Clinical Focus on ART

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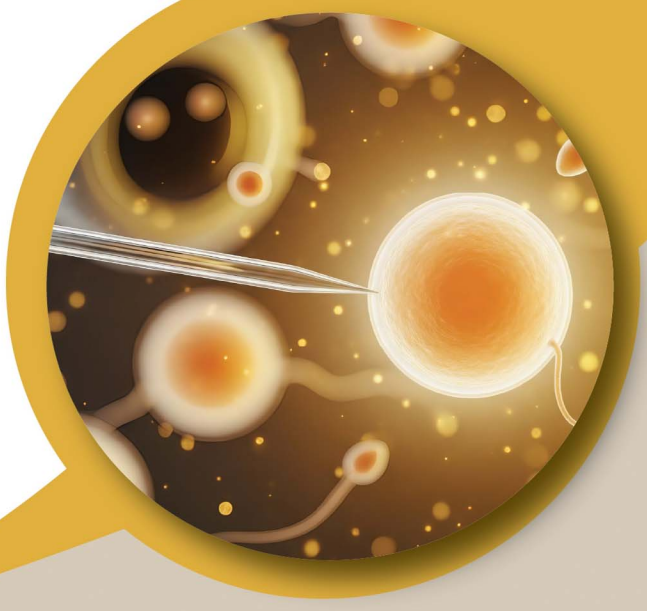

Foreword
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CHAPTER 27

Endometriosis and Assisted Reproductive Technology

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INTRODUCTION

"He who knows Endometriosis knows gynecology."

–William Osler

Endometriosis is a benign, estrogen dependent, and progressive gynecological disease in women of reproductive age which is extremely common. Yet, there is much that is still not understood and involves a lot of controversies.

HOW ENDOMETRIOSIS LEADS TO INFERTILITY: PATHOPHYSIOLOGY

Possible Mechanisms

Mechanical Causes

- Altered tubo-ovarian relationships because of distorted anatomy resulting impaired oocyte pickup
- Tubal damage—hydrosalpinx and hematosalpinx—altered tubal motility prevents egg capture.

Molecular Mechanisms: Alterations in Peritoneal Fluid

- Local hostile environment and peritoneal fluid abnormal macrophages and cytokines affect sperm motility, sperm oocyte interaction, and implantation failure.
- Prostanoids, cytokines, growth factors, interleukins, etc., cause chronic inflammation—impairing ovarian, tubal, and endometrial function.[1]

Alteration of Systemic Immune Response

- ↑Antiendometrial antibody (autoimmune reaction)[2]
- Increased polyclonal B cell activity, T cell, natural killer (NK) cell, and monocyte activation
- ↑Cell-mediated gametocyte injury.

Reactive Oxidative Species (ROS) and Free Radicals

Iron is sequestrated by macrophages as ferritin and, thus, macrophages are overloaded with iron. During its attempt to destroy iron, it produces large amount of ROS which leads to many adverse fertility-related issues.

IMPACT OF ENDOMETRIOSIS ON IN VITRO FERTILIZATION OUTCOME

Defective ovarian steroidogenesis and folliculogenesis affect oocyte quality, oocyte fertilization, embryogenesis, and implantation, resulting in fertilization and implantation failure due to:

- Poor ovarian reserve (POR)

- Abnormal and slow follicular and oocyte development
- Lower cytoplasmic mitochondrial content and oocyte defects; alteration in structure and function of oocyte mitochondria
- Spindle abnormalities
- Increased apoptosis of granulosa cells
- Low ovarian response
- Increased gonadotropin requirement
- Atretic follicles and ovulation failure—lesser number of follicles and low oocyte yield
- Number of fertilized oocytes and high-quality embryos are less
- Decreased estrogen production
- Dysregulated endometrial function
- Lower implantation rates
- Lower clinical pregnancy rate (CPR) and increased miscarriage rates luteinized unruptured follicle (LUF) (4–35%)
- Attenuated luteinizing hormone (LH) surge
- Luteinized unruptured follicle
- Luteal phase defect (LPD)
- Deep dyspareunia affects sexual performance.

Assisted reproductive technology (ART) is the first choice for infertility associated with endometriosis. Many studies demonstrated that endometriosis has adverse effects on all aspects of the reproductive process and consequently on in vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI) success rates.[3]

Cycle cancellation rate is three times higher in women with endometriosis. Monthly fecundity rate is lower in women with mild disease (5–11% vs. 25%). Endometriosis reduces per cycle conception by half.[4] The study by Basheer Alkudmani[5] supports the same reporting clinical and ongoing pregnancy rates (PRs) per cycle to be lower than the control group by 1.8 and 2.2% in patients, respectively, with mild endometriosis, and 17 and 22% in patients with severe endometriosis irrespective of the protocol.[5]

STATISTICS

- Prevalence of endometriosis—1 in 10 women suffer from endometriosis.
- 25–50% of infertile women have endometriosis.
- 30–50% of women with endometriosis are infertile.
- Infertile women are 6–8 times more likely to have endometriosis than fertile women.
- The frequency of endometriosis among women with infertility subjected to diagnostic hysterolaparoscopy was found to be 48%.
- The result of IVF in advanced endometriosis is 36% reduced.
- About 25% conceive after surgery.

TREATMENT

It depends on:

- Woman's age
- Symptoms
- Obstetric status
- Stage of the disease
- Ovarian reserve
- Previous ovarian surgery
- Effects of medical therapy
- Other infertility factors like tubal factor and male factor.

No Single Optional Treatment for Endometriosis

Medical management of endometriosis indicated in:

- Young women with shorter duration of infertility
- Early endometriosis and without much anatomical distortion should be offered

controlled ovarian hyperstimulation (COH) with intrauterine insemination (IUI) without surgery
- Endometrioma <3–4 cm in size
- Those which do not come in the way of ovum pick up (OPU)
- Infertile women with POR, elderly, or advanced disease
- Recurrent endometrioma.

MEDICAL MANAGEMENT

Medical management for pain by suppression of ovulation with oral contraceptive pills (OCP), dienogest, and progesterone are of no benefit for fertility treatment.

Medical management for infertility includes:[4]
- Controlled ovarian hyperstimulation and intrauterine insemination
- In vitro fertilization
- Aromatase inhibitors (AI)
- Gonadotropin-releasing hormone analog (GnRHa)—before and after surgical treatment.

INTRAUTERINE INSEMINATION EUROPEAN SOCIETY FOR HUMAN REPRODUCTION AND ENDOCRINOLOGY) GUIDELINES 2014

- Women with endometriosis must be referred to ART earlier.
- Endometriosis has decreased per cycle conception rate in comparison with male factor and unexplained infertility.[6]
- Controlled ovarian hyperstimulation with IUI should be considered within 6 months following surgery in the treatment of subfertile women with American Fertility Society (AFS)/American Society for Reproductive Medicine (ASRM) stage I/II endometriosis, when at least one tube is patent instead of expectant management, as it increases live birth rates (LBRs).
- In minimal and mild endometriosis, success rate per cycle with superovulation with IUI for consecutive 3–4 cycles is 10–15%. They have a plateau effect after 3–6 cycles. However, pregnancy rate is lower than with unexplained infertility.[7]

CONTROLLED OVARIAN HYPERSTIMULATION AND INTRAUTERINE INSEMINATION

There is no exact method to distinguish which stimulation protocol is the best for such patients.
- Clomifene citrate (CC) and IUI triples mean fertility rate from 3.3 to 9.5%
- Clomifene citrate and IUI versus letrozole and IUI gave similar results
- Follicle-stimulating hormone (FSH)/human menopausal gonadotropin (HMG) and IUI—stages I and II (15%) and stages III and IV (8%).

INDICATIONS FOR IN VITRO FERTILIZATION—INTRACYTOPLASMIC SPERM INJECTION IN ENDOMETRIOSIS

- Diminished ovarian reserve
- Failed COH–IUI three cycles
- Presence of adenomyosis
- Female age >35 years
- Recurrent endometrioma
- Presence of other factors like male or tubal factor
- Bilateral endometrioma
- Infertility duration >5 years
- Stage III/IV disease

In Vitro Fertilization or Intracytoplasmic Sperm Injection—Which is Better?

Intracytoplasmic sperm injection is always better than IVF. In endometriosis, it is "ICSI

for all" instead of IVF. Barnhart et al.[8] reported less fertilization in IVF in patients with endometriosis.

IVF protocols in women with endometriosis: The debate about the best protocol is ongoing.

- Extended GnRH analog treatment
- Ultralong protocol
- Gonadotropin-releasing hormone analog long protocol
- Antagonist protocol
- Prolonged OCP or danazol before IVF
- Short protocol
- Clomiphene plus gonadotropins
- Aromatase inhibitors plus gonadotropins
- Natural cycle IVF.

Extended Gonadotropin-releasing Hormone Agonist Protocol

There is evidence to suggest that the use of prolonged downregulation (extinguishes the disease) with GnRH agonist (11.25 mg, 3 months) prior to ovarian stimulation for IVF increases CPR by fourfold.[4]

The administration of extended GnRHa to patients with diminished ovarian reserve (DOR) may further diminish ovarian response to subsequent gonadotropin treatment. Hence, stimulation prior to GnRHa, vitrification of all those embryos, and transferring in a thaw cycle following extended GnRHa treatment may be more appropriate.

Ultralong Protocol

The ultralong protocol extends the usual 3–4 weeks of GnRHa administration with a 3.75 mg depot dose. Despite mixed findings, with one study showing no enhancement in reproductive outcomes, several retrospective studies and a Cochrane review involving three randomized controlled trials (RCTs) suggest that this protocol could indeed improve the likelihood of conception, particularly in women with stages III–IV endometriosis. This review specifically noted higher CPR and LBR in women following the ultralong protocol compared to shorter ones.[9]

Gonadotropin-releasing Hormone Agonist Long Protocols

Gonadotropin-releasing hormone analogs used in the long protocol for COH are the gold standard in fertility treatments, especially recommended for women with a good ovarian reserve. However, its efficacy decreases in women with a low ovarian reserve, who require higher doses of gonadotropins and longer stimulation periods (supported by significant statistical findings: $p < 0.001$ for dosages and $p < 0.05$ for duration).[10]

A review of six RCTs involving 286 patients showed that using GnRH agonists for 3–6 cycles before IVF-ICSI significantly increased the CPR by fourfold and reduced miscarriage rates. This efficacy is attributed to the modulation of uterine NK cells and the normalization of endometrial aromatase expression by GnRH agonists. NK cell modulation suggests an improved immune environment for embryo implantation and aromatase is crucial for estrogen synthesis, essential for a pregnancy-supportive environment.[11]

Higher number of embryos were available for cryopreservation in agonist group.[12]

The Cochrane database reviews from 2006 and 2007 collectively highlight the effectiveness of GnRHa in fertility treatments. The 2006 review, analyzing three trials with 165 women, showed that GnRHa significantly increased LBR and CPR emphasizing its potency in improving fertility outcomes (OR: 9.19; 95% CI: 1.08–78.22). The CPR per woman was also significantly higher (three studies: OR: 4.28; 95% CI: 2.00–9.15).

The 2007 review compared depot and daily GnRHa in 552 women in six studies and found no difference in CPR between the two, suggesting equal effectiveness (OR: 0.94; 95% CI: 0.65–1.37). However, it noted that depot GnRHa required more gonadotropin ampules and longer ovarian stimulation, highlighting practical differences in administration.

In a retrospective analysis comparing three groups of patients with endometriosis undergoing assisted procreation procedures, distinct approaches were evaluated:

1. The use of GnRHa (buserelin) for 3 months, followed by COH with HMG
2. The administration of GnRHa for 3 weeks, then continuing with ovarian stimulation using HMG
3. Treatment with clomiphene citrate in combination with HMG.

The results indicated that the use of GnRHa significantly increased the number of oocytes retrieved. Notably, the group treated with GnRHa for 3 months exhibited the highest fertilization rate. Comparatively, treatment with GnRHa for either 3 months or 3 weeks was found to be more effective than the combination of clomiphene citrate and HMG. This suggests that for patients with endometriosis, GnRHa based treatments, particularly the longer duration of 3 months, are more efficient in enhancing the outcomes of assisted reproduction.

The use of GnRHa in fertility treatments for endometriosis patients yields mixed effectiveness. GnRHa administration before IVF is associated with improved fertilization rates, but not necessarily higher implantation rates. While cleavage, pregnancy, and delivery rates are generally higher with GnRHa, not all studies show statistical significance. A key retrospective study by Liu et al.[13] found that the long agonist protocol in IVF significantly increased cumulative conception rates (50.3%) compared to short or ultrashort protocols (8.3%). This highlights the long agonist protocol's superior efficacy in enhancing fertility outcomes in endometriosis patients.

In evaluating the effectiveness of different approaches to enhancing pregnancy rates, two specific approaches were compared. The use of GnRH agonists (GnRHa) showed an odds ratio (OR) of 1.68 for achieving pregnancy while surgical intervention had the OR of 1.63 for the same outcome. Both these approaches resulted in pregnancy rates within the range of 25–35%. This data suggests that both GnRH agonists and surgical methods are comparably effective in increasing the likelihood of pregnancy.

Gonadotropin-releasing Hormone Antagonist Protocol

Gonadotropin-releasing hormone antagonists (cetrorelix and ganirelix) help to avoid prolonged pituitary suppression. Antagonist protocols reduce the cost and time of gonadotropin treatment compared to long and ultralong ones.

Agonist and Antagonist Protocol—Comparison

A GnRH agonist protocol appears to result in higher PR and LBR after fresh ET in women with endometriosis associated infertility suggesting that antagonist protocol might negatively impact endometrial receptivity.[14]

No significant difference was observed between the groups with freeze—thaw embryo transfer. In frozen embryo transfer (FET) cycles, the antagonist protocol has comparable clinical pregnancy outcome with long or prolonged agonist protocol, especially in those with DOR.[15]

Studies by Canis et al.[16] and Pabuccu R[12] highlight the effectiveness of COH using

TABLE 1: CPR in fresh embryo transfers of agonist versus antagonist cycles.

	Agonist cycle	*Antagonist cycle*
CPR per ET (embryo transfer) (fresh)	25%	13%
LBR per ET (fresh)	22%	10%

(CPR: clinical pregnancy rate; ET: embryo transfer; LBR: live birth rate)

both GnRH agonist and antagonist protocols. These treatments are equally effective in terms of IR and CPR in FET cycles, as evidenced in randomized trials.[14,17]

The findings, therefore, show that GnRH agonist protocol leads to higher PR and LBR after fresh embryo transfer in women with endometriosis-associated infertility, as mentioned in **Table 1** whereas the antagonist protocol might have encouraging response in FET cycles.

Anti-Müllerian Hormone and Protocol Selection

Although the mean number of oocytes retrieved was higher in the agonist group compared to the antagonist group, there was a trend for higher number of embryos and pregnancy rates in the antagonist group compared to the agonist group in low AMH population.

In a recent study, Hosseini et al.[3] showed that the expression levels of some genes involved in the cytoplasmic maturity, antiapoptotic process, and ATP production were higher in human oocytes of the women in the GnRH antagonist protocol versus those in the GnRHa protocol. For these reasons, antagonist protocol may have a positive influence on both oocyte and embryo quality; consequently, on the PR.

However, in the normal range of AMH (1.1–2.8), long agonist protocol is the best choice for these patients. Therefore, individualized IVF protocols, according to various ranges of AMH, may improve clinical outcomes of IVF/ICSI in patients with endometriosis.

Letrozole

Letrozole is an interesting drug resulting in improved endometrial receptivity. Those with poor prognosis for IVF might be improved with letrozole cotreatment. The administration of letrozole 5 mg daily for days 2–6 of gonadotropin stimulation. Letrozole gives better IVF–ET result of CPR 61 versus 14% and LBR 50 versus 7% by improving endometrial receptivity.[18]

A study of 84 patients with 121 cycles with letrozole—GnRH antagonist protocol was associated with significantly better implantation rate (IR), CPR, and LBR per embryo transfer concordant with the theory that letrozole may correct endometrial receptivity defects.

Other Protocols

Short protocol with GnRH analog should be avoided in these women because it results in lower number of oocytes yield when compared with the long protocol.

With *natural cycle IVF* protocol, possible problems such as disease progression and poor responsiveness to hyperstimulation can be avoided.

The use of combined oral contraceptive pills (COCPs) prior to ART may increase IVF success and should be considered like longer GnRH agonist downregulation. Pretreatment with OCP for 6–8 weeks before IVF–ET improves outcome.[19]

Surgery is indicated in:

- Pain attributable to endometrioma or other related symptoms

- Potential for rupture
- Size >4 cm (>3 cm as added by Donnez et al.[20]), because it may give compression effect on follicles and interfere with ovarian responsiveness during COH
- Inability to access follicles during OPU and, thus, avoid technical difficulties and follicular fluid contamination
- Concern of occult malignancy/for histological diagnosis
- Associated with infection or ovarian abscess
- Deep infiltrating endometriosis (DIE).

Presence of large endometriomas at the time of OPU significantly reduces the number of oocytes retrieved compared to the healthy ovary in contrast to normal ovaries: 31 versus 69%.[21] Cumulative pregnancy rate is 43–60% following laparoscopic surgery.

Counseling

The woman should be counseled thoroughly regarding the risks of recurrence, reduced ovarian function after surgery and sometimes, even loss of the ovarian function. ART can be offered as first-line treatment or after surgery. The decision to proceed with surgery should be considered carefully if the woman has had previous ovarian surgery.

Advantages of Laparoscopy

- Prevents endometriosis progression
- Decreased toxicity to the embryos and gamete
- Enhances uterine receptivity.

What are the Limitations of the Surgery?

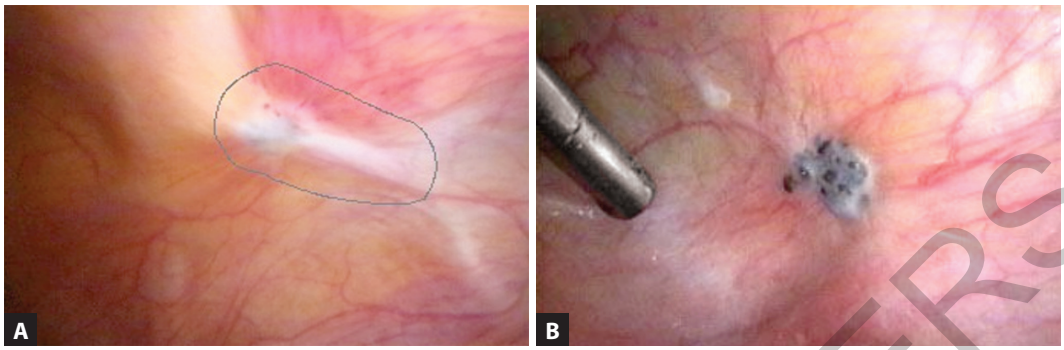
- Surgery has risk of incomplete surgery and recurrence. High risk of recurrence: 25% at the end of 2 years and 40–50% at 5 years.
- Postoperative medication is required to reduce the recurrence.
- Excision/cystectomy is preferable because of less recurrence (6 vs. 20%), but excision results in more reduction of ovarian reserve as mentioned in **Table 2**.
- Unable to reverse the inflammatory and biomolecular changes.

Negative Impact of Surgery on Ovarian Reserve

Surgical intervention, particularly the excision and ablation of endometriotic lesions **(Figs. 1 and B)**, raises concerns about the balance between benefits and potential harm, such as the loss of ovarian reserve. Studies highlight the cautious approach of "less is more," with evidence showing healthy ovarian tissue (found in 97% of the cyst specimen) often removed during cyst wall stripping, as mentioned in **Table 2**. Stripped cyst wall consisted of primordial, primary, and secondary follicles in 69% cases leading to the loss of primordial follicles, especially in larger cysts.[20]

TABLE 2: Pros and cons: Laparoscopic ablation versus cystectomy.

Ablation	*Cystectomy*
• Cyst wall is ablated, not excised • Diathermy is more used • Less bleeding • A proportion of follicles may be destroyed because of thermal injury • Lesser loss of primordial follicles • Higher risk of recurrence because cyst wall is not removed	• Internal cyst wall is excised by stripping from underlying stroma–traction and countertraction • Diathermy less used, more bleeding • A proportion of follicles may get lost along with the stripped cyst wall • More loss of primordial follicles • Lower risk of recurrence as cyst wall is removed



Figs. 1A and B: Endometriotic spots on the peritoneal surface.

Extensive coagulation and surgery close to the ovarian hilum are best avoided to preserve ovarian blood supply. Also, there is a negative correlation between the stage of endometriosis and the pregnancy rate postsurgery, indicating that more advanced stages of the disease can lead to lower chances of conception following surgical intervention.[22]

Proper operative laparoscopy increases pregnancy rates than just diagnostic.

Excision of the endometriotic capsule increases spontaneous PR compared to drainage and electrocoagulation of the cyst wall.

Patients with complete removal of endometriotic lesion had spontaneous PR of 25% and LBR of 19%. After surgical ablation and fulguration in stages I and II with superovulation with gonadotropins and IUI, there was 2–3 times higher LBR compared to just medical treatment. It gave shorter time to pregnancy and LBR with IVF. In patients who had IVF-ICSI after laparoscopic surgery, 48.9% conceived in stage I/II and 28.3% conceived in III/IV.[23,24] Conception rates were maximum in first 6 months and dropped after 1 year of surgery.

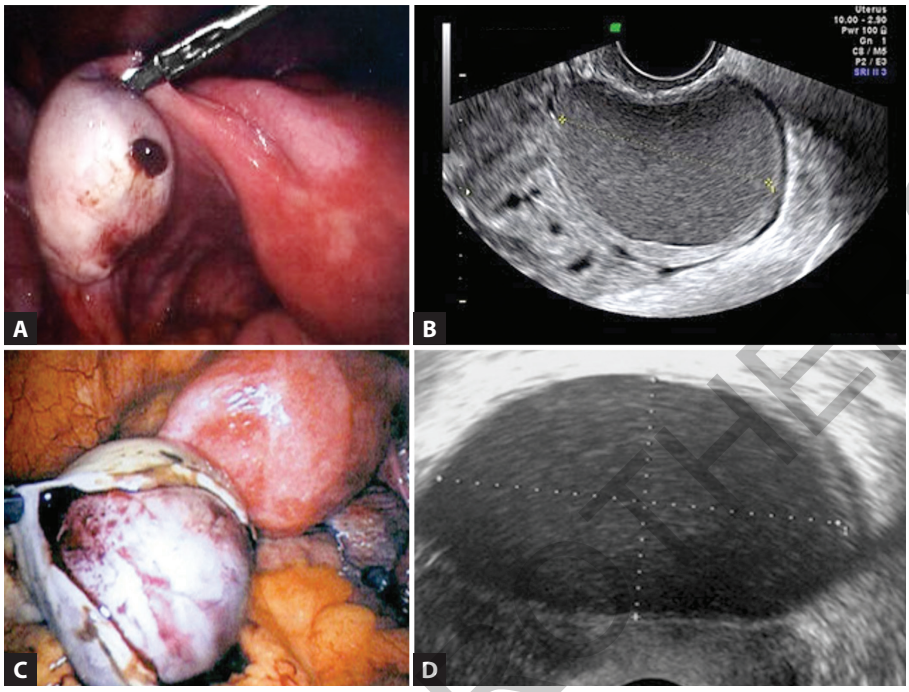
For small endometriomas (<3 cm), initial medical management with ovarian stimulation and IUI is advised for 3–4 cycles before considering laparoscopy, as cystectomy prior to ART does not significantly improve pregnancy rates. However, for larger endometriomas (over 3 cm), laparoscopic cystectomy before ART is recommended, improving follicle accessibility, (as mentioned in **Table 3**) and reducing pain, followed by GnRHa treatment and IVF-ICSI[25] and, thus, higher fertility rates.

Challenges with endometriomas >4 cm **(Figs. 2A to D)** include difficulties in oocyte retrieval, the risk of cyst puncture, follicular-fluid contamination, and potential infection.[21]

TABLE 3: Advantages and disadvantages of surgery for endometrioma.

Advantages of surgery	*Disadvantages of surgery*
• Better IVF success rate • Prevents rupture • Facilitates oocyte retrieval • Avoids contamination of follicular fluid with contents • Occult malignancy can be detected • Prevents progression	• Cystectomy prior to IVF does not improve PR • Surgery and anesthesia risks • Potential risk of reduction of ovarian reserve • Aspiration prior to IVF does not increase PR

(IVF: in vitro fertilization; PR: pregnancy rate)



Figs. 2A to D: Endometrioma presentation. (A and C) Laparoscopic and (B and D) Sonography.

TABLE 4: Comparison of benefits and risks of expectant management versus surgical management.

	Expectant management	*Surgical management*
Potential benefits	• Avoids surgery and its complications • No further compromise on ovarian reserve • Avoids delay in commencing ART	• Alleviates symptoms • Histological confirmation and excludes malignancy • Decreased risk of cyst complication • Facilitates ovarian access during OPU
Potential risks	• Pain of various presentation persists • Cyst rupture • Difficult ovarian access during OPU • Infection of endometrioma • No histological diagnosis • May accelerate	• Surgical and anesthetic risks • Decreased ovarian reserve • Postoperative adhesions • Potential delay of ART

(ART: assisted reproductive technology; OPU: ovum pick up)

Surgery is generally avoided in older patients, those with low ovarian reserve, asymptomatic cases, bilateral or recurrent endometrioma due to risks such as reduced ovarian response, decreased oocyte yield, and a higher likelihood of recurrence (as mentioned in **Table 4**).

In vitro fertilization or intracytoplasmic sperm injection cycles postendometrioma excision can face these difficulties:

- Reduced ovarian volume and antral follicle count (AFC)
- Reduced ovarian response on stimulation and oocyte yield

- So, COH needs more gonadotropins and longer stimulation days
- Reduced E2 (estradiol) level.

Advantages of Preoperative Gonadotropin-releasing Hormone Agonist

- Reduction in cyst size
- Reduction of hypervascularization and inflammation
- Reduction in cyst wall thickness
- Reduction of adhesions.

Endometriotic Cyst Aspiration

No statistically different response is seen, with or without cyst aspiration. So, it is not recommended to make ultrasound-guided aspiration with or without sclerotherapy. It is reserved in cases of recurrent endometrioma that may hinder oocyte retrieval like ones >4 cm or in symptomatic infertile women with low-ovarian reserve.

Sclerotherapy

Ethanol sclerotherapy decreases the recurrence rate of endometrioma without altering the results of IVF, where a second surgery would have a deleterious effect. CPR was same in both cystectomy and sclerotherapy, in some clinical trials.[26]

Precautions to be Taken During Ovum Pick Up in the Presence of Endometrioma

- Antibiotic prophylaxis
- 2% betadine vaginal wash followed by thorough saline wash before OPU
- Strict asepsis to be maintained during OPU
- Avoid repeatedly exposing needle tip to vagina and outside
- Avoid puncture and aspiration of the endometrioma.

Fertility Preservation in Women with Endometriosis

Vitrification of the embryos, cryopreservation of the oocytes, or of ovarian tissue is a good practical option in women with bilateral endometriomas or POR.[27]

To summarize, the management of endometriosis-related infertility requires a comprehensive and nuanced approach without delay, prioritizing both fertility restoration and symptom relief. Laparoscopy is the gold standard for diagnosis, offering precision with minimal invasiveness and respectful handling of ovaries. In treating endometriosis, particularly large endometriomas, cystectomy is often the preferred surgical option. For early-stage endometriosis (I/II), combining COH with IUI has proven more effective than expectant management. In advanced stages (III/IV), operative laparoscopy increases pregnancy rates compared to a nonintervention approach.

In IVF treatments for endometriosis, downregulation for 3–6 months prior to ART improves the success, although overall ART success rates are low. Ovulation stimulation, regardless of the protocol chosen, does not appear to exacerbate endometriosis.

Gonadotropin-releasing hormone agonist protocol is associated with improved fertilization rates and a higher yield of mature oocytes and embryos for cryopreservation, thereby increasing the cumulative fecundity rate. Conversely, the antagonist protocol with FET is particularly advantageous for patients with low AMH.

Objectives of the treatment should be not only on restoring fertility at the earliest but also on alleviating pain and other

symptoms to improve the patient's quality of life. Controlling the underlying disease to prevent recurrence and regular monitoring are critical.

CONCLUSION

Endometriosis reduces the fertility potential because of many mechanisms, right from egg, embryo, and endometrial quality to take-home baby rates. Once diagnosed, women should initiate her fertility treatment as early as possible rather than wait -and -watch policy. Surgery improving the fertility is not necessary in all the cases. ICSI is always better than IVF for these oocytes. Though there are many treatment protocols, success rates of all appear almost same. The reproductive physician's previous experience has a great impact in deciding the protocols and the ART success.

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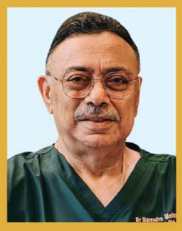
Clinical Focus on ART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Clinical Focus on Assisted Reproductive Technology (ART) is a concise, clinically oriented guide addressing the unique challenges of infertility care in India and South Asia. The book integrates scientific evidence with practical decision-making relevant to everyday ART practice in resource-variable settings.

Covering the complete spectrum—from epidemiology, psychosocial aspects, lifestyle and environmental factors to advanced diagnostics, genetics, fertility preservation, AI-based embryo selection, and regenerative therapies—this volume emphasizes individualized, ethical, and patient-centric care. Special focus is given to common regional clinical scenarios such as PCOS, endometriosis, male factor infertility, poor ovarian response, and unexplained infertility.

With balanced discussions on ethical, legal, cultural, and access-related issues, this book serves as a valuable resource for reproductive Medicine Specialists, Clinicians, and Trainees seeking evidence-based, context-appropriate ART solutions.

Shelving Recommendation
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