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Academy of ART

Vol: 10/2022

i-Ceat

**RESONANCE**



# Endometriosis in ART



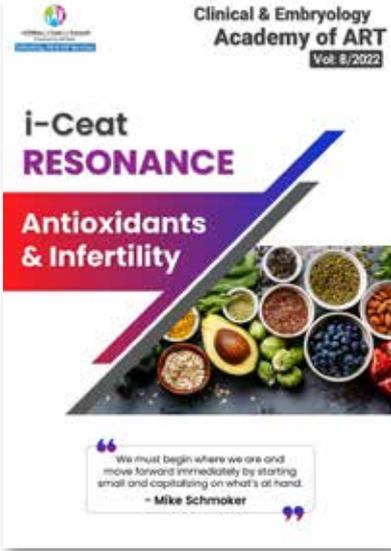
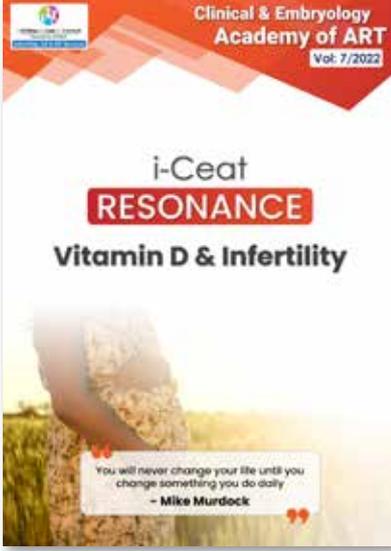
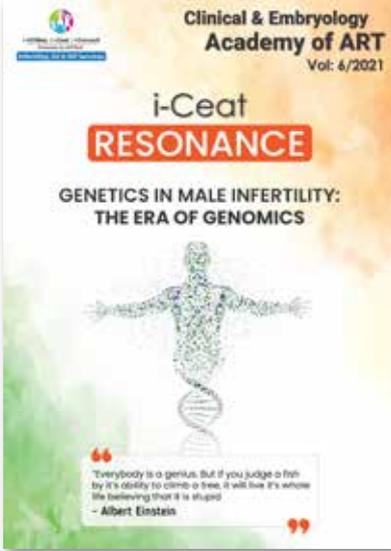
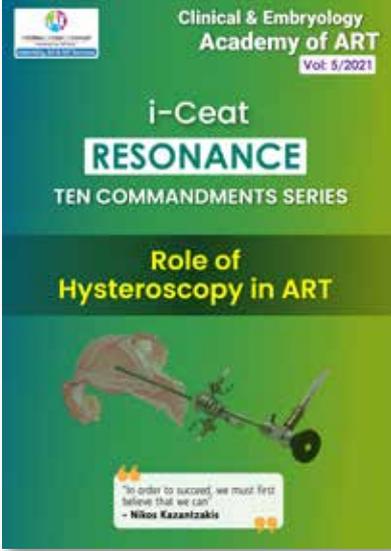
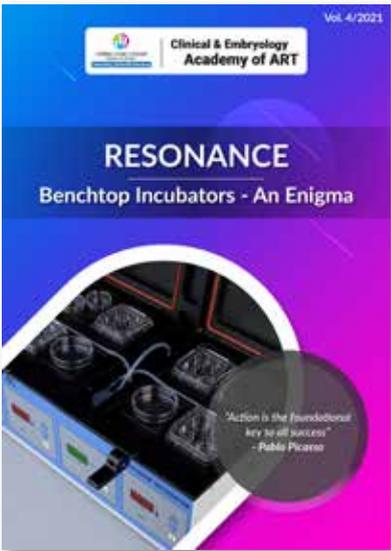
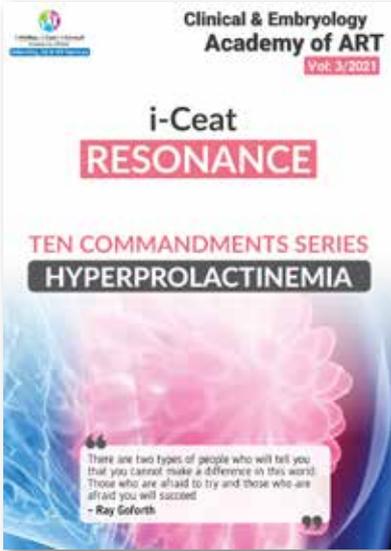
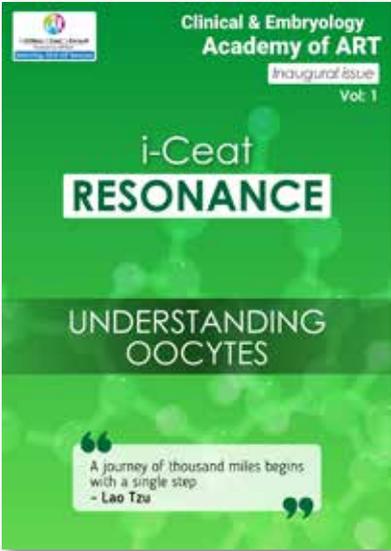
*You will never change your life until you  
change something you do daily.*

— Mike Murdock



# Resonance

## Previous Volumes



# Hands-On Training



# Preface

It has always been a great pleasure and privilege for our team to write on various topics related to infertility/subfertility in order to make it effortless and comprehensive to read for you all. Our academy has released nine volumes of Resonance over the past few months and we are launching the tenth one today. The supreme aim of this bulletin is to cover common as well as burning issues pertaining to infertility and ART in a great detail.

Through this volume, we are hoping to empower your knowledge about endometriosis, one of the most debatable topics in our field. Without any doubt this bulletin will immensely benefit you all to understand endometriosis in great depth and assist you in choosing the best plan of management for women affected with this emotionally and physically disturbing disorder. Along with medical and surgical treatment these women need a lot of empathy and support.

At the end, we would like to wish you all happy reading and learning.

## Guest Editor

### **Dr Sushma Ravi**

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Ambikapur, Chhattishgarh

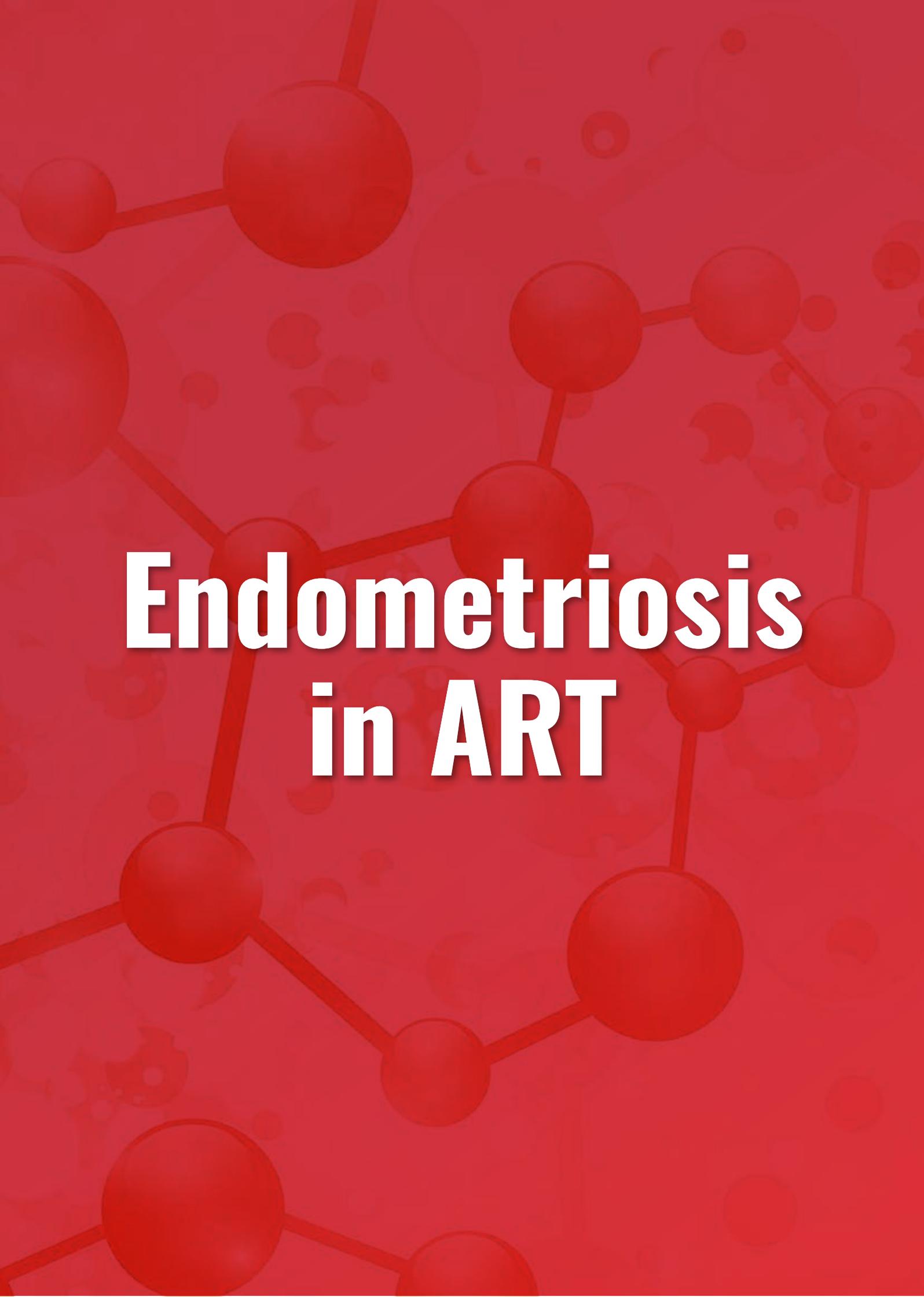
## Series Editor

### **Dr Aakriti Shukla**

MBBS MS (LHMC, New Delhi) MRCOG (UK)  
National Faculty i-Ceat, India

*"I've learned the important little baby steps,  
which teach us how to grow.  
Moving up just one small notch will help us  
more than we know."*

**– Tom Baker**



# **Endometriosis in ART**

# How to approach a patient with endometriosis

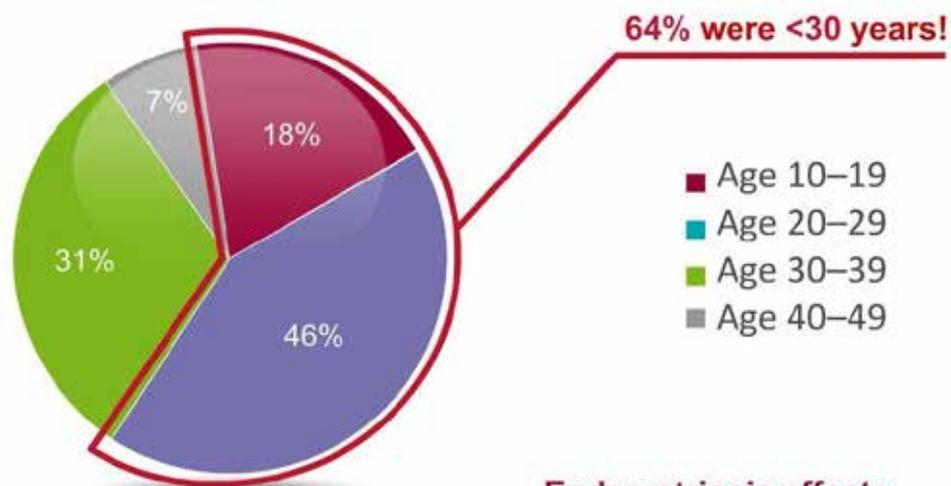
## 1. Introduction

**Endometriosis** is a disease characterized by ectopic endometrial implants throughout the pelvis, sometimes negatively impacting the fertility. Although endometriosis impairs reproduction, it does not usually completely prevent pregnancy. A combination of surgery, ovulation induction with intrauterine insemination, and assisted reproductive technology can help these women conceive.

## 2. Prevalence

The prevalence of endometriosis varies with age and clinical presentation. The prevalence of asymptomatic endometriosis is 1-7%. The overall prevalence of endometriosis in reproductive age women is between 3-10%. Among women in the reproductive age group, 12-32% women with complaint of pelvic pain have endometriosis and 9-50% women with infertility have endometriosis(Fig. 1).

**Fig. 1: Prevalence according to age of females**



**Endometriosis affects women during the prime years of their lives!**

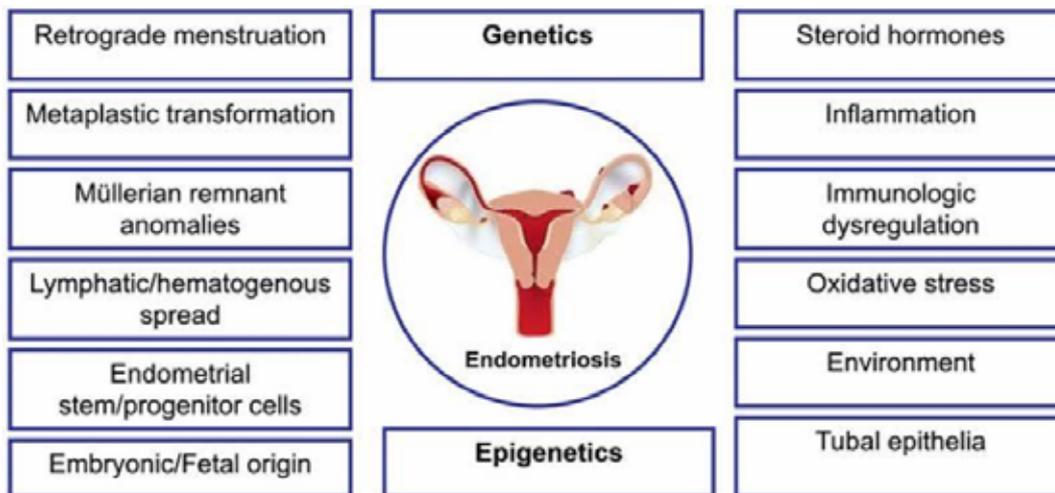
### 3. Pathogenesis

The pathogenesis of infertility in women with endometriosis varies by the stage of the disease, with mild disease inciting inflammatory pathways and advanced disease involving anatomic disruption in addition to inflammation. Various inflammatory cells play a major role in its pathophysiology in different ways as shown in (Fig. 2,3).

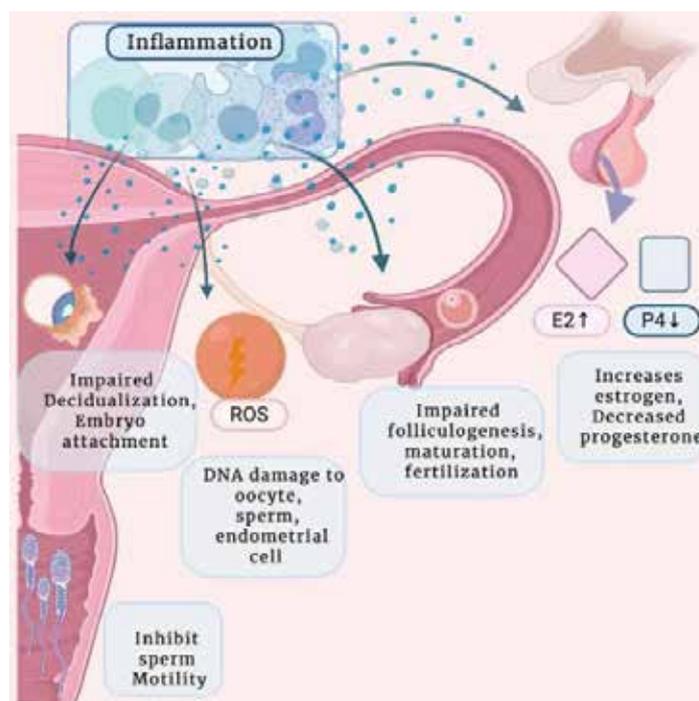
#### Genetic involvement

The disease is frequently observed in monozygotic and dizygotic twins pairs. The risk of endometriosis is also seven times higher if a first degree relative has history of endometriosis. These findings suggest a genetic predisposition to the disease. **Activation of k-RAS gene** contributes to the genetic basis of endometriosis.

**Fig. 2: Pathogenesis of endometriosis**



**Fig. 3: Role of inflammatory factors in endometriosis**



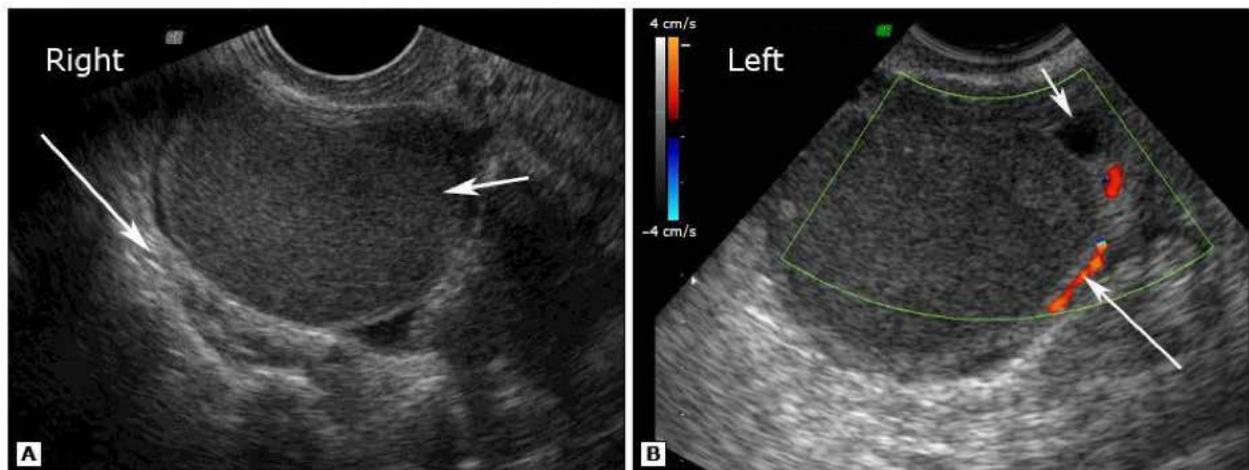
## 4. Factors affecting Endometriosis

Increase the risk of Endometriosis	Decrease the risk of Endometriosis
1. Nulliparity	1. Pregnancies
2. prolonged exposure to endogenous estrogen (eg, early menarche and late menopause)	2. Extended intervals of lactation
3. Shorter menstrual cycle	3. High BMI
4. Heavy menstrual flow	4. Increased waist-to-hip ratio
5. Obstruction of menstrual outflow eg. Mullerian anomalies, cervical stenosis	5. Diet rich with fruits and vegetables
6. Exposure to diethylstilbestrol in utero	

## 5. Diagnosis of endometriosis

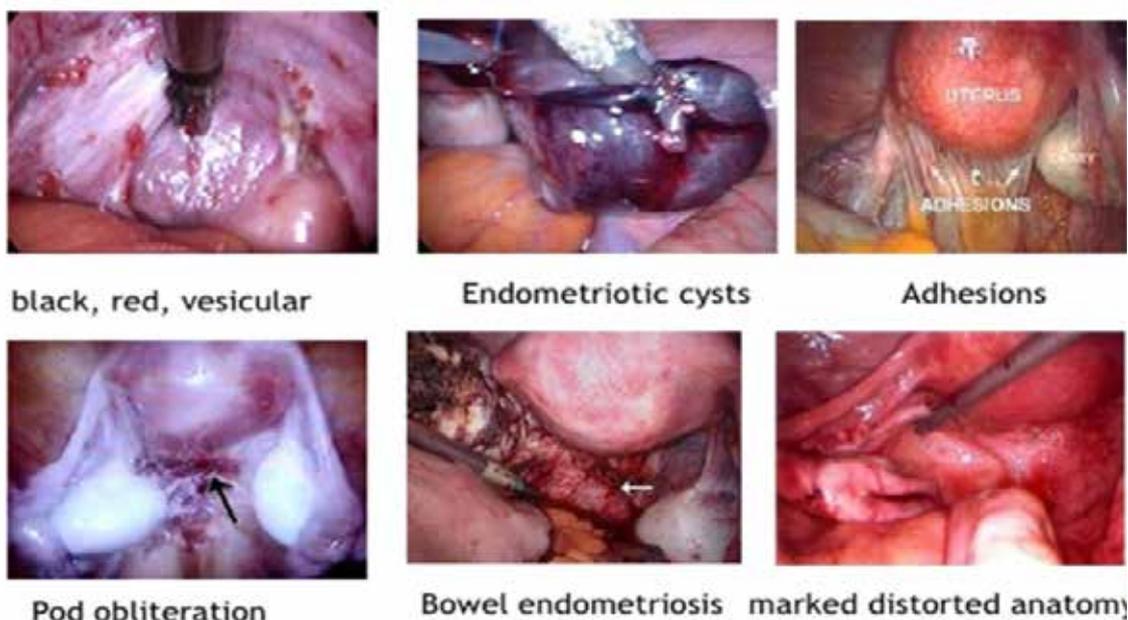
- a. Clinical examination:** It is always advisable to perform a per vaginal examination in all infertile women with suspected endometriosis for vaginal nodules, mobility of uterus, to palpate rectovaginal septum, to feel ovarian size for endometrioma, tenderness.
- b. Transvaginal Sonography:** Image of the right adnexa showing an **endometrioma**. The homogeneous echo pattern of the cyst contents (ie, "**ground-glass appearance**") is characteristic of an endometrioma. (short arrow); the cystic nature of the endometrioma is also indicated by the **acoustic enhancement** (long arrow) (**Fig 4A,4B**).
- c. Transvaginal ultrasound with color doppler:** Image of the left adnexa showing a benign endometrioma of the left ovary viewed with color Doppler imaging. No flow within the cyst can be demonstrated; however, blood flow is demonstrated within the wall of the cyst in the ovarian tissue itself (long arrow). Also identified within the left ovary is a small follicle (short arrow) (**Fig 4B**).

**Fig. 4: Ultrasound image of an endometrioma**



- d. Magnetic resonance imaging (MRI):** The usefulness of MRI in diagnosing endometriosis is not well established.
- e. Biomarkers:** It is **not recommended** to use biomarkers, for instance, CA125 to diagnose endometriosis. However, it might be used to monitor treatment response in patients with endometriosis and high level of CA125.
- f. Laparoscopy:** Laparoscopy is the gold standard technique to diagnose endometriosis although it is an invasive one. It is the standard technique for inspection of pelvis and to establish a definitive diagnosis of endometriosis. Laparoscopic examination should include a complete inspection in a clockwise or counterclockwise direction with a blunt probe, with palpation of lesions to check for nodularity as a sign of deeply infiltrative endometriosis of the bowel, bladder, uterus, tubes, ovaries, cul-de-sac, or broad ligament. The GDG recommends that clinicians confirm a positive laparoscopy by histology, since positive histology confirms the diagnosis of endometriosis, even though negative histology does not exclude it. **Diagnostic Laparoscopy is not recommended to be carried out until indicated (Fig. 5).**

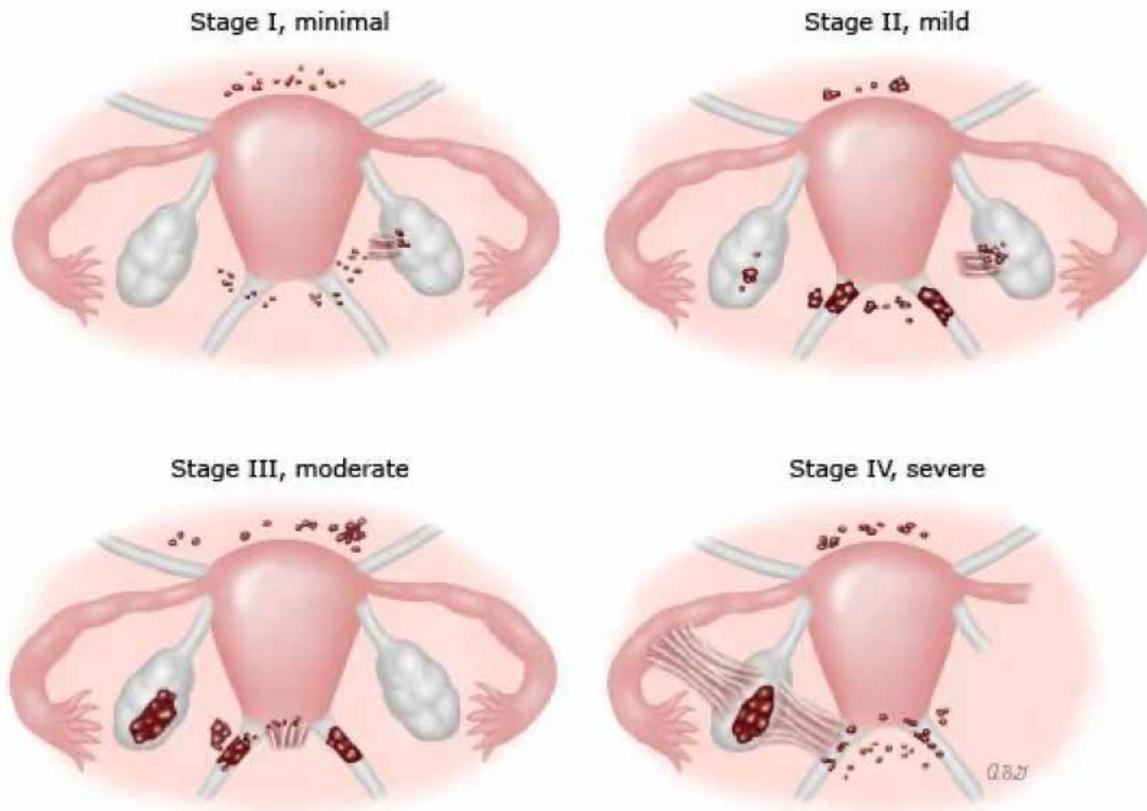
**Fig. 5: Laparoscopic images of endometriosis**



## 6. Classification of endometriosis

Grading of endometriosis is done by laparoscopy from minimal to severe. According to the **revised American society for Reproductive Medicine classification of endometriosis**, this disorder is classified in four stages (**Fig. 6**).

**Fig. 6: Staging of Endometriosis**



**Chart 1: Laparoscopic scoring of endometriosis according to revised ASRM classification**



**AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE  
REVISED CLASSIFICATION OF ENDOMETRIOSIS**

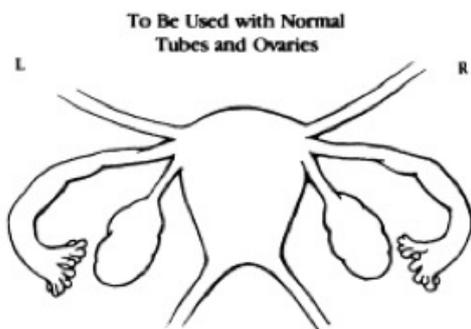
Patient's Name \_\_\_\_\_ Date \_\_\_\_\_  
 Stage I (Minimal) - 1-5      Laparoscopy \_\_\_\_\_ Laparotomy \_\_\_\_\_ Photography \_\_\_\_\_  
 Stage II (Mild) - 6-15      Recommended Treatment \_\_\_\_\_  
 Stage III (Moderate) - 16-40  
 Stage IV (Severe) - >40  
 Total \_\_\_\_\_ Prognosis \_\_\_\_\_

PERITONEUM	ENDOMETRIOSIS	< 1cm	1-3cm	> 3cm	
	Superficial	1	2	4	
Deep	2	4	6		
OVARY	R Superficial	1	2	4	
	Deep	4	16	20	
	L Superficial	1	2	4	
	Deep	4	16	20	
POSTERIOR CULDESAC OBLITERATION	Partial	4		Complete	
		4		40	
OVARY	ADHESIONS	< 1/3 Enclosure	1/3-2/3 Enclosure	> 2/3 Enclosure	
	R Filmy	1	2	4	
	Dense	4	8	16	
	L Filmy	1	2	4	
	Dense	4	8	16	
	TUBE	R Filmy	1	2	4
		Dense	4*	8*	16
		L Filmy	1	2	4
Dense		4*	8*	16	

\*If the fimbriated end of the fallopian tube is completely enclosed, change the point assignment to 16.  
 Denote appearance of superficial implant types as red [(R), red, red-pink, flamelike, vesicular blobs, clear vesicles], white [(W), opacifications, peritoneal defects, yellow-brown], or black [(B) black, hemosiderin deposits, blue]. Denote percent of total described as R\_\_\_%, W\_\_\_% and B\_\_\_%. Total should equal 100%.

Additional Endometriosis: \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_

Associated Pathology: \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_



## 7. Approach to a patient with infertility attributed to endometriosis.

Endometriosis is a challenging disease and requires decision making at every stage by the clinician & the patient. Infertility may be caused by endometriosis alone or endometriosis combined with other factors, both male and female. For women who present with endometriosis and infertility, we proceed with an infertility evaluation. We then assess the need to perform primary surgery for staging and treatment of endometriosis or repeat surgery to treat pain symptoms. Choice of infertility therapy is based on the combination of findings from the infertility evaluation and surgical staging.

### » **Medical management**

Medical management improves the quality of life for patients with endometriosis. Therapies for endometriosis cause hormonal suppression and most of them have contraceptive effects. According to Cochrane review subfertile women should not be prescribed hormonal ovarian suppression to improve fertility as first line treatment in patients of endometriosis who wish to conceive.

### » **Surgical management**

- a. In infertile women with **ASRM stage I/II endometriosis**, clinicians should perform operative laparoscopy (**excision or ablation of the endometriosis lesions**) including **adhesiolysis**, rather than performing diagnostic laparoscopy only, to increase ongoing pregnancy rates.
- b. According to the recommendations, clinicians should counsel the women with endometrioma regarding the **risks of reduced ovarian function after surgery and the possible loss of the ovarian function**. The decision to proceed with surgery should be considered carefully if the woman has had previous ovarian surgery.
- c. In women with **endometrioma larger than 3 cm**, it recommends clinicians might **consider cystectomy** prior to assisted reproductive technologies to improve endometriosis-associated pain or the accessibility of follicles.
- d. **The excision of the endometrioma capsule should be done, instead of drainage and electrocoagulation of the endometrioma wall**, to increase spontaneous pregnancy rates.
- e. In infertile women with **ASRM stage I/II endometriosis**, clinicians **may consider CO<sub>2</sub> laser vaporization** of endometriosis, instead of monopolar electrocoagulation, since **laser vaporisation is associated with higher cumulative spontaneous pregnancy rates**.
- f. In infertile women with **ASRM stage III/IV endometriosis**, clinicians **can consider operative laparoscopy**, instead of expectant management, to increase spontaneous pregnancy rates.

## 8. Stimulation protocol and endometriosis

- A. In patients with endometriosis planned for Intra uterine Insemination, gonadotropins are preferred over Clomiphene or Letrozole alone.
- B. **Ultra-Long Protocol:** Down regulation for **2–3 months with GnRH** depot in women with endometriosis increases the odds of clinical pregnancy by more than 4-fold. With the use of GnRH agonist and transvaginal oocyte retrieval there is increased success in use of IVF for endometriosis associated infertility.
- C. **GnRH agonist protocol:** Women with all stages of endometriosis who underwent **luteal phase GnRH agonist down-regulation followed by IVF/ICSI treatment** had a similar pregnancy and live birth rate and lower miscarriage rate compared with women with tubal factor infertility. GnRH-agonist not only prevent, deleterious effects of premature endogenous LH surge but also suppress a number of inflammatory cytokines (modulate NK cells of the uterus and also reduce uterine aromatase production). The long down-regulation pretreatment with GnRH<sub>a</sub> suppression with hormonal therapy add back 3 months (and up to 6 months) before IVF or ICSI will increase the clinical pregnancy rates.
- D. **GnRH antagonist protocol:** There are good choices for poor responders, patients with poor ovarian reserve due to ovarian endometrioma or after its surgical excision in IVF cycles as they cause **immediate suppression** of LH surge.

## 9. Impact of endometriosis in ART

The impact of endometriosis on ART outcomes is variable. Mild endometriosis (**ie, Stage I/II disease**) does **not appear to negatively impact** ART results. In contrast, the body of evidence suggests **Stage III/IV disease** negatively impacts outcomes, although the data are conflicting. The mechanism appears to decrease ovarian reserve, effect on receptivity of endometrium, inflammatory effect etc.

**There is no evidence that ART increases the recurrence of endometriosis.** In addition, the use of ART in women with endometriosis does not appear to increase the risk of poor birth outcome, particularly preterm birth.

## 10. Fertility preservation

As endometriosis can be associated with ovarian depletion and infertility, fertility preservation therapies such as embryo, oocyte, and ovarian tissue freezing have been proposed for women diagnosed with endometriosis. Women who may benefit from this approach include those with bilateral endometriomas, prior ovarian surgery, and young age at diagnosis. **More data are needed before a recommendation can be made regarding fertility preservation treatment in women with endometriosis.**

## 11. Ten Commandments

1. Laparoscopy is the best diagnostic tool but being an invasive procedure is **not recommended** as a routine test for infertility.
2. In infertile women with endometriosis, clinicians **should not** prescribe ovarian suppression treatment to improve fertility.
3. Clinicians **not to prescribe** adjunctive hormonal treatment before surgery or after surgery to improve spontaneous pregnancy rates.
4. Clinicians **may consider** operative laparoscopy for the treatment of endometrioma (more than 3cm) associated infertility as it may increase their chance of natural pregnancy. However, it can lead to loss of ovarian cortex and thus reducing the level of AMH. Nowadays we recommend **leaving the endometrioma untouched** until it comes in the way of needle during the ovum pick-up.
5. In infertile women with ASRM stage I/II endometriosis, clinicians **may perform** intrauterine insemination (IUI) with ovarian stimulation, instead of expectant management or IUI alone, as it increases pregnancy rates.
6. **ART can be performed** for infertility associated with endometriosis, especially if tubal function is compromised, if there is male factor infertility, in case of low Endometriosis Fertility Index (EFI) and/or if other treatments have failed [**EFI is a scoring system which includes assessment of historical factors at the time of surgery (age, duration of infertility and pregnancy history), of adnexal function at conclusion of surgery (functional score of Fallopian tubes, fimbriae and ovaries bilaterally), and of the extensiveness of endometriosis**].
7. Clinicians are **not recommended** to routinely perform surgery prior to ART to improve live birth rates in women with stage I/II endometriosis, as the potential benefits are unclear.
8. A specific protocol for ART in women with endometriosis **cannot be recommended**. Both antagonist and agonist protocols can be offered based on patient's and physician's preferences as no difference in pregnancy or live birth rate has been demonstrated.
9. In women with endometrioma, clinicians **may use antibiotic prophylaxis** at the time of oocyte retrieval, although the risk of ovarian abscess formation following follicle aspiration is low.
10. There is **insufficient evidence** to recommend prolonged administration of the COC/progestogens as a pre-treatment to ART to increase live birth rates.

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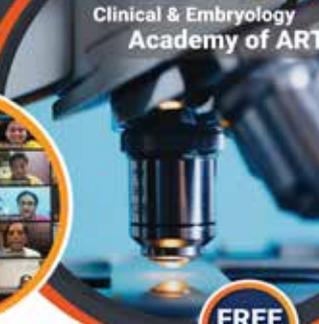
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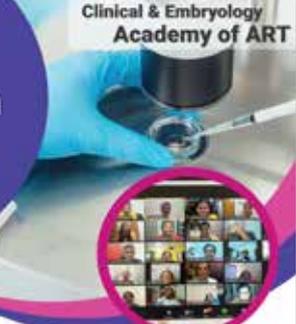
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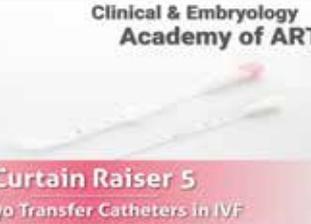
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**CURTAIN RAISER 7**  
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**AZOOSPERMIA**

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Tips & Tricks

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**CURTAIN RAISER 12**  
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**Curtain Raiser 13**  
Adjuvants in IUI, IVF & Embryology

**FREE REGISTRATION**

**SUNDAY 11<sup>th</sup> July 2021**  
08:30 - 09:30 AM (IST)

For **FREE Registration** Whatsapp 'ADJ' on

+91 8287883005, 8375994958

400+ Candidates have been trained so far across the globe

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**Curtain Raiser 14**  
**HSG**  
Interpretation, Tips & Tricks

**FREE REGISTRATION**

**i-Ceat CSR Initiative**

**Sunday 1<sup>st</sup> Aug. 2021**  
08:30 - 09:30 AM (IST)

For **FREE Registration** Whatsapp 'HSG' on

+91 8287883005, 8375994958

450+ Candidates have been trained so far across the globe

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**Curtain Raiser 15**  
Hormonal Evaluation in Infertility

**FREE REGISTRATION**

**i-Ceat CSR Initiative**

**SUNDAY 15<sup>th</sup> Aug. 2021**  
08:30 - 09:30 AM (IST)

Zoom Meeting ID: 812 9073 7036  
Pass code: ICEAT

For **FREE Registration** Whatsapp 'HEI' on

+91 8287883005, 8375994957

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## Curtain Raiser 16

### Ovarian Reserve Assessment



**SUNDAY**  
5<sup>th</sup> Sep. 2021  
08:30 - 09:30 AM (IST)

**FREE REGISTRATION**

Zoom Meeting ID: 846 0663 7351  
Pass code: ICEAT

For **FREE** Registration Whatsapp '**ORA**' on  
**+91 8287883005, 8375994957**

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## Curtain Raiser 17

### Endometriosis: IUI and IVF



**FREE REGISTRATION**

**SUNDAY**  
10<sup>th</sup> Oct. 2021  
08:30 - 09:30 AM (IST)

For **FREE** Registration Whatsapp '**ENDO**' on  
**+91 8287883005, 8375994957**

551+ Candidates have been trained so far across the globe

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## Curtain Raiser 18

### Male Sexual Dysfunction



**SUNDAY**  
31<sup>st</sup> Oct. 2021  
08:30 - 09:30 AM (IST)

**FREE REGISTRATION**

For **FREE** Registration Whatsapp '**MSD**' on  
**+91 8287883005, 8375994957**

551+ Candidates have been trained so far across the globe

[www.i-ceat.com](http://www.i-ceat.com)

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## Curtain Raiser 19

### Selecting the best sperm for IUI and IVF



**FREE REGISTRATION**

**SUNDAY**  
14<sup>th</sup> Nov. 2021  
08:30 - 09:30 AM (IST)

**i-Ceat CSR Initiative**

For **FREE** Registration Whatsapp '**SBS**' on  
**+91 8287883005, 8375994957**

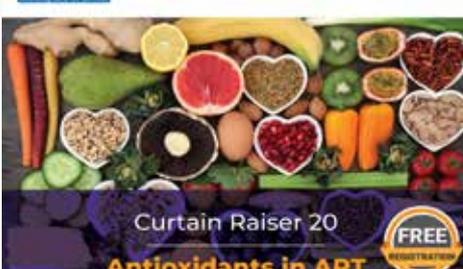
551+ Candidates have been trained so far across the globe

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## Curtain Raiser 20

### Antioxidants in ART



**FREE REGISTRATION**

**SUNDAY**  
5<sup>th</sup> Dec. 2021  
08:30 - 09:30 AM (IST)

**i-Ceat CSR Initiative**

For **FREE** Registration Whatsapp '**AOA**' on  
**+91 8287883005, 8375994957**

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## Curtain Raiser 21

### PCOS in ART



**SUNDAY**  
26<sup>th</sup> Dec. 2021  
08:30 - 09:30 AM (IST)

**FREE REGISTRATION**

**i-Ceat CSR Initiative**

For **FREE** Registration Whatsapp '**PCOS**' on  
**+91 8287883005, 8375994957**

551+ Candidates have been trained so far across the globe

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## Curtain Raiser 22

### ART ACT 2021



**FREE REGISTRATION**

**SUNDAY**  
9<sup>th</sup> Jan. 2022  
08:15 - 09:30 AM (IST)

**i-Ceat CSR Initiative**

For **FREE** Registration Whatsapp '**ART**' on  
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## Curtain Raiser 23

### THIN ENDOMETRIUM



**FREE REGISTRATION**

**SUNDAY**  
16<sup>th</sup> Jan. 2022  
09:30 - 10:30 AM (IST)

**i-Ceat CSR Initiative**

For **FREE** Registration Whatsapp '**ENDO**' on  
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## Curtain Raiser 24

### Best Incubators for an IVF Laboratory



**FREE REGISTRATION**

**SUNDAY**  
23<sup>rd</sup> Jan. 2022  
09:30 - 10:30 AM (IST)

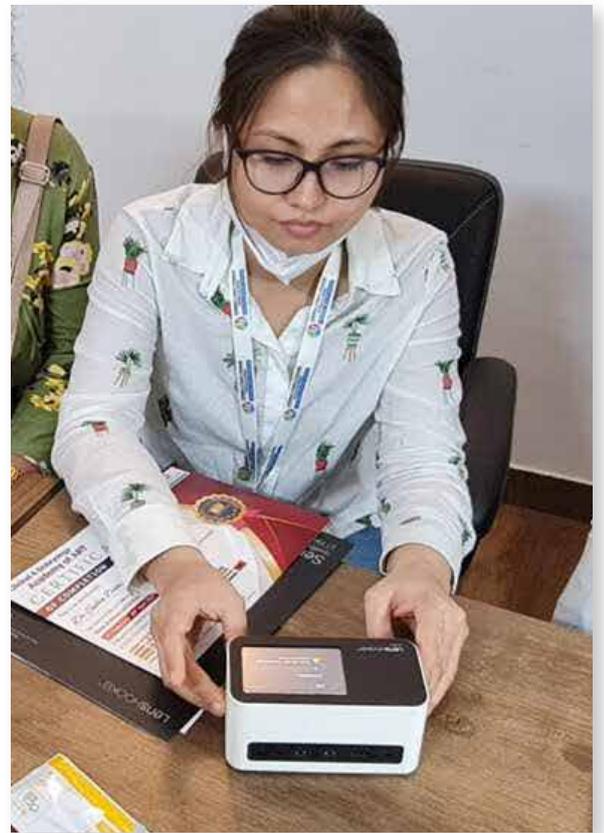
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10<sup>th</sup> Edition



27<sup>th</sup> February, 2022

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& QA/QC

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OPU-ET, Reproductive  
Ultrasound & QA/QC

> E - learning > Digital Learning Modules > Online Exams > Online Lectures  
> Recorded Video Lectures > Certification at the end of Course



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