

Review Article

Adenomyosis and Infertility

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Abstract:

Adenomyosis is an abnormal growth of endometrial glands and stroma into the myometrium causing diffusely enlarged uterus. Due to the abnormal growth of endometrial glands and stroma it causes severe pain during menstruation. Though USG and MRI can help, histopathology of the lesion is confirmatory diagnosis of the disease. It is one of the important causes of infertility with very poor prognosis. Any treatment modalities can fail when lesion is diffuse in nature. Surgery in the form of total hysterectomy is the definitive treatment for complete cure but hysterectomy is not logical for infertile patients. So, fertility sparing surgery can be done to improve fertility. Medical treatment in the form of GnRHa and different form of progesterones can be used to eliminate symptoms and to reduce the adenomyotic mass, which may improve the fertility status. Non-surgical High Intensity Focused Ultrasound (HIFU) is another option to reduce the size of the lesion. For reproduction active treatment is ideal to accelerate live birth. Controlled ovarian hyperstimulation and Intrauterine Insemination (IUI) can be done if tube(s) are patent. If not, Assisted Reproductive Technology (ART) is the treatment of choice for this group of patients.

Introduction:

Adenomyosis may be defined as the benign invasion of endometrium into the myometrium, producing a diffusely enlarged uterus which microscopically exhibits ectopic non-neoplastic, endometrial glands and stroma surrounded by the hypertrophic and hyperplastic myometrium¹. It is the disease of multiparous women and commonly found in women between the ages of 35 and 50 years. But younger women with adenomyosis is not very uncommon².

Types of Adenomyosis

Based on myometrial invasion and histologic characteristics adenomyosis is classified as

1. Diffuse adenomyosis: When ectopic endometrial, glands and stroma are scattered throughout the whole musculature of the uterus, then this extensive disease is called diffuse adenomyosis³.
2. Focal adenomyosis: When disease is confined in a particular area of uterus, then it is focal

adenomyosis. The histologic characteristics of focal adenomyosis may vary from almost solid to only cystic in nature. Thus, this form could be subdivided to:

- a. *Adenomyoma*: When disease infiltrates any particular area with clear border and felt as circumscribed masses is called adenomyoma^{4,5}.
 - b. *Cystic adenomyosis*. A rare form of adenomyosis characterized mainly by the presence of a single adenomyotic cyst within myometrium. It is described as juvenile cystic adenomyosis (JCA). It is usually cystic, occur in younger women of < 30 years, lesion is >1cm and associated with severe dysmenorrhea⁶.
3. Polypoid adenomyomas. Circumscribed endometrial masses composed of predominantly endometrioid glands and a stromal component predominantly of smooth muscle⁴.

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- a. *Typical polypoid adenomyomas*. Polypoid adenomyomas without architectural or cellular atypia⁴.
 - b. *Atypical polypoid adenomyomas*. A rare variant of polypoid adenomyomas characterized by atypical endometrial glands, often squamous metaplasia, and a cellular smooth muscle stroma⁷
4. Other forms:
- a. *Adenomyomas of the endocervical type*. Occasionally adenomyomatous polyps are present in the cervix, which contains endocervical type of epithelium. These lesions must be differentiated from adenoma malignum⁸
 - b. *Retroperitoneal adenomyomas*. At the lowest part of the uterus and in the upper rectovaginal septum these may present, which are thought to arise from metaplasia of mullerian remnants beneath the peritoneum⁹

Prevalence of Adenomyosis:

Diagnosis of both early stage adenomyosis and endometriosis is difficult. But early endometriosis can be diagnosed by laparoscopy while early adenomyosis cannot be diagnosed without histopathology. An accurate determination of its incidence or prevalence has therefore not been carried out¹⁰. Post surgical series report an extremely variable detection rate of 5% to 70%¹⁰. This variation is probably due to method of histopathological analysis. When extensive cut section of specimen is histopathologically examined incidence is increased. In a study it shows that incidence is 31% when 3 cut section is examined whereas 61% when six cut section is examined¹. In a meta-analysis of more than 500 cases, the detection rate was 21–47% with a mean of approximately 30%.¹⁰

Risk Factors for Adenomyosis

Age

Though 70-80% adenomyosis was diagnosed after hysterectomy at their fourth and fifth decades of life,¹¹⁻²⁰ modern MRI criteria of diagnosis suggest that the disease may cause dysmenorrhea and chronic pelvic pain in adolescents and younger women than previously appreciated^{21,22}.

Parity

Usually women with adenomyosis are multiparous¹⁵⁻¹⁷. Pregnancy and pregnancy related procedure like caesarean section D&C might facilitate the formation of adenomyosis due to the invasive nature of the trophoblast to the extension of the myometrial fibers and breaking of the endomyometrial barrier due to the procedure.

Uterine surgery

Both dilation curettage and caesarean section have association with higher rate of adenomyosis^{14,23,24}. However, other studies reported no relationship of cesarean section or other uterine surgical procedure with adenomyosis^{16,17,25}.

Smoking

Some studies found association between smoking and adenomyosis^{17,26} but other did not show any association¹⁴

Ectopic pregnancy

Implantation in adenomyotic lesion could result in an ectopic pregnancy developing within the myometrium^{27,28}. It has been hypothesized that women with adenomyosis are more likely to have a history of ectopic pregnancy, since adenomyosis may be a risk factor for the development of intramural ectopic pregnancy^{17,27,28}.

Depression and antidepressant

Abnormalities of prolactin dynamics is associated with adenomyosis. Increased prolactin appears to be sufficient to cause histological adenomyosis and is associated with up-regulation of the uterine prolactin receptor messenger RNA. Depression and antidepressant use can act through prolactin dynamics and in both human and animal studies shown an increased risk of depression, and antidepressant use in formation of adenomyosis²⁹⁻³¹.

Tamoxifen

Adenomyosis is relatively rare in postmenopausal women but a higher incidence of adenomyosis has been reported in women treated with tamoxifen for breast cancer³²

Etiology and Pathogenesis

Exact etiology of adenomyosis is not known. Two separate pathogenetic theories have been proposed to explain its formation.

Theory-one: An origin from the invagination of the deepest portion of the endometrial mucosa (usually >2.5 mm beneath the basal endometrium) between bundles of smooth muscle fibers of the myometrium has been proposed.

Theory-2 two: De novo along the intramyometrial lymphatic system; a metaplastic process initiating from ectopic intramyometrial endometrial tissue produced *de novo*³.

Uterine auto-traumatization and initiation of the mechanism of tissue injury and repair (TIAR) have been considered as the primary events in the disease process³³. The auto-trauma of the junctional zone or physiological damages due to placental implantation most likely results in the same pathological cascade³⁴. This also explains that adenomyosis often gets more severe after each pregnancy and childbirth. In multiparous women trauma by pregnancy and delivery, dilatation and curettage or trauma by endometrial ablation can cause breakdown of endometrial basal layer and invagination of the basal endometrium into the subendometrial myometrium at the endometrial–myometrial interface (EMI). But this theory is not applicable for nulliparous women. Theory of uterine hyperperistalsis during early reproductive life induces micro-injury (auto-trauma) at the EMI region is the suggestive cause in nulliparous women³⁵. In order to heal this damage local oestrogen production increases, which in turn causes increased peristalsis of the uterus. Thus, a vicious circle of auto-trauma phenomenon and increased intrauterine pressure particularly during menstruation enhance the entry of endometrial tissue into EMI and myometrium. This process is thought to be facilitated by the lack of intervening submucosa between the endometrial–myometrial interface. The infiltrated endometrial gland and stroma induces a reaction in myometrium causing hypertrophy and hyperplasia of surrounding myometrial smooth muscle leads to development of focal adenomyoma or diffuse adenomyosis.

Hormonal, genetic, immunological and growth factors possibly play a role in this sequence of events. Tamoxifen treatment is also associated with a higher incidence.

Clinical Features of Adenomyosis

Severity of symptoms vary widely according to occupancy of myometrium by abnormal growth of

endometrial tissue. It may remain totally asymptomatic or sometimes being a severe and debilitating condition, which incapacitate the woman to do any work. Severity of symptoms is associated with the extent of the disease

Symptoms:³⁶

- Asymptomatic (33%)
- Chronic pelvic pain (77%)
- Menorrhagia or heavy menstrual bleeding (40-60%): It is more common when lesion is deep seated and associated with endometriosis. Sometimes bleeding is so heavy that woman suffers from anemia with symptoms like fatigue and dizziness.
- Abnormal uterine bleeding: Abnormal and heavy uterine bleeding is common in presence of adenomyosis.
- Dysmenorrhoea (15-30%): Sometimes cramping painful menstruation is so severe that it cannot be controlled by analgesic. Any such painful menstruation should be suspected as adenomyosis and investigation should be done accordingly.
- Dyspareunia (7%)
- Pressure symptoms due to pressure on bladder and rectum
- Radiation pain or dragging feelings in thighs and legs.
- Feeling of fullness in lower abdomen due to enlargement of uterus (30%).
- Infertility (11-12%) and poor reproductive outcome. Miscarriage, premature labour and premature rupture membrane is common in adenomyosis^{37,38}

Clinical examination findings:

Associated Condition

- Fibroid uterus: Adenomyosis is frequently associated with hormone-dependent pelvic lesions. Up to 80% of women with adenomyosis also have other lesions, the most frequent being leiomyomas. Endometrial polyps, hyperplasia (with and without atypia) and adenocarcinoma may be associated with adenomyosis²⁵
- Endometriosis: Pelvic endometriosis is observed in 6–24% of women with adenomyosis uteri.

Almost 50% cases of endometriosis are associated with some form of adenomyosis³⁹. One third of young women with clinically suspected, deeply infiltrating endometriosis had MRI features of uterine adenomyosis⁴⁰.

Role of Adenomyosis in infertility

Adenomyosis alters the normal myometrial architecture that disturbs the uterine cavity environment, uterine peristalsis and sperm transport⁴¹. There may be fertilization failure due to disturbed sperm transport. Abnormal myometrial architecture and increased uterine peristalsis eventually result in implantation failure^{42,43}.

The ectopic endometrium of adenomyosis leads to reduced endometrial receptivity and impaired decidualization⁴⁴⁻⁴⁷. The ectopic endometrium displays a dysregulation of immune factors, markers of apoptosis or proliferation, inflammatory mediators, and oxidative stress, which reduces uterine receptivity⁴². A number of cellular and humoral immune responses are observed in adenomyosis, causing an immunological 'vicious cycle' in the endometrium. Thus multiple factors are responsible for infertility in adenomyosis.

Diagnosis

Histopathology of the specimen is the confirmatory diagnosis of adenomyosis. With the evolution of magnetic resonance imaging (MRI) and high-quality transvaginal ultrasound (TVUS), today the diagnosis can be made with a level of accuracy of 80%–90% without the need for excisional surgery.^{48-50,38} Among ultrasonography 3D is better as it can identify the thickened and irregular junctional zone. Overall diagnostic accuracy of adenomyosis for 2D and 3D USG is 83% and 89% respectively⁵¹.

Sonographic diagnostic features of adenomyosis

Features of diffuse adenomyosis:

- Globular uterine enlargement in the absence of any fibroid uterus.
- Asymmetrical enlargement of the anterior and posterior wall of the uterus.
- Linear striations or fingerlike projections, indistinct endometrial stripe.
- Heterogenous poorly circumscribed anechoic areas within the myometrium.

- Abnormally dense or especially varied density within the myometrium
- Anechoic lacunae or cystic spaces of varying sizes, which may be blood filled. Rarely adenomyosis may present as a cystic lesion lined with endometrial tissue and surrounded by myometrial tissue, when it is called cystic adenomyoma. This sometimes difficult to differentiate from an accessory cavitated uterine mass (ACUM) with functional endometrium. ACUMs represent a variety of the Mullerian anomaly.
- Diffuse spread of small vessels within the myometrium by colour Doppler USG. Doppler ultrasonography can differentiate adenomyoma from fibroid uterus. In uterine fibroid blood vessels arranged around the margin of the capsule⁵²⁻⁵⁴ but in adenomyosis the vessels are differently spread.
- Junctional zone by 3D ultrasonogram.

Features of focal adenomyoma:

- Elliptical shape
- Absence of mass effect
- Discrete hypo-echoic nodule with poorly defined margins between a normal and abnormal myometrium
- Presence of anechoic cysts of varying diameter

Magnetic resonance imaging (MRI):

Magnetic resonance imaging (MRI) provides slightly better diagnostic capability compared to TVUS. MRI is the gold standard imaging modality for assessing the JZ in the diagnosis of adenomyosis⁵⁵. Dueholm et al pointed out that MRI diagnostic accuracy improves when uterine volume is less than or equal to 400mL and concluded that the combination of MRI and TVS produces the highest level of accuracy for exclusion of adenomyosis⁴⁹.

Features of adenomyosis on MRI:

- A myometrial mass with indistinct margins of primarily low intensity.
- Diffuse or local widening of junctional zones on T2 weighted images.
- Thickening of the JZ, ≥ 12 mm, or irregular junctional thickness with a difference of >5 mm between the maximum and minimum thickness.

- An ill-defined area of low signal intensity in the myometrium on T2-weighted MR images.
- Islands of ectopic endometrial tissue identified as punctate foci of high signal intensity on T1-weighted image.^{48,55,56}
- Uterine enlargement.
- Small hypointense myometrial spots.
- Swiss cheese appearance with exuberant myometrial cysts and nodules on contrast enhanced T2 sequences.

MRI is expensive and may not be readily available in every facilities. Moreover, different prospective studies and systematic review shown that there is no significant difference in sensitivity and specificity between TVUS and MRI. Researchers agreed that both TVS and MRI show high levels of accuracy as the noninvasive diagnostic method of adenomyosis. However, MRI may be particularly useful in the assessment of focal adenomyoma and provides important information regarding surgery.

Treatment of Adenomyosis

The aim of treatment is to relieve symptoms like dysmenorrhea and menorrhagia, to improve quality of life, to reduce the size of adenomyosis and to enhance fertility.

Hysterectomy is the definitive treatment of adenomyosis particularly for diffuse symptomatic one as the woman passed her childbearing age or completed her family. But treatment of diffuse adenomyosis in infertile patients is extremely challenging as preservation of the uterus for future childbearing is the target of all women. Treatment strategy for infertile or who have not completed their family remains controversial and challenging. Because the causative relationship between adenomyosis and subfertility has not been fully understood. To date there is no agreement on the most appropriate therapeutic methods to manage infertile patients with adenomyosis. Multiple treatment modalities including hormonal therapies with gonadotropin releasing hormone agonist (GnRHa) and conservative surgical procedures have been used to treat patients with adenomyosis with success. In general, clinical pregnancy rate is lower after both medical treatment or conservative surgical procedures.

The options of treatment for this type of patients are various. As symptom is severe and patient is desirous of pregnancy, after proper counselling and explaining the advantages, disadvantages and reproductive outcome of individual treatment, any of the options can be chosen by the patient.

A. For Symptomatic Relieve

1. Medical Treatment

Analgesics: Nonsteroidal anti-inflammatory drugs (NSAIDs) work by inhibiting the cyclooxygenase (COX-1 and COX-2) and decreasing the production of prostaglandins. It is usually the first-line treatment for pain relief of adenomyosis. NSAIDs have been proved to be effective in the treatment of primary dysmenorrhea⁵⁷.

Hormones: To make pseudopregnancy state which eliminate dysmenorrhoea and menorrhagia. In addition, long term use reduces the bulk of the mass. Commonly used hormones are:

- i) **Combined Oral Contraceptive Pills (OCPs):** OCP work by inhibiting ovulation. Many studies have shown that these are effective in the treatment of dysmenorrhea. Mansouri et al. have shown regression of adenomyosis on MRI after using oral contraceptive pills for 3 years in adolescents with adenomyosis presenting with chronic pelvic pain⁵⁸.
- ii) **Oral progesterone (Dienogest):** Dienogest is a selective synthetic oral progestin. A prospective clinical trial has shown Dienogest to be a valuable alternative to depot triptorelin acetate for treatment of premenopausal pelvic pains due to uterine adenomyosis as both treatment were highly effective for dysmenorrhea, dyspareunia, and chronic pelvic pain associated with adenomyosis⁵⁹
- iii) **Levonorgestrel-Releasing Intrauterine System (LNGs):** LNGs is a progesterone containing intrauterine device. LNGs acts locally and causes decidualization of the endometrium and adenomyotic deposits. By improving uterine contractility and reducing local prostaglandin production within the endometrium, LNGs appears to be an effective method in relieving dysmenorrhea associated with adenomyosis and more effective than the combined OCP in improving the quality of life.

- iv) **GnRH Agonists:** GnRH agonists are effective in alleviating dysmenorrhea and relieving menorrhagia associated with adenomyosis⁶¹. To avoid the risk of osteoporosis, treatment with GnRH agonists is usually restricted to a short duration of 3–6 months although the duration of use may be extended with add-back estrogen therapy⁶².
- v) **Aromatase Inhibitors:** Aromatase inhibitors prevent development of adenomyosis by inhibiting conversion of androgen to estrogen. It is as effective as GnRH agonist in reducing the volume of adenomyoma as well as improving symptoms⁶³. Combined use of aromatase inhibitors with GnRH agonist also give good results in severe uterine adenomyosis who wished to preserve fertility. There was a reduction in uterine volume of 60% after 8 weeks of treatment as determined by magnetic resonance imaging and ultrasound.

2. High Intensity Focused Ultrasound (HIFU)

High intensity focused ultrasound (HIFU) is another nonsurgical and novel noninvasive treatment for adenomyosis. It is effective in both focal and diffuse lesions^{69,70}. The treatment is performed under the guidance of ultrasound or MRI. MRI-based thermal mapping offers real-time temperature monitoring during HIFU treatment; thus, it enhances safety and efficacy during HIFU treatment. Ultrasound-guided HIFU (USgHIFU) differs from MRI-guided HIFU (MRgHIFU) in that it is silent and does not require the patient to be enclosed in a confined space.

Efficacy of HIFU treatment

Symptomatic relieve:

Ultrasound guided HIFU was shown to be technically successful in up to 94.6% of patients with symptomatic adenomyosis⁶⁹. Different studies shown success rate of HIFU treatment in symptomatic relieve and significant improvement of quality of life from 82.3%-100%⁷¹⁻⁷⁴.

A two-year follow up in the relief rate of dysmenorrhea was 82.3% and the relief rate of menorrhagia was 78.9%⁷⁵.

Fertility outcome:

A single case report showed that one session MRgHIFU treatment reduced the focal adenomyotic lesion of an infertile woman from 84cm³ to 33cm³.

There was significant reduction in menorrhagia and a remarkable decrease in size of the lesion, six weeks after the treatment. The patient conceived spontaneously and delivered a healthy term baby via vaginal route⁷⁶. Zhou et al. reported 54 pregnancy and 21 delivery out of 64 cases of post HIFU at a median of 10 months period (range:1-31 months)⁷⁷.

No uterine rupture occurred during gestation or delivery⁷⁷. The results suggested that HIFU seems to be a safe treatment option for patients who wish to conceive; however, there is an urgent need for randomized clinical trials (RCTs) comparing HIFU with other treatment options such as hormone intrauterine devices.

Complications:

No life threatening complications occurred after HIFU treatment. Minor complications like skin burns and leg pain were frequently reported.^{71,72} Pain in the treated region, lower abdominal pain, vaginal discharge, urinary retention, and mild sacral or sacrococcygeal pain^{73,74} are other complications. Skin burns, leg pain, or numbness of the lower limbs were reportedly seen in less than 1% of the treated patients⁷⁴. Bowel injury during HIFU treatment for adenomyosis is a rare complication but the consequences can be devastating⁶⁹. Adenomyosis and endometriosis can cause pelvic adhesions and if the bowel adheres to the uterus or the abdominal wall, it can significantly increase the risk of bowel injury.

Contraindications:

Pelvic endometriosis with adhesions or scars >10 mm in width are contraindication for HIFU. If there is endometriosis with pelvic adhesion it is increased risk for bowel injury. Scar tissue is more fibrotic and less vascular than normal tissue, and thus difficult for ultrasound to penetrate. Ultrasound energy is readily absorbed by scar tissue and may cause thermal damage to skin.

3. Surgical Treatment

Uterus sparing surgery in the form of cytoreduction or complete excision of adenomatous lesion as far as possible can cause significant reduction of dysmenorrhea and menorrhagia^{64, 65}. There was no significant difference in the reduction of dysmenorrhea, menorrhagia and pregnancy rate by complete and partial adenomyomectomy. Before surgery application of GnRHa to reduce the size of

the adenomyotic growth is helpful. *Triple-flap method* of adenomyomectomy was done by Osada, where adenomyotic tissues were radically excised and the uterine wall was reconstructed by a triple-flap method without overlapping suture lines to prevent uterine rupture in subsequent pregnancies.

Complications of surgery:

- a. **Intraoperative hemorrhage**
- b. **Post-operative adhesion formation and tubal factor infertility**
- c. **Adenomyosis and uterine rupture:** The most important and dangerous risk of conservative surgery of adenomyosis is uterine rupture during pregnancy or labor⁶⁶. After adenomyomectomy, it is presumed that subsequent uterine scars may conceal dense residual adenomyotic foci, and as a consequence the tensile strength of the uterus may decline leading to possible rupture of pregnant uterus. Wang et al, described this risk as one out of eight women experiencing uterine rupture in pregnancy/labor after cytoreductive surgery for adenomyosis⁶⁷.
- d. **Post-partum haemorrhage:** Sporadic reports have outlined the risk of severe atonic postpartum hemorrhage in women with known adenomyosis, which can necessitate a peripartum hysterectomy⁶⁸. Because of the absence of data and experience, an elective caesarian delivery after adenomyomectomy seems to be preferable regarding patients safety, especially in nonorganized centers.

B. For Reproduction

1. **Spontaneous or Induction of ovulation:** After prolonged GnRHa, HIFU or surgery spontaneous pregnancy may occur. After complete excision, reduction of dysmenorrhea, menorrhagia and pregnancy rate were 82.0%, 68.8%, and 60.5%, respectively. After partial excision it was 81.8%, 50.0%, and 46.9%, respectively⁷⁸.
2. **COH and IUI:** For infertile patients if there is no spontaneous pregnancy, COH and IUI is an option of treatment provided tube (s) is /are patent and husband's semen report is applicable for IUI.
3. **Assisted Reproductive Technology (ART):** If there is no spontaneous pregnancy within a

reasonable period or tubes are removed or damaged during fertility sparing surgery or bilateral tubal block or husband's semen analysis report shows severe semen problem ART is indicated. Study shows that adenomyosis was associated with a 28% reduction in clinical pregnancy who underwent IVF/ICSI with autologous oocytes. There is higher chances of miscarriage, independent of oocyte or embryo quality⁷⁹. Thalluri and Tremellen also showed that the adenomyosis was associated with a significant reduction in successful implantation of good-quality embryos in patients undergoing IVF treatment, 23.6% vs 44.6% with and without adenomyosis respectively⁸⁰. The use of short-term GnRH agonists to shrink the size of the adenomyotic lesion has been shown to improve conception rate within 6 months of cessation of GnRH agonist therapy^{81,82}.

Several studies have shown that pretreatment with GnRH analogue improved pregnancy outcome. Zhou et al.⁸³ analyzed the clinical efficacy of leuprorelin acetate in treatment of uterine adenomyosis with infertility. They found that, after 2–6 months of leuprorelin acetate therapy, the mean uterine volume was significantly reduced from $180 \pm 73\text{cm}^3$ to $86 \pm 67\text{cm}^3$, leading to an improvement in embryo implantation and clinical pregnancy rates.

Selection of stimulation protocol

As mentioned previously that GnRHa pretreatment improved pregnancy rate, long GnRHa protocol should be considered as it helps to induce decidualization of the adenomyotic deposits rendering the disease inactive. Tao et al. showed that GnRH antagonist protocol appears to be inferior to GnRH agonist long protocol cycle. GnRHa long protocol is associated with increased pregnancy and decreased miscarriage rates⁸⁴.

Two staged IVF

In women with adenomyosis, a two-staged in vitro fertilization could be considered. Particularly if uterine sparing surgery is done in adenomyosis with associated endometriosis and in elderly patients, there is possibility of reducing ovarian reserve. Elderly patients may lose their follicular pool as medical treatment for preparation of uterus may take long time. In those cases, patients can undergo ovarian

stimulation, oocyte retrieval, and fertilization followed by frozen-thawed embryo transfer (FET) at a later stage. Prior to the FET, GnRH analogue suppression therapy for 3 months or so leads to shrinkage of the adenomyosis and improve the result. The clinical pregnancy, implantation and ongoing pregnancy rates were 51.35% vs 24.83%, 32.56% vs 16.07%, and 48.91% vs 21.38% respectively in long GnRHa + HRT vs only HRT FET cycle⁸⁵.

Conclusion:

There is no strong evidence to indicate a definite technique that secures the best clinical and reproductive performance. Investigators are trying best and investigators describe the advantages of their technique, which did not show any statistically significant clinical differences in practice. Treatment planning finally depends on patient's severity of symptoms, desire of pregnancy and fertility potential.

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