutes of Health.

Pre-Congress Workshops & 7th Annual Conference

Old Questions, New Answers .....all about PCOS!

16–18th September 2022

16th September 2022 – PRE-CONGRESS WORKSHOPS

Convenor: Sujata Kar & Padma Rekha Jirge

9:30 am to 6:30 pm – Workshop I:
BASICS OF FERTILITY MANAGEMENT IN PCOS

9.30 am – Welcome and introduction to the Workshop

9:45 to 11:00 am – Session 1: Diagnosis in PCOS

9:45 am – Diagnosis of PCOS– Do's and Don'ts
10:00 am – Differential diagnosis of PCOS
10:15 am – Assessment of Ovarian Reserve
10:30 am – Case Presentation followed by discussion with Experts & Moderators

11.00 to 12.15 pm – Session 2: Impact on Fertility in PCOS

11.00 am – Insulin Resistance
11.15 am – Hyperandrogenism
11.30 pm – Obesity
11.45 pm – Case Presentation followed by discussion with Experts & Moderators

12.15 to 1.30 pm – Session 3: Fertility Management

12.15 pm – Use of Oral Ovulogens in Non-ART cycles
12.30 pm – Use of Gonadotropins in Non-ART cycles
12.45 pm – Prevention and management of OHSS
1.00 pm – Case Presentation followed by discussion with Experts & Moderators

1.30 pm to 2.30 pm Lunch

2.30 to 3.45 pm – Session 4: Monitoring the stimulated cycle

2.30 pm – Follicular Monitoring with US + hormones
2.45 pm – Triggering Ovulation.
3.00 pm - Managing the Luteal Phase.
3.15 pm – Case Presentation followed by discussion with Experts & Moderators

3.45 to 5.00 pm – Session 5 – Optimizing Fertility Outcomes in PCOS

3.45 pm – Role of Adjuvants
4.00 pm – Laparoscopic ovarian drilling
4.15 pm – Nutrition for Lean & Obese
4.45 pm – Case Presentation followed by discussion with Experts & Moderators

5.00 to 6.15 pm – Session 6.: The Final Step: Assisted Reproduction

5.00 pm – Advanced Reproductive Age
5.15 pm – Intrauterine Insemination
5.30 pm – Assisted Reproduction
5.45 pm – Case Presentation followed by discussion with Experts & Moderators

6.15 to 6.30 – Take Home Messages from the Workshop

6.30 pm – Tea / Coffee Break

7:30 pm – 8:30 pm Convocation

8:30 pm – Paid Banquet

9:15 am to1:30 pm – Workshop II:
PCOS AND ASSISTED REPRODUCTION

……..In collaboration with ASPIRE (Asia Pacific Initiative on Reproduction)

Convenors: Duru Shah, Madhuri Patil

9:15 – Welcome and Introduction to Workshop

9.30 am to 10.45 am – Session 1: Follicular Phase in PCOS

9:30 am – How does Pre-stimulation treatment impact success?
9:45 am – How should we customise Ovulation Induction Protocols?
10:00 am – Do adjuvants help?
10:15 am – Discussion

10.45 am to 12.00 noon – Session 2: Luteal Phase in PCOS

10.45 am – Does the trigger matter?
11.00 am – Which Luteal Phase Support is safe and effective?
11.15 am – How do we prevent OHSS?
11.30 am – Discussion

12.00 noon to 1.30 pm – Session 3: Implantation phase in PCOS

12:00 pm – What is the optimum endometrium needed fo implantation?
12:15 pm – How do we enhance the thin Endometrium in a freeze all cycle?
12:30 pm – Do adjuvants help?
12:45 pm – Discussion

1:15 pm to 1:30 pm – Take Home Messages from the workshop

1.30 pm to 2.30 pm Lunch

2.30 pm to 6.45 pm – Workshop III:
HORMONES IN PCOS AT PERI MENOPAUSE

……In collaboration with International Menopause Society

Convenor: Sudha Sharma

2:30 – Welcome and Introduction to Workshop

2.35 pm to 3:50 pm – Session 1: Androgens, Estrogens, Progesterones at midlife

2:35 pm – Do hyper androgenic women have an increased libido?
2:50 pm – Are vaginal oestrogens effective for sexual function?
3:05 pm – Do OC pills affect the sex drive?
3:20 pm – Discussion

3:50 pm to 5.20 pm – Session 2: Menopausal Hormone Therapy in PCOS Women

3:50 pm – Which MHT is ideal for Menopausal symptoms?
4:05 pm – What are the benefits v/s risks in PCOS women?
4:20 pm – Can we offer MHT to women in special situations?
4:35 pm – Discussion

5.05 pm to 6:20 pm – Session 3: The Obese PCOS woman

5:05 pm – How do we manage dermatological issues in midlife PCOS women?

5:20 pm – How do lean PCOS and obese PCOS differ at Perimenopause and beyond?

5.35 pm – How do we best manage metabolic syndrome in PCOS women?

5:50 pm – Discussion

6.20 pm to 6.30 pm – Take Home Messages from the Workshop

6.30 pm to Tea / Coffee Break

7:30 pm to 8:30 pm Convocation

8:30 pm – Paid Banquet

DAY 1: CONFERENCE – 17th September 2022

9.00 am to 10.30 am – Session 1: Hormones in PCOS

9.00 am – Should Serum AMH replace PCOM as a diagnostic marker?

9.20 am – How does hormonal monitoring assist ultrasound monitoring in ART cycles?

9.40 am – Is it important to assess thyroid disorders in PCOS?

10.00 am – Discussion

10.30 am to 11.00 am – Session 2: Key Note Address: "Cognition and Mood: The role of reproductive hormones in PCOS"

11.00 am to 11.30 – Coffee Break

11.30 am – 01.00 pm – Session 3: PCOS and Pregnancy ……In collaboration with RCOG

11.30 pm – Progesterone therapy in the first Trimester- What is the best protocol?

11.45 pm – What is the significance and risk of excessive weight gain in the mid-trimester?

12.00 pm – Does maternal hyperandrogenaemia and obesity lead to PCOS in the future generation?

12.15 pm – How do we prevent PCOS in adulthood in an Obese prepubertal girl?

12.30 pm – Discussion

1.00 pm to 2.00 pm – Lunch

2:00 to 2.30 pm – Session 4: Keynote Address: "Advocacy and mentorship in PCOS"

2.30 pm to 4:00 pm – Session 5: Gut Dysbiosis, the "Leaky Gut" and PCOS

2:30 pm – What is the "Leaky Gut" and can it lead to PCOS?

2:50 pm – What is the connection between Vaginal or Gut Dysbiosis and Fertility?

3:10 pm – How should we manage Dysbiosis?

3:30 pm – Discussion

4.00 pm to 5.30 pm – Session 6: Managing the Adolescent with PCOS – Which OC Pill and when?

4.00 pm – Acne & Hirsutism

4.20 pm – Endometriosis

4.40 pm – Abnormal Uterine Bleeding

5.00 pm – Discussion

5.30 pm – Coffee Break

6.00 pm to 7.00 pm – Session 7: Posters Judging Session

6:00 pm to 7:00 pm – Annual General Body Meeting.

7.00 pm to 8.30 pm – Inauguration

8.30 pm onwards Banquet with Entertainment

DAY 2: CONFERENCE – 18th September 2022

8.30 am to 9.30 am – Session 8: Poster Prize Winners – Invited Oral Presentation Session

9.30 am to 11.00 am – Session 9: Adjuvants in PCOS

9.30 am to 09:50 am – Can Metformin prevent Diabetes?

9.50 am to 10:10 am – Do Inositols work?

10:10 am to 10:30 am – Melatonin - Does it improve sleep and reduce androgens?

10.30 am – Discussion

11.00 am to 11.30 Coffee Break

11.30 to 12.30 pm – Session 10: Key Note Lectures

11.30 to 12.00pm – "Sexuality in PCOS"

12:00 to 12.30pm – "Adipose tissue in PCOS: linking metabolic & reproductive dysfunction."

12.30 to 1.30 pm – Session 11: "Grand Finale of PCOS Quizzes"

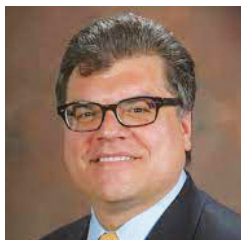
1.30 to 2.30 pm – Lunch

2:30 to 3:30 pm – Youth Brigade Session

3:30 to 4:00 pm – Valedictory Session with Lucky Dip Prizes

4:00 to 5:00 pm – Tea/Coffee

Our International Faculty



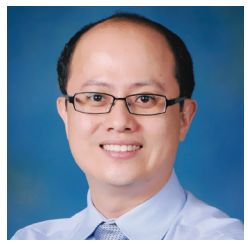
Dr. Ricardo Azziz
(USA)

Prof. Anuja Dokras
(USA)

Prof. T.C.Li
(Hong Kong)

Prof. Pauline M. Maki
(USA)

Dr. Virgilio Novero
(Philippines)



Prof. Ang Sengbin
(Singapore)

Strategies to Reduce Multiple Pregnancy in Medically Assisted Reproduction (MAR)

Dr. Mohan S Kamath
- MS (AFMC),DNB, Fellow (Reproductive Medicine, CMC, Vellore)
- Professor and Head, Department of Reproductive Medicine and Surgery CMC, Vellore

Dr. Treasa Joseph
- MS, Fellow (Reproductive Medicine, CMC, Vellore)
- Assistant Professor, Department of Reproductive Medicine and Surgery, CMC, Vellore

Multiple pregnancy is one of the commonest preventable adverse outcomes associated with Medically Assisted Reproduction (MAR). The Human Fertilisation Embryology Authority(HFEA) from the UK reported that around 15% of conceptions following assisted reproductive technology (ART) were multiple pregnancy (1). There is a reported five-fold increase in still birth and a seven-fold increase in neonatal death in multiple pregnancy compared to singleton pregnancy (2). Additionally,multiple pregnancy is associated with an increased risk of maternal adverse outcomes such as hypertensive disorders of pregnancy, gestational diabetes and post-partum haemorrhage along with a four-fold rise in healthcare cost (3). It is worthwhile to note that the increase in maternal and perinatal risks are directly related to the number of foetuses. As a result, regulatory authorities governing ART practices have recommended different strategies in order to reduce multifoetal pregnancy. A decreasing trend has been reported in the European population with reduction in the incidence of twin pregnancy from 20.6% in 2010 to 14.5% in 2016. (2)

Elective single embryo transfer (eSET) is the principal strategy adopted for primary prevention of multiple pregnancy following ART. The recent Cochrane review reported significantly lower live birth rate (LBR) following a single cycle of eSET (Risk Ratio, RR 0.67; 95% CI 0.59–0.75; women = 1,904) as compared to double embryo transfer (DET) (4). This was associated with a significant decrease in multiple pregnancy rates with eSET (4). However, the same review reported that women with a 42% chance of live birth following DET had a comparable 34-46% chance of live birth after two successive SETswith 0-3% risk of multiple pregnancy(4). It must be noted that the decrease in the effectiveness of eSET following a single transfer could be substantially negated with successive frozen embryo transfers. The availability of a robust vitrification program and couples'acceptance for multiple transfers is an essential requirement for the success of the eSET policy.

Non-ART treatment such as Ovulation Induction (OI) and controlled ovarian stimulation (COS) with Intrauterine insemination (IUI) have a reported incidence of 8.9% twin deliveries in the European population (1). There is convincing evidence to suggest that multiple pregnancy rates are higher with increase in the number of follicles (5). Strategies for reduction of multiple pregnancy include strict cancellation policies for COS cycles in case of more than three follicles, or aspiration of excess follicles prior to the trigger (6).In a recent network metanalysis which included 2098 women, authors reported that LBR following ovulation induction with gonadotrophins were found to be comparable with oral agents such as clomiphene and letrozole (7). The same review reported a significant linear increase in multiple gestations with gonadotrophins as compared to oral agents specifically when cancellation policies were liberal (>3 follicles) (7). **Therefore it would be worth considering oral ovulogens for OI especially in treatment of women with PCOS or IUI for mild male factor which aims at monofollicular response.**

Monozygotic twining which occurs due to splitting of the zygote could be considered a possible adverse effect of ART procedures possibly due to manipulation or extended culture of the embryos prior to transfer (8,9). Evidence is limited to conflicting results based on observational studies with a paucity of adequately powered randomised trials reporting monozygotic twinning. Pooled results of 16 observational studies reported increased incidence of monozygotic twinning with assisted hatching (OR 1.17; 95% CI 1.09–1.27) (8). A similar association has also been reported with extended blastocyst culture of embryos and monozygotic twinning (OR 2.16; 95% CI 1.74–2.68) (9). However, the results are limited by heterogeneous nature of the included studies. Embryo biopsy is the core step required for preimplantation gestational test (PGT). In a large cohort study including more than two lakh SET cycles, authors reported a significant increase in monozygotic splitting in biopsied embryos for PGT (OR 1.64, 95% CI 1.19–2.27) as compared to non-biopsied embryos (10).Younger maternal age was also found to have an association with monozygotic twinning (OR 1.29; 95% CI 1.03–1.62) following ART(8). **Avoidance of untoward manipulation of embryos and restricted use of invasive techniques is probably an important step in order to reduce the incidence of monozygotic twinning following ART.**

In conclusion, it is important to highlight that multiple pregnancy must be prevented following ART and non-ART treatments in order to prevent detrimental effects on the maternal and perinatal outcomes as well as the indirect effects on healthcare costs and psychological well-being of the couple. **Legislative regulations for implementation of the eSET policy and universal recommendations for embryo transfer number are central to reducing the incidence of multiple pregnancy following ART.** Guidelines and regulatory policies are

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Hot off the Press

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Treatment of Lean PCOS Teenagers: A Follow-up Comparison Between Myo-Inositol and Oral Contraceptives[1]

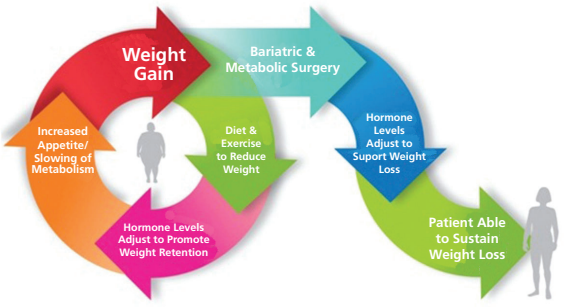
Treatment of PCOS is challenging, more so when it is a lean adolescent. The authors evaluated a suitable therapeutical approach for these patients. The diagnosis was assigned according to Adolescent Diagnostic Criteria in two age groups 13-16 years and 17-19 years. They treated 118 lean PCOS teenagers for 3 months either with oral contraceptive pills (OCP) drospirenone/ethinylestradiol, Myo-Inositol (MI) or OCP plus MI.

13-16 years old lean teenagers treated with MI and in 17-19 years group, MI with OCP exhibited a significant decrease in weight and body mass index (BMI), and an effective improvement in the metabolic and hormonal profile. They found a different scenario in the two age ranges.

With the older teenagers a combination of MI with OC seems more effective. They concluded that MI alone or in combination with OCP could be effective to improve both metabolic and hormonal parameters of PCOS adolescents.

Metabolic Surgery on Patients with Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis[2]

This systematic review and meta-analysis aimed to evaluate the therapeutic effects of metabolic surgery on obese patients with PCOS. A total of 14 studies involving 501 obese patients with PCOS undergoing metabolic surgery were included. Incidence of PCOS in obese women ranged from 5.5% to 63.5%. The results showed the incidence of abnormal menstruation decreased from 81% to 15% (OR=0.03, 95% confidence interval (CI): 0.01-0.08), while the incidence of hirsutism dropped from 71% to 38% (OR=0.21, 95% CI: 0.06-0.74). Serum total testosterone and free testosterone levels decreased by 25.92 ng/dL (MD = -25.92, 95% CI: -28.90- -22.93) and 2.28 ng/dL (SMD = -2.28, 95% CI: -3.67- -0.89), respectively. Sex hormone-binding globulin (SHBG) levels increased by 26.46 nmol/L (MD = 26.46, 95% CI: 12.97-39.95). Serum anti-Mullerian hormone (AMH) levels decreased by 1.29 ng/mL (MD = -1.29, 95% CI: -1.92- -0.66). Pregnancy rates ranged from 95.2% to 100% postoperatively. These findings



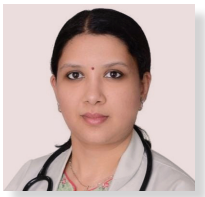
indicate that patients with PCOS are expected to benefit from metabolic surgery, and could help potentially improve their reproductive outcomes. **Metabolic surgery contributed to marked improvement of oligomenorrhea, hirsutism, and free testosterone, total testosterone, SHBG, and AMH in patients with PCOS and could thus be a viable option for the clinical treatment of obese PCOS**.

References

1. Pkhaladze L, Russo M, Unfer V, Nordio M, Basciani S, Khomasuridze A. Treatment of lean PCOS teenagers: a follow-up comparison between Myo-Inositol and oral contraceptives. Eur Rev Med Pharmacol Sci. 2021 Dec;25(23):7476-7485. doi: 10.26355/eurrev_202112_27447. PMID: 34919250.
2. Yue W, Huang X, Zhang W, Li S, Liu X, Zhao Y, Shu J, Liu T, Li W, Liu S. Metabolic Surgery on Patients With Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis. Front Endocrinol (Lausanne). 2022 Mar 10;13:848947. doi: 10.3389/fendo.2022.848947. PMID: 35360056; PMCID: PMC8961297.

Comparison of clinical pregnancy rate between progestin primed ovarian stimulation protocol and gonadotropin releasing hormone antagonist protocol in polycystic ovarian syndrome patients in in-vitro fertilization cycles

A randomised control study was done on 60 PCOS women. 30 women underwent GnRh antagonist Flexible protocol cycle where they received 0.25ug cetrorelix acetate subcutaneously when the follicle size measured around 14 mm till day of trigger. Remaining 30 women who followed the same inclusion and exclusion criteria received Medroxy progesterone acetate 10 mg twice a day till the day of the trigger. All the patients underwent freeze thaw cycle. The ovarian stimulation and clinical outcome was assessed in both the groups. There was no significant difference in the dose or duration of gonadotrophin required. The present study did not have any difference with respect to oocyte retrieved, matured oocytes and embryos. The clinical pregnancy rate was higher in the PPOS group as compared to GnRH antagonist group but it was not significantly higher. In both the protocols, incidence of prevention of OHSS



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and suppression of premature LH was similar. However, cost was significantly lower in the PPOS protocol group as compared to GnRH antagonist group.The clinical pregnancy rate though was high in PPOS group but it is not found to be statistically significant.

Progestin given daily inhibiedt the synthesis and secretion of LH by reducing the frequency of the GnRH pulse, thus correcting the abnormally high LH levels and hyperandrogenism in the intrafollicular environment. Due to increased LH , the progesterone is converted to androstenedione in the theca cells, thus leading to decrease in the intrafollicular environment. Theoretically administration of progesterone leads to normal follicle development and improved oocyte quality, thus improving pregnancy outcomes.

In view of good patient compliance and patient friendly, with decrease cost burden progestin can be considered as an alternative regimen.

Dr. Neelam Kabra , Dr. Nymphaea Walecha , Dr. M. Gouri Devi . IOG, 2022: 12(1);30-36.

Pregnancy, perinatal and childhood outcomes in women with and without polycystic ovary syndrome and metformin during pregnancy: a nationwide population based study.

Romina Fornes, Johanna Simin, Minh Hanh Nguyen

Reproductive Biology and Endocrinology (2022) https://doi.org/10.1186/s12958-022-00905-6

This article is a retrospective cohort study conducted nation wide in Sweden, where it was investigated if PCOS, metformin intake or a combination of both had an influence on the pregnancy, perinatal and childhood outcomes. The cohort included 1,016,805 singleton pregnancies from 686,847 women. Multivariable logistic regression was used to assess the risk of pregnancy and perinatal outcomes, while to determine the risk of obesity during childhood the Cox proportional Hazard modelling was used. Te results were expressed as multivariable adjusted odds ratios (OR) and hazard ratios (HR) and 95% conifdence intervals (CIs), respectively, using the group of women without PCOS and without metformin exposure as reference.

It was seen that PCOS is associated with

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Events Held

	Month	Date	Topic	Supported by
WHAT WHEN WHY W3 Webinar Series	March	26-03-2022	Menstrual Dysfunction in Adolescent PCOS "Why, When & How	Inca Life Sciences a SUN PHARMA division
	April	16-04-2022 30-04-2002	Optimizing success in fertility treatment in PCOS: Role of Adjuvants How important is luteal Support for PCOS women with Infertility?	EDENCE LIFE SCIENCES USV
	May	21-05-2022 28-05-2022	Do PCOS women have an increased risk of Postpartum Haemorrhage? Does Bariatric Surgery help the obese PCOS?	torrent PHARMA USV
	June	18-06-200 25-06-2022	Which investigations during infertility treatment help? Vitamin D, a Hormone or a Vitamin?	METROPOLIS The Pathology Specialist torrent PHARMA
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Newer Dimensions in the Management of PCOS

Date	Topic
26-3-22	Is there any connection between Gut & PCOS?
02-4-22	Insulin Resistance & Hyperandrogenism: The Connection
09-4-22	Lean vs Obese PCOS & ART
23-4-22	Multidisciplinary approach to PCOS

Continued from page 4 (Laparoscopic Ovarian Drilling by Kaberi Banerjee)

finally the Metformin only group (47.5%). CC, but not LOD, increases the complication rate in pregnant patients who received metformin.

One is concerned regarding complications associated with laparoscopy. In a study by Fuentes et al in 2014, of all 2888 laparoscopies included, most were procedures of moderate difficulty (adnexal surgery) (54.2%). The overall frequency of major complications was 1.93%, and that of minor complications was 4.29%. The level of technical difficulty and existence of prior abdominal surgery were associated with a higher risk of major complications and conversions to laparotomy. Since, laparoscopic ovarian drilling is usually done in a pelvis with hardly any adhesions, the complication rate is very low, especially in skilled hands.

Thus, for anovulatory infertility in women with PCOS, LOD is a successful second-line treatment for ovulation induction after the failure of CC. In addition to being as effective as Gn, LOD avoids OHSS and multiple pregnancies. Moreover, several follow-up studies provided evidence of long-term reproductive and endocrinological benefits of LOD.

LOD thus not only helps in regulating ovulation and enhancing conception rates but also provides an opportunity to assess the pelvis for other potential causes of subfertility which could be treated at the same time. We therefore believe that diagnostic hysteroscopy and laparoscopy should be offered quite high-up in the hierarchy of infertility investigations and treatment.

Continued from page 5 (PCOS diagnosis in adolescents)

particularly challenging due to the overlap of PCOS diagnostic features with normal physiological changes during early years post-menarche. Therefore, diagnosis of PCOS during adolescence requires menstrual cycle irregularity well defined according to time post menarche and clinical hyperandrogenism (severe acne and/or hirsutism)/biochemical hyperandrogenism as the two essential criteria. **PCOM should not be used as a criterion for PCOS diagnosis within eight years of menarche. Adolescents meeting one of the PCOS diagnostic criterion may be considered to be "at risk" of PCOS and require follow up in addition to symptom management.**

References

1 Treloar, A.E., Boynton, R.E., Behn, B.G. & Brown, B.W. (1967) Variation of the human menstrual cycle through reproductive life. Int J Fertil 12, 77-126.

2 Legro, R.S., Lin, H.M., Demers, L.M. & Lloyd, T. (2000) Rapid maturation of the reproductive axis during perimenarche independent of body composition. J Clin Endocrinol Metab 85, 1021-1025.

3 Assens, M., Dyre, L., Henriksen, L.S., Brocks, V., Sundberg, K., Jensen, L.N., Pedersen, A.T. & Main, K.M. (2020) Menstrual Pattern, Reproductive Hormones, and Transabdominal 3D Ultrasound in 317 Adolescent Girls. J Clin Endocrinol Metab 105.

4 Peña, A.S., Witchel, S.F., Hoeger, K.M., Oberfield, S.E., Vogiatzi, M.G., Misso, M., Garad, R., Dabadghao, P. & Teede, H. (2020) Adolescent polycystic ovary syndrome according to the international evidence-based guideline. BMC Med 18, 72.

5 Teede, H.J., Misso, M.L., Costello, M.F., Dokras, A., Laven, J., Moran, L., Piltonen, T. & Norman, R.J. (2018) Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Fertil Steril 110, 364-379.

6 Radivojevic, U.D., Lazovic, G.B., Kravic-Stevovic, T.K., Puzigaca, Z.D., Canovic, F.M., Nikolic, R.R. & Milicevic, S.M. (2014) Differences in anthropometric and ultrasonographic parameters between adolescent girls with regular and irregular menstrual cycles: a case-study of 835 cases. J Pediatr Adolesc Gynecol 27, 227-231.

7 Venturoli, S., Porcu, E., Fabbri, R., Pluchinotta, V., Ruggeri, S., Macrelli, S., Paradisi, R. & Flamigni, C. (1995) Longitudinal change of sonographic ovarian aspects and endocrine parameters in irregular cycles of adolescence. Pediatr Res 38, 974-980.

8 (2018) International evidence-based guideline for the assessment and management of polycystic ovary syndrome. Monash University, Melbourne, Australia.

9 Witchel, S.F., Oberfield, S., Rosenfield, R.L., Codner, E., Bonny, A., Ibanez, L., Pena, A., Horikawa, R., Gomez-Lobo, V., Joel, D., Tfayli, H., Arslanian, S., Dabadghao, P., Garcia Rudaz, C. & Lee, P.A. (2015) The Diagnosis of Polycystic Ovary Syndrome during Adolescence. Horm Res Paediatr 83, 376-389.

10 Bozdag, G., Mumusoglu, S., Zengin, D., Karabulut, E. & Yildiz, B.O. (2016) The prevalence and phenotypic features of polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod 31, 2841-2855.

Continued from page 8 (Strategies to Reduce Multiple Pregnancy in Medically Assisted Reproduction)

important for improving the uptake and acceptance of eSET. The use of techniques such as assisted hatching and PGT must be adopted after proper counselling and awareness of possible risks of such invasive procedures.

References

1 C De Geyter, C Calhaz-Jorge, M S Kupka, C Wyns, E Mocanu, T Motrenko, G Scaravelli, J Smeenk, S Vidakovic, V Goossens, The European IVF-monitoring Consortium (EIM) for the European Society of Human Reproduction and Embryology (ESHRE), ART in Europe, 2015: results generated from European registries by ESHRE, Human Reproduction Open, Volume 2020, Issue 1, 2020, hoz038, https://doi.org/10.1093/hropen/hoz038.

2 Perinatal risks associated with assisted reproductive technology. Committee Opinion No. 671. American College of Obstetricians and Gynecologists. ObstetGynecol 2016;128:e61–8.

3 Luke B, Brown MB. Contemporary risks of maternal morbidity and adverse outcomes with increasing maternal age and plurality. FertilSteril 2007;88:283–93.

4 Kamath MS, Mascarenhas M, Kirubakaran R, Bhattacharya S. Number of embryos for transfer following in vitro fertilisation or intra- cytoplasmic sperm injection. Cochrane Database of Systematic Reviews 2020, Issue 8. Art. No.: CD003416. DOI: 10.1002/14651858.CD003416.pub5. Accessed 08 May 2022.

5 Van Rumste MM, Custers IM, van der Veen F, van Wely M, Evers JL, Mol BW. The influence of the number of follicles on pregnancy rates in intrauterine insemination with ovarian stimulation: a meta-analysis. Hum Reprod Update 2008; 14:563–70.

6 Danhof NA, Wang R, van Wely M, van der Veen F, Mol BWJ, Mochtar MH. IUI for unexplained infertility-a network meta-analysis. Hum Reprod Update 2020; 26:1–15.

7 Zolton JR, Lindner PG, Terry N, DeCherney AH, Hill MJ. Gonadotropins versus oral ovarian stimulation agents for unexplained infertility: a systematic review and meta-analysis. FertilSteril 2020; 113:417–25.

8 Busnelli A, Dallagiovanna C, Reschini M, Paffoni A, Fedele L, Somigliana E. Risk factors for monozygotic twinning after in vitro fertilization: a systematic review and meta-analysis. FertilSteril 2019; 111:302–17.

9 Glujovsky D, Farquhar C, QuinteiroRetamar AM, Alvarez Sedo CR, Blake D. Cleavage stage versus blastocyst stage embryo transfer in assisted reproductive technology. Cochrane Database Syst Rev 2016;6:CD002118.

10 Kamath, M. S., Antonisamy, B., & Sunkara, S. K. (2020). Zygotic splitting following embryo biopsy: a cohort study of 207 697 single-embryo transfers following IVF treatment. BJOG: an international journal of obstetrics and gynaecology, 127(5), 562–569. https://doi.org/10.1111/1471-0528.16045

Continued from page 9 (Hot off the Press)

gestational diabetes, preeclampsia, preterm birth and caesarean section. Metformin during pregnancy, regardless of presence or absence of PCOS, was not associated with an increased risk of caesarean section, preterm birth, lower birth weight and low Apgar scores. In conclusion, findings confirm that maternal PCOS may increase the risk of several adverse pregnancy and obesity in children, whereas exposure to metformin may lower this risk. Metformin in women without PCOS was associated with an increased risk of obesity in children yet confounding by indication cannot be ruled out.

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