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Endometriosis update

CLINICAL REVIEW
A Relationship between Endometriosis and Obstetric Complications

IN THIS ISSUE:

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Dear Colleagues,

Endometriosis is a painful chronic condition that demands more attention. Endometriosis affects an estimated 176 million women worldwide, making it one of the most common gynecological conditions. Despite its prevalence, the condition remains underdiagnosed, and many women suffer for years before receiving a proper diagnosis and treatment. It's important for gynecologists to recognize the signs and symptoms and diagnosis typically involves a combination of medical history, physical examination, and imaging tests.

This EndoUpdate covers intriguing aspects of endometriosis. It is an excellent source of knowledge with relevant references. Articles of this journal cover a wide range of sections important in endometriosis from update on pathogenesis to alternate therapies, useful for management of endometriosis. The article on "Update on aetiopathogenesis of endometriosis" provides succinct information on pathogenesis of Endometriosis. "Images in Endometriosis" provides knowledge on presentation of different phenotypes of endometriosis with imaging findings. It has compared transvaginal ultrasound versus MRI (Magnetic Resonance Imaging) for detection of deep infiltrating endometriosis with special mention on IDEA (International Deep Endometriosis Analysis) group proposed ultrasound-based approach to detect endometriosis.

It also included recent ESHRE guideline-based recommendations for assessment of endometriosis. The article on "A relationship between endometriosis and obstetric complication in the Clinical review" imparts sharp idea on impact of endometriosis on pregnancy, related potential obstetric complications and management. "Tips & Tricks - Endometriosis- when & How" gives insight and knowledge on taking decision for surgical management of endometriomas. The article on "Alternate therapies in Endometriosis -Psychological and mind-body interventions for endo-metriosis" speak on the topic with epigrammatic brevity. It covers psychological impact of endometriosis with inclusion of information on biofeedback, behavioural treatment.

We hope you will enjoy reading this issue of EndoUpdate. Please reach us at Endometriosis Society of India @ endosocindia@gmail.com

The membership form of Endometriosis Society of India is included. We encourage all gynecologists to join us.

TABLE OF Content

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A Relationship Between Endometriosis and Obstetric Complications

INTRODUCTION

It was traditionally believed that pelvic endometriosis completely gets cleared in pregnancy due to high levels of progesterone and there was little concern about maternal or perinatal consequences of pre-pregnancy endometriosis.

However, there has been a paradigm shift in this concept over the last decade and we now have growing evidence that endometriosis and/or adenomyosis do have many significant impacts on pregnancy outcome[1].

In this review article, we will discuss the pathophysiological relationship between endometriosis and pregnancy, the potential obstetric complications of endometriosis and some suggestions on how to manage these.

Possible mechanisms of adverse effect of Endometriosis on pregnancy.

We know that endometriosis including adenomyosis are basically inflammatory conditions involving remarkable alterations in the pelvic biomolecular microenvironment. Some of these well-known changes, which may be responsible for pregnancy complications of endometriosis, are described below in brief.

1. Altered endomyometrial junction or junctional zone causes defective trophoblastic invasion and remodeling of spiral arteries in pregnancy.
2. Inflammation associated with endometriosis leads to enhanced local activity of cytokines viz. IL6, IL8, prostaglandin F2 alpha (PGF2 alpha) and prostaglandin E2 (PGE2).
3. Endometriosis itself is associated with raised levels of reactive oxygen species (ROS). The high hemosiderin content in the endometriomas and local endometriotic deposits further add to the increased oxidative stress in the pelvic micromilieu.
4. Adenomyosis, which is an intra-myometrial endometriosis, causes abnormality in myometrial structure and function. This leads to abnormal myometrial contraction or uterine hyperperistalsis.

Until recently, most of the suggestions regarding obstetric complications of endometriosis came from anecdotal evidence or case reports or case series.

In 2020, Duffy et al[2] conducted an international consensus study for standard reporting, data collection and selection of obstetric outcomes across randomized control trials and meta-analyses.

The following discussion of the possible complications of endometriosis will be based upon the

final consensus. However, the evidence for every complication is not fullproof and studies have shown that risks may not be the same following natural conception and assisted reproduction techniques (ART) even after excluding the cofounders. Therefore, we should be cautious to interpret the inferences and practice according to our expertise and overall patient scenario.

POTENTIAL ADVERSE OBSTETRIC OUTCOMES OF PRE-PREGNANCY ENDOMETRIOSIS:

1. Miscarriage:

Excessive oxidative stress in the pelvic environment jeopardizes the ovum quality and hampers blastocyst implantation into an unfavorable endometrium. Even if implantation is successful, uterine hyperperistalsis and unsynchronized myometrial growth may dislodge the embryo. All these factors would lead to an early pregnancy failure. However, there are differences in opinion and some studies[3] did not find any significant difference in miscarriage rate in control and endometriosis groups.

2. Gestational Hypertension and Pre-Eclampsia (PE):

Association between pre-pregnancy endometriosis and PE is not very clear. Whereas some studies say there is none, others have shown a modest association with Odds Ratio 1.21 to 1.29[4]. The possible explanations for this association are oxidative stress causing generalized endothelial dysfunction and failed spiral artery remodeling at endomyometrial junctional zone.

3. Placenta Previa and Placenta Accreta:

There is strong evidence that women who conceive with a background history of endometriosis, are at increased risk for placenta previa (OR 2.04 - 3.17)[1,3].

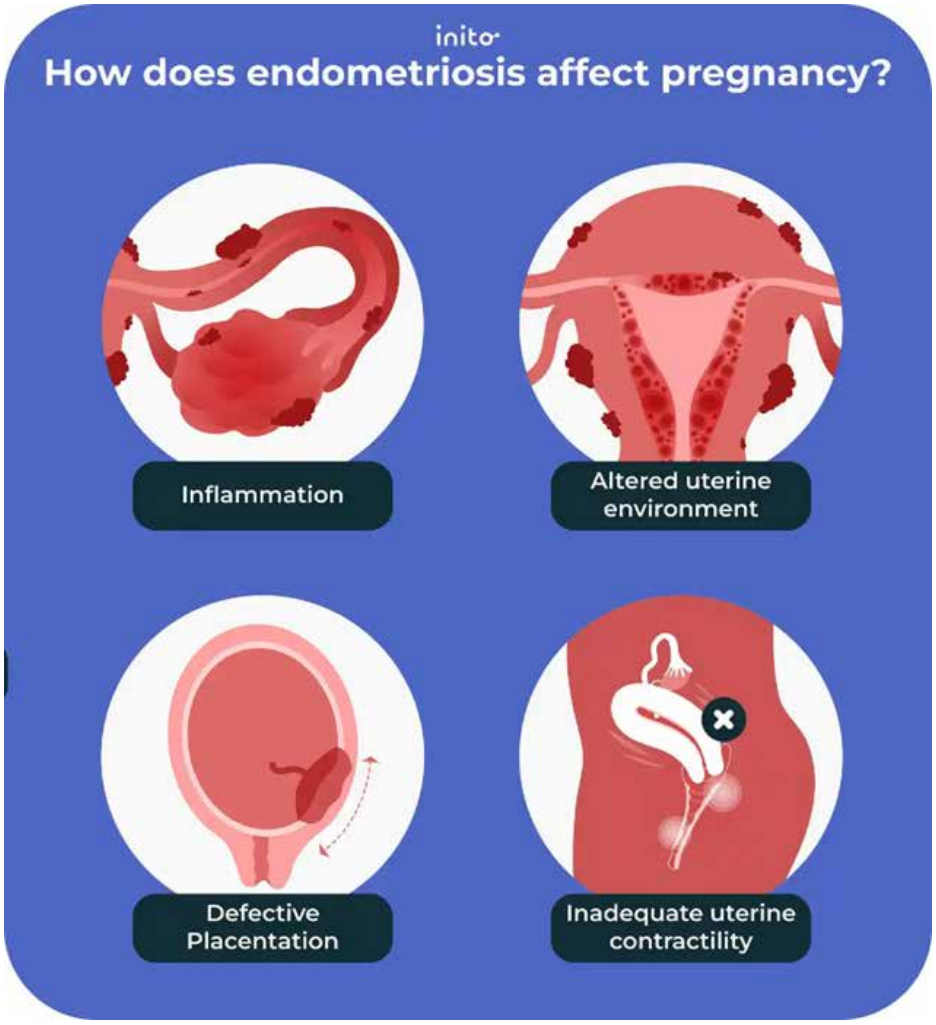
This risk is quite high in women who have had deep endometriosis (DE) and even higher in women who were surgically treated for DE by either radical or non-radical excision (6.75% and 17.8% respectively)[5,6]. It is believed that adhesion and fibrosis in DE might have increased the chance of abnormal placental location. Adenomyosis also greatly enhances the risk of placenta previa (adjusted OR 16.68)[3] and placenta accreta spectrum[7]. Furthermore, the risk increases with severity of adenomyosis and the chance of placenta previa may be as high as 23.08% in women who conceived with severe adenomyosis[3]. Whereas ART is itself a risk factor of placenta previa (OR 2.96), it is further increased in those who had ART for endometriosis or adenomyosis[1].

4. Placental Abruption:[4]

It is stated that risk of placental abruption increases by 87% in women with pre-pregnancy endometriosis, especially adenomyosis.

5. Preterm prelabour rupture of membranes (PPROM), preterm birth (PTB) and their consequences:

Evidence shows these women are at higher risk of PPROM and PTB (OR 2.33 and 1.7 respectively[4]. The possible explanations are that ongoing inflammation leads to PPROM whereas enhanced activity of PGF2



alpha and PGE2 results in cervical ripening and uterine contractions[8]. As a corollary of increased risk of PPROM and PTB, admission to neonatal intensive care unit and neonatal death are also increased (OR 1.39 and 1.78 respectively)[4].

6. Fetal growth restriction (FGR) and Intrauterine fetal death (IUFD):

Studies have shown that endometriosis slightly increases the risks of FGR (OR 1.28) and IUFD (OR 1.29)[3]. These may stem from defective trophoblastic invasion and abnormal placentation leading to placental hypoperfusion and stillbirth. Increased chance of PE, placental abruption and PTB may also add to the risk of IUFD.

7. Malpresentation and Uterine dystocia:

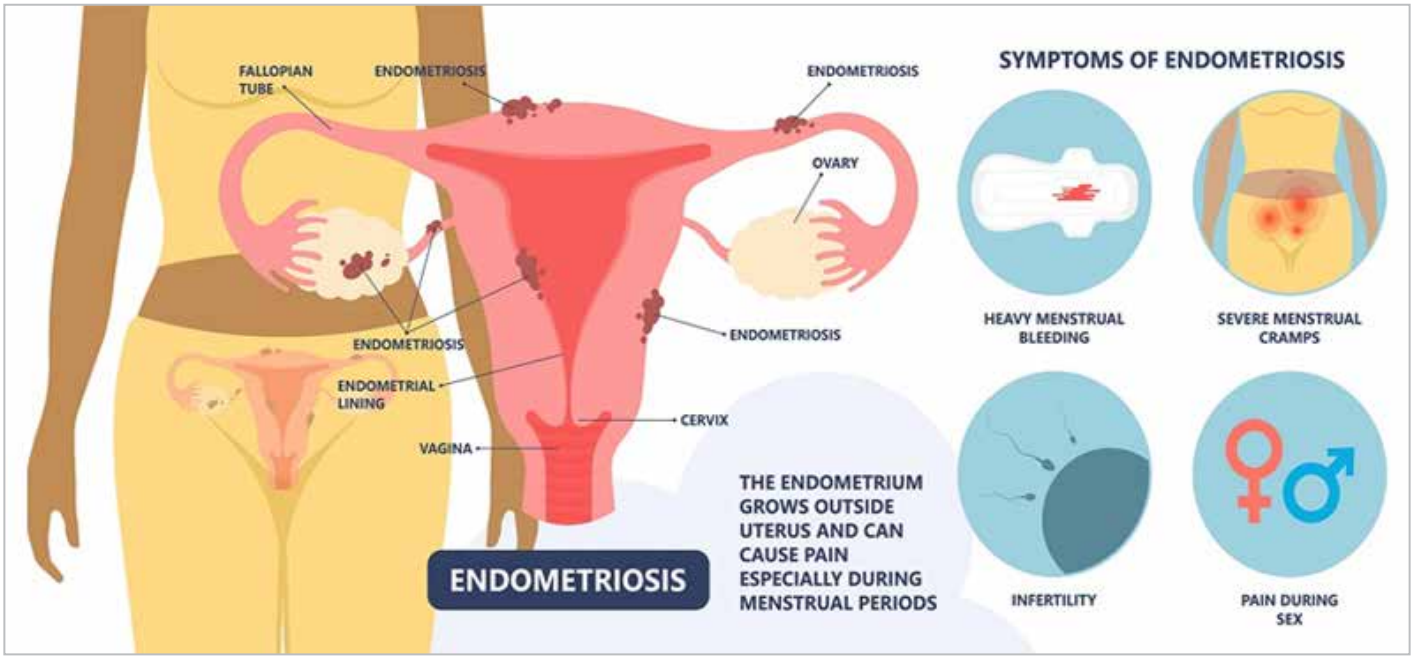
There are evidence that endometriosis and especially adenomyosis increases chance of malpresentation and delayed labour due to uterine dystocia [4,9].

8. Need for Caesarean Delivery (CD):

Evidence about increased chance of caesarean in women with endometriosis is heterogeneous. Nevertheless, even if no direct cause-effect relationship between endometriosis and CD exists, some primary complications of endometriosis in pregnancy themselves may increase the risk of CD. Another concern is quite relevant to the current practice in our country. As many of the women with endometriosis undergo some form of fertility treatment including ART, the pregnancy becomes especially precious to the couple. Most of them insist their obstetricians to deliver their baby at 36 weeks or earlier. This also increases the rate of unnecessary CD.

9. Spontaneous Hemoperitoneum in Pregnancy (SHiP):

This is an extremely rare (1 in 10,000) complication of pregnancy where unprovoked intra-abdominal haemorrhage may lead to catastrophic shock. Most commonly, the bleeding occurs from decidualized endometriotic implants. Rarely, massive hemoperitoneum can occur due to scar rupture following adenomyomectomy or bleeding from endometriotic implants on gut surface or parametrial veins [10]. The maximum incidence is in the third trimester and manifests with acute abdominal pain, signs of shock and abdominal wall rigidity and tenderness. Timely management depends on clinical suspicion and diagnosis by ultrasound or laparotomy with delivery of the fetus.



MANAGEMENT OF A PREGNANT WOMAN WITH PRE-PREGNANCY ENDOMETRIOSIS:

Most of these women complete their pregnancy with an uneventful outcome. However, a subset of that is at higher risk and should be managed with extra vigilance.

They are as follows[1]:

- History of adenomyosis

- Pregnancy by ART
- History of surgery for endometriosis, especially DE.

These women need sensitive counseling about the risks of aforesaid complications and an agreed management plan should be achieved.

There is yet no guideline on management of women with pre-pregnancy endometriosis. Nevertheless, some practice points can be applied based on knowledge about the impact of endometriosis on pregnancy and standard management plan of the potential complications.

Following are some suggestions:

1. Management by an experienced obstetrician at a well-equipped center.
2. A viability scan at 9 weeks to exclude silent miscarriage.
3. Low dose aspirin (150 mg / day) prior to 12 weeks to prevent potential pre-eclampsia.
4. Placental localization at the time of anomaly scan. If low lying, subsequent management should follow the standard pathway.
5. Measurement of cervical length at the scanning opportunities. If less than 2.5 cm, management should be done as threatened PTB.
6. Serial growth scan at 28, 32 and 34 weeks to detect FGR at earliest and minimize risk of fetal demise.
7. Judicious delivery plan without undue bias towards CD. However, malpresentation and prolonged labour will need delivery mode on their own merit. Though most women would be a candidate for vaginal delivery, those with previous rectovaginal endometriosis have a higher chance of obstetric anal sphincter injury[1].
8. Awareness about potential serious complications e.g., placental abruption and SHiP.

CONCLUSION:

Pregnancy after endometriosis is increasing because of rising prevalence of endometriosis and increased ART procedures. As most of these women have their obstetric care from general obstetricians, awareness about the potential complications and their management are of utmost importance.

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Update on the Aetiopathogenesis of Endometriosis

INTRODUCTION:

The history of endometriosis spans a time period of more than 160 years, beginning with the nosography of Rokitansky - who laid the foundations of what we now know to be endometriosis - which was further built upon by Cullen and Von Recklinghausen, and with the help of Casler's 'menstruating ovary' in 1919, this led to Sampson's theory of retrograde menstruation, which was the first step in trying to elucidate the clear pathogenesis of endometriosis[1]. Since 1919 there have been many emergent theories such as haematogenous and lymphatic spread, coelomic metaplasia and the stem cell recruitment theory, however despite all of these theories synergising with one another, there has still not been a single unifying theory which is able to successfully integrate all aspects of this pathology.

AETIOLOGY:

Sampson's theory of retrograde menstruation.

The retrograde menstruation theory is the most cited and well-known theory which has been supported over time by a variety of studies including analyses of patient demographics showing a positive correlation between outflow tract obstruction and endometriosis[2]. Retrograde menstruation induction in primates has shown endometriotic lesions analogous to those in humans which further adds weight to this theory[3].

Although retrograde menstruation provides a plausible evidence base for endometriosis, it raises more questions than it answers. Firstly, it does not explain extraperitoneal manifestations of the disease, nor does it explain the presence of endometriotic lesions in patients outside the demographic of women of reproductive age. Secondly, it only accounts for the physical deposition of endometrial tissue but does not provide an adequate mechanism of attachment, immune system evasion, and survival of these tissues.

STEM CELL RECRUITMENT THEORY

To function normally, endometrial tissue must regenerate in a cyclical pattern for most of a woman's reproductive life following menstruation, injury or iatrogenic interventions such as curettage.

Stem cells have been hypothesised to be the driving force behind this regeneration however the source of these stem cells - bone marrow or endometrium - had been a divisive force when this theory was first gaining traction.

Multiple studies have confirmed the presence of stem cells in endometrial tissue such as a 2012 study showing a cell surface marker SUSD2 - found in pluripotent stem cells in the basalis layer of the endometrium[5], this supports Leyendecker's theory that women with endometriosis are more likely to have 'hyperperistaltic movements' causing parts of the basalis layer to dislodge and be transported via retrograde menstruation into the peritoneal cavity and proliferate under the influence of paracrine and endocrine signals[6].

Bone marrow derived stem cells (BmSC) have also been shown to contribute to endometrial regeneration, which was replicated in a study done in 2012, the results of which show that when murine bone marrow is transplanted from male mice into female mice BmSCs localise and engraft to the endometrium[7].

MULLERIAN REMNANT ABNORMALITIES

Mullerian ducts are the precursor to the female reproductive system, and through a complex system of molecular and hormonal signalling they eventually give rise to the uterus, cervix, fallopian tubes, and upper vagina. The Mullerian remnant theory posits that during this duct migration some cells get dislodged and spread across the posterior pelvic floor where they retain foetal endometrial properties such as progesterone resistance.

This theory is supported by the presence of endometrial cells in female foetuses at autopsy and thus partially explains the presence of endometriosis in pre-pu-bertal female populations[8].

COELOMIC METAPLASIA

Grunwald's theory of coelomic metaplasia suggests that the driving force behind endometriosis is a metaplastic change in coelomic tissues due to their similarity to Mullerian ducts, this theory would explain the presence of endometriosis in patients without a uterus such as in Mayer-Roki-tansky-Kuster-Hauser syndrome (MRKH) where retrograde menstruation is not physically possible. A 2005 study showed that metaplastic changes in ovarian stromal tissue were associated with endometriosis [9].

PATHOGENESIS

Steroid dependence

The pathogenesis of endometriosis stems from a complex interplay of a variety of factors. Endometriosis can be considered a steroid dependent disorder which can be broadly characterised by excess oestrogen and a resistance to progesterone which in combination with epigenetic changes leads to the hormonal milieu that is most conducive to ectopic tissue survival. Steroid hormones use nuclear receptors (NRs) to exert their effects on organ systems, and there have been many aberrantly expressed NRs which are thought to be implicated in the pathogene-sis of endometriosis.

One particular cascade is that the transcription factor (TF) NR5A1 is involved, and it upregulates the expression of the steroidogenic acute response protein (StAR) which leads to excessive production of oestradiol[11]. NR5A1 is almost directly opposed by the action of a transcriptional repressor (TRs) named NR2F2, which has the opposite effect and inhibits expression of StAR.

Observing the differential expression of these TFs and TRs in ectopic vs. eutopic endometrium, the presence of NR5A1 mRNA is ~12000 times higher in ectopic endometrial tissue which can be explained by the aberrant epigenetic changes detected in GWAS studies across various populations[12].

Oestrogen receptors also play a

similar role as the TFs, in particular ESR1 and ESR2 which have the same oppositional effect as NR5A1 and NR2F2, where ESR1 is responsible for the proliferative effects of oestradiol by binding to oestrogen promoter sequences and ESR2 suppresses these same sequences, however above a certain threshold of expression, ESR2 inhibits apoptosis via the expression of the SGK1 gene and facilitates inflammation via the COX-2 pathway[13], and another study showed that ESR2 predominance leads to evasion from immune surveillance by interfering with the inflammasome producing IL-1β which contributes to better cell to cell adhesion enabling the endometriosis lesions to take root[14]

In a similar fashion to the two-hit hypothesis, excess oestrogenic effects are not enough to drive the progression of endometriosis, and a second 'hit' is required which comes in the form of progesterone resistance.

Epigenetic changes are seen across many domains relating to the pathogenesis of endometriosis, and these changes provide the second 'hit'.

One of these changes is the differential expression of progesterone receptors (PGRs) in endometrial tissue. Eutopic endometrial tissue has both PGRs A and B (PGR-A and PGR-B respectively) and these have been found to be downregulated via epigenetic mechanisms such as the expression of miR196a directly downregulating PGR and thus causing progesterone resistance in eutopic endometrium, PGR-B is also selectively downregulated via hypermethylation of its promoter[15].

The suggestion that endometriosis is an epigenetic disease is supported by the fact that three DNA methyltransferase genes which are responsible for methylation are all found in abundance in endometriosis [16] and so are thought to further add to the dysregulated steroid-dependent pathways.

CELLULAR SIGNALLING AND INFLAMMATION

Cellular properties enabling survival are the second step in establishing endometriotic deposits after the hormonal milieu has been set up.

After retrograde menstruation the immune system will remove the excess tissue deposited outside the uterus, however in endometriosis these cells are able to persist because of two hypothetical reasons. The first one is that endometrial cells secrete a soluble molecule (ICAM-1) which interferes with NK cells apoptotic abilities, and the second is that due to an intrinsically dysregulated immune system - due to endometriosis being associated with other autoimmune diseases - the immune cells would not function normally.

Another ability that ectopic deposits have to acquire is that of neo-angiogenesis because their native environment - the richly vascularised endometrium - has to be replicated for survival.

Upregulation of TNF-a, IL-8 and MMP3 contribute to angiogenesis and these are found in higher concentrations in women with endometriosis in addition to elevated levels of vascular endothelial growth factor (VEGF). A study has also demonstrated that neuroangiogenesis occurs in conjunction with neovascularization which significantly contributes to dysmenorrhea, and has a positive correlation with disease severity.[17]

Analysing the cytokine and chemokine profile of peritoneal fluid of women with endometriosis, there are several cytokines that promote inflammation such as TNF-a and IL-6, and there are also chemoattractants such as MCP-1 which recruit macrophages that further promote angiogenesis and the formation of reactive oxygen species (ROS) through the processing of iron from erythrocytes, these ROS then damage peritoneal tissue leading to cyclical proliferation of endometrial tissue.[18]

A NEW UNIFIED THEORY

Given all the new and emerging research on epigenetic changes and micro and macroscopic alterations of the endometriotic environment, a new theory can be formed by

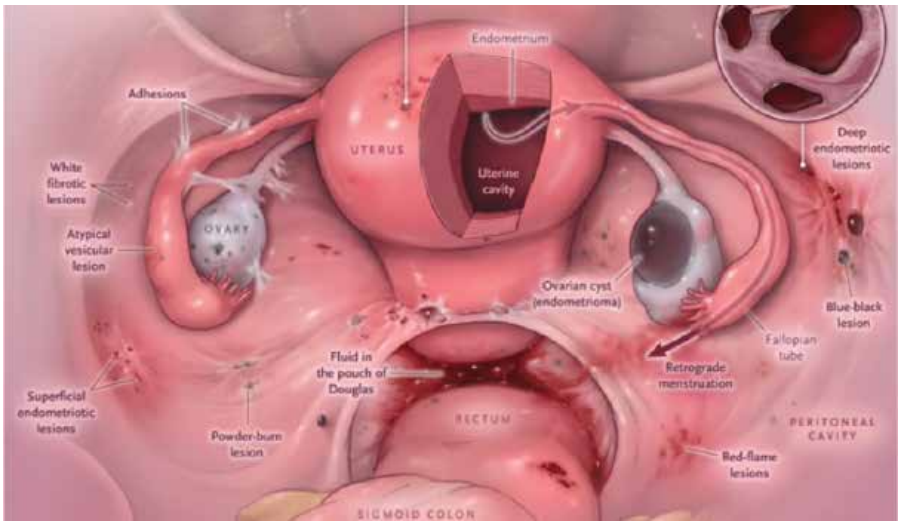

Figure 1: Subtypes of endometriosis. (Figure from Zondervan et al. (2020)

collating various aspects of previous mechanisms of pathogenesis. This unification of theories shows that the aetiopathogenesis of endometriosis is extremely complex and comes from various factors interacting together in a specific niche which is challenging to replicate in vitro, however the discovery of aberrant miRNAs, NR expression and steroid hormone imbalances can provide us with new targets for pharmacological therapies in the future.

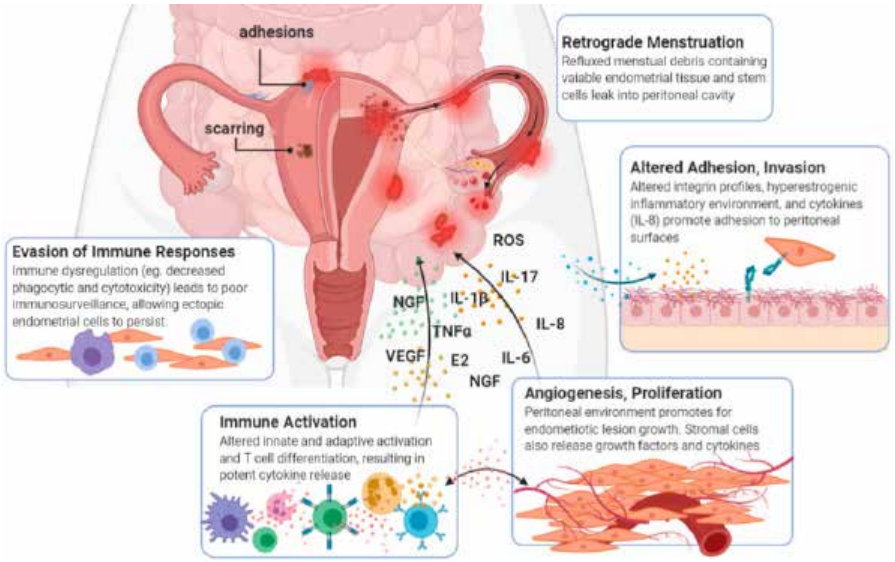

Figure 2 : Factors contributing to the pathogenesis of endometriosis Jiang et al., 2021(10)

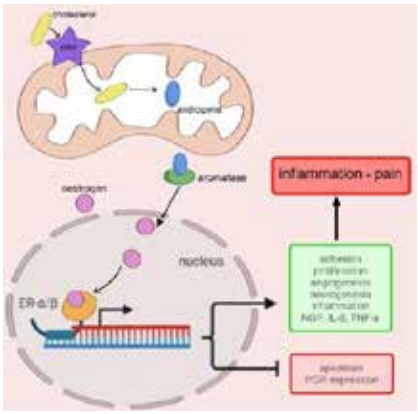

Figure 3 : Steroidogenic factors contributing to the pathogenesis of endometriosis. Figure adapted from Jiang et al., 2021[10]

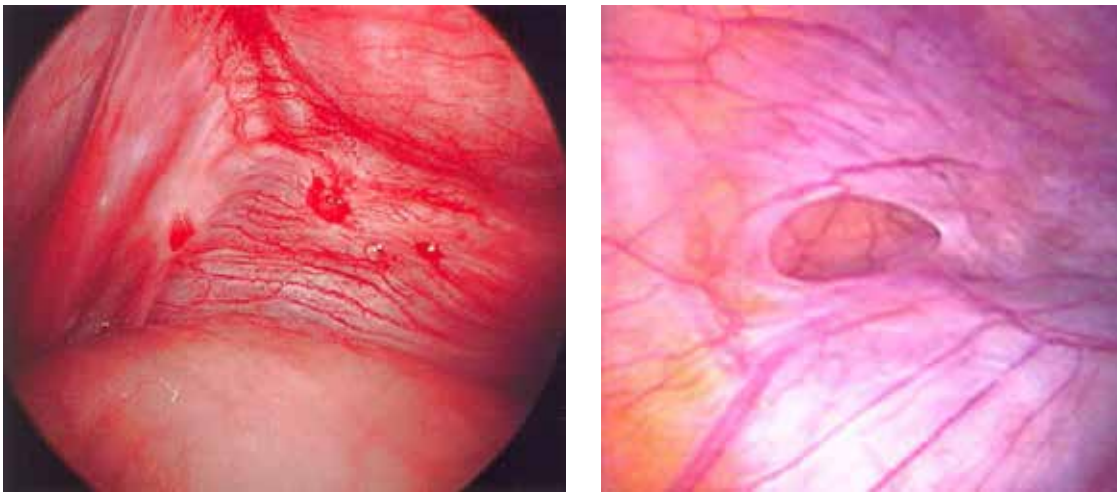

Figure 4, 5 : From left to right - 4) focal haemorrhage with surrounding angiogenesis, 5) an Allen-Masters peritoneal defect Burney and Giudice, 2012[18]

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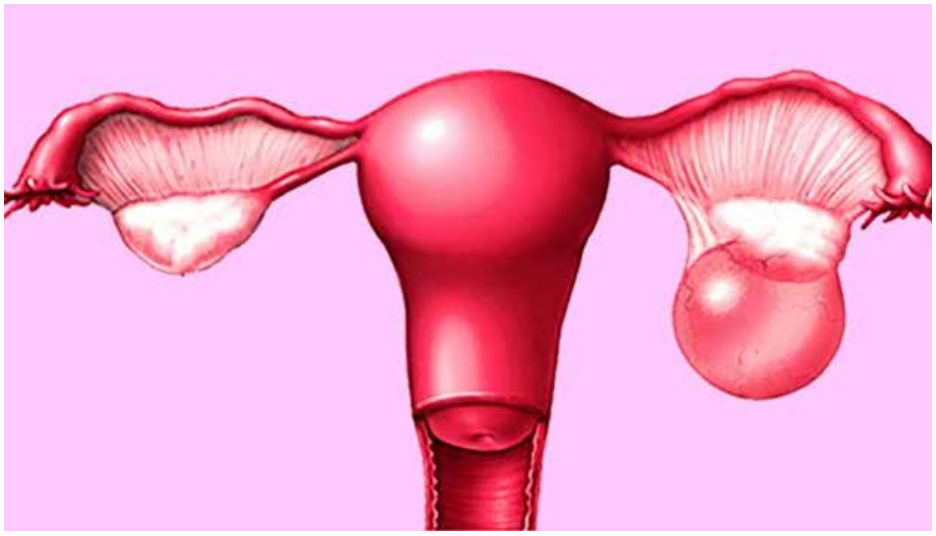
Endometrioma- When & How?

INTRODUCTION:

When the ectopic endometrial tissues are localized to the ovaries, they present as “chocolate” cysts called Endometriomas, the presence of which, almost always indicates the presence of the disease in other areas of the pelvis, such as rectosigmoid area and POD (Pouch of Douglas). It is associated with extensive adhesions secondary to reactive fibrosis and smooth muscle metaplasia. It is one of the most common ovarian cysts to present in a woman during her life, affecting 2 to 10% of the female



general population.[1] It usually presents as severe dysmenorrhea, dyspareunia, subfertility, infertility, chronic pelvic pain, dyschezia, irritable bowel syndrome.[2]

DIAGNOSIS OF ENDOMETRIOSIS:

Clinical history and clinical examination including per-vaginal and per-rectal examination can reveal palpable ovarian endometriotic cysts as adnexal mass, deep infiltrating endometriosis (DIE) as painful nodules in the rectal mucosa and POD. This can be confirmed by USG TVS" (ultrasound-guided transvaginal scan) and MRI with adequate accuracy.[3][4]

Diagnostic laparoscopy is still considered to be gold standard in diagnosing Endometriosis, followed by biopsy for histopathological confirmation.

Imaging techniques along with biochemical markers such as CA125 is useful in preoperative assessment of the severity of Endometriosis.[8]

In this article we discuss in detail about Ovarian Endometriomas and its surgical treatment modalities.

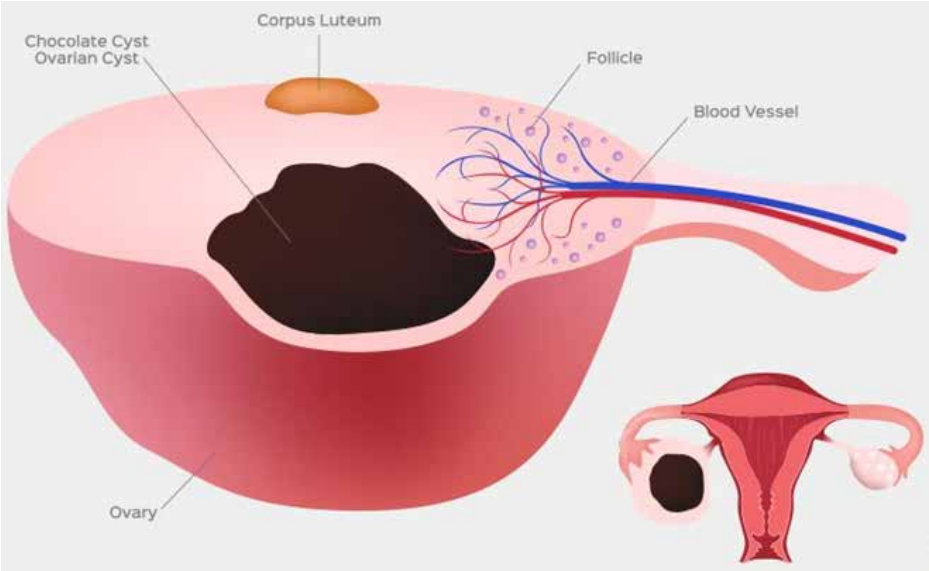
TREATMENT OPTIONS FOR ENDOMETRIOSIS: WHEN TO OPERATE?

Both medical management and combined surgical with medical management is advocated based on symptoms, extent of the disease and the desire for fertility. Treatment modality needs to be customized and curated to individual patient as inadequate treatment has high rates of recurrence and overzealous management will lead to affection of ovarian reserve, inadvertently contributing to subfertility/ infertility.[5][6]

Endometriomas < 3cm size can be managed medically with Dienogest, OCPs or GnRH analogs. Dienogest is a synthetic progestin, given in the dose of 2mg per orally daily, which can be used in endometriosis associated pain relief effective in up to 70% cases, and >50% reduction in cyst size. It is well tolerated and has a good safety profile[12]

Endometriomas >3cm or Endometriomas associated with severe dysmenorrhea, chronic pelvic pain or infertility needs surgical intervention in the form of Ovarian cystectomy.

Various operative methods of treating Endometriomas exist such as, Cyst fenestration with drainage or deroofing of the cyst, coagulation, or ablation with electrical or laser energy of the cyst base. These are associated with high rates of recurrence (~30%). (7) Laparoscopic stripping and cystectomy proves to be the most effective way of treating Endometriomas. The use of bipolar energy for achieving hemostasis may adversely affect the ovarian reserve.

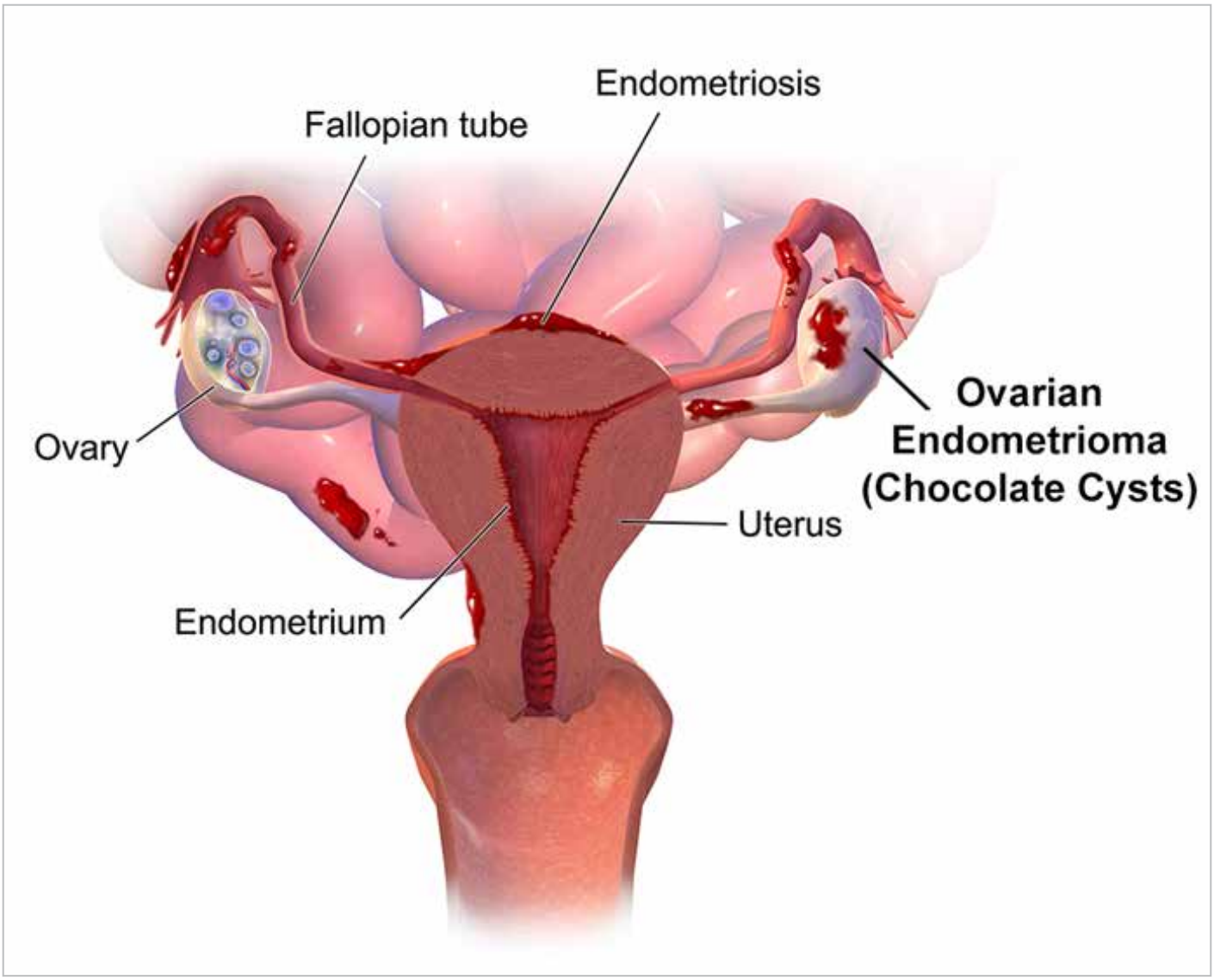


ROLE OF CA125 IN ENDOMETRIOMA MANAGEMENT PLAN:

CA 125 levels are often elevated in patients with endometriosis. CA125 levels directly correlate with the extent of the disease, size of the endometrioma and presence of pelvic adhesions.[8] CA125 value also correlates with the histological follicular loss of the ovary prior to laparoscopic stripping of the endometrioma capsule from the surrounding normal ovarian tissue. The follicular loss is unrelated to the surgical stripping techniques but directly or indirectly due to the biologic inflammatory process happening within the ovarian parenchyma adjacent to the endometrioma.[8]

ROLE OF TVS IN ENDOMETRIOMA MANAGEMENT PLAN:

Endometrioma typically appear as a complex cyst, unilocular or multilocular, with a typical homogeneous ground- glass appearance[6] with absent or moderate vascularization of the cyst walls.[5] USG helps in preoperative mapping of the endometriotic lesions, associated adenomyosis and to an extent the presence of adhesions and extraovarian endometriosis such DIE. Adhesions appear as fine septa



or strands of tissue in the pelvic fluid. Pouch of Douglas obliteration is assessed by pressing the USG probe on the cervix or placing a hand abdominally to see if the rectosigmoid freely glides over the posterior uterine surface (Sliding sign).[5] DIE is suspected when the anterior or posterior compartment shows abnormal hypoechoic retroperitoneal linear or nodular thickening with irregular contours and no vascular signals on Doppler.[5]

SURGICAL FLOWCHART FOR ENDOMETRIOMA SURGERY:

- Number of Ovarian Endometriomas, presence of pelvic adhesions noted by USG.
- Appropriate preoperative counseling done and consent for surgery taken.
- Patient is placed in modified lithotomy position, under general anesthesia. Veress needle insertion done at Palmer's point which is relatively free of adhesions in most cases, to achieve pneumoperitoneum. Initially insufflation flow is kept at 1L/min. 5mm trocar is inserted blindly about 2 inches below the Palmer's point and lateral to inferior epigastric artery surface landmark and first port created. Insufflation flow rate is then increased to 30 L/min once abdominal cavity is safely entered.
- Primary 10 mm trocar is inserted above the umbilicus mid-way between xiphisternum and umbilicus under visual inspection by 5 mm camera via the 1st port. This placement enables thorough inspection of the abdominal and pelvic cavity as well as the under surface of the diaphragm, liver and spleen by providing a panoramic view. Two more 5 mm trocars are inserted under vision at the left iliac fossa and contralateral side mid-way point between the other two 5mm ports lateral to

the Inferior epigastric artery (Fig 2). This port placement forms a triangle in relationship to one another and avoids chop stick effect during surgery. Insufflation pressure is set at 14 mmHg.

- Thorough inspection and exploration of the abdominal cavity done in clock view manner to look for endometriotic lesions and assess the extent of the disease.
- Endometriotic cysts/ Endometriomas are isolated, freed from any adhesions. (Fig 4)
- Cysts are punctured using monopolar energy source by making a small sharp nick over the cortical surface over the cyst, large enough for the suction cannula to pass through. (Fig 6)
- Contents of the cysts are aspirated, through irrigation and suction alternatively until the irrigation fluid becomes clear. Initial incision over the cyst is enlarged and the inner wall of the cyst is checked for possible vegetations.
- Cleavage plane is identified and the capsule of the cyst is stripped from the surrounding normal ovarian tissue using two toothed grasping forceps pulled gently in opposite directions.
- Hemostasis is then achieved with bipolar forceps applied on the ovarian parenchyma on the specific bleeding points of the inner surface where the cyst was stripped off. This judicious use of bipolar energy in the long term does not seem to adversely affect the ovarian reserve.[9] Care is taken not to use any energy on the outer surface of the ovary to avoid adhesions formation and loss of follicles.
- Cyst wall is subjected to Histopathological examination to confirm the diagnosis.

RECENT ADVANCES IN ENDOMETRIOMA SURGERY:

- Vasopressin injection in the dilution of 10% solution using 10U vasopressin in 100 ml is injected in the plane between the cyst wall and the normal ovarian tissue which causes ballooning and hydro dissection of the cleavage plane, ensuring easy stripping of the cyst wall and lesser need of energy source to achieve hemostasis.[10] When injected in the correct plane, side effects of intravenous vasopressin are prevented.
- Alternatively, Floseal, a topical hemostatic agent containing collagen granules and human thrombin or Surgicel powder (Oxidized regenerated cellulose) may be used to achieve control over minor bleeding points after stripping of the endometrioma and is predicted to preserve ovarian function.[11]

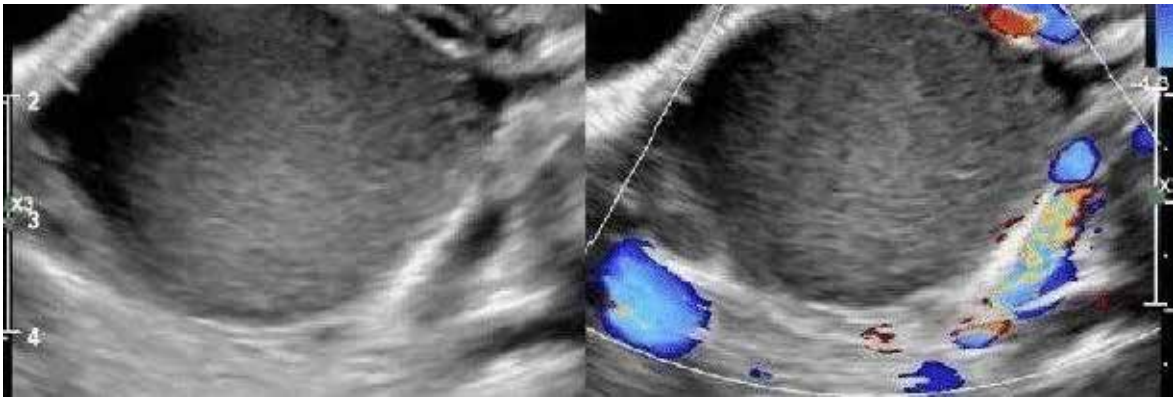


Figure 1: TVS image of Endometrioma showing ground glass appearance (Left), Figure 2: Doppler showing minimal peripheral vascularity (Right)

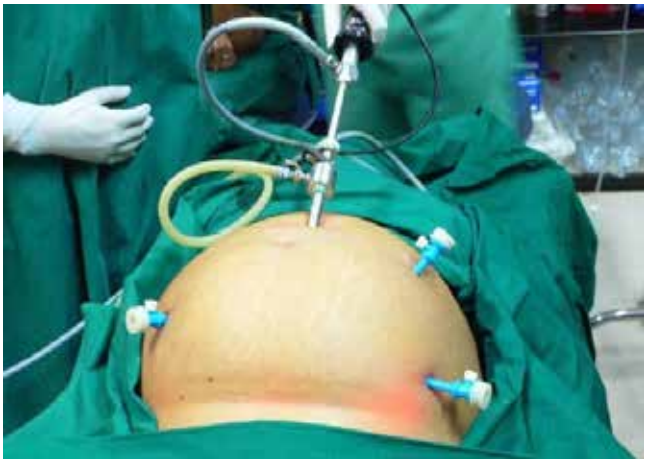


Figure 2: Picture showing Port placements

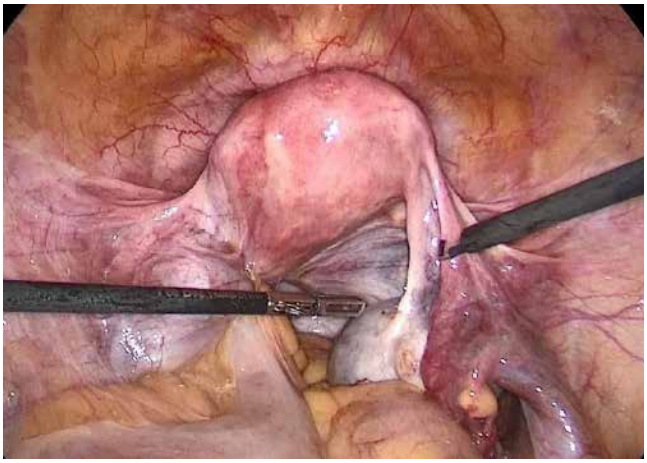


Figure 3: Inspection of Abdominal and Pelvic cavity

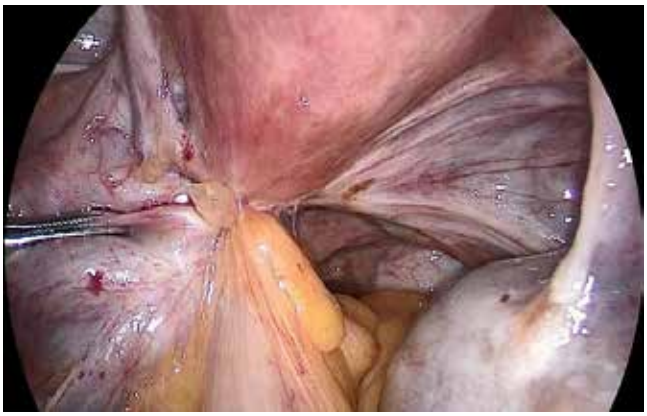


Figure 4: Inspection and assessment of adhesions

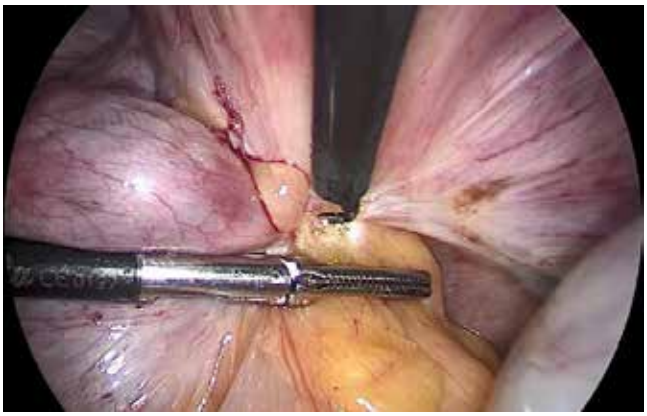


Figure 5: Adhesiolysis

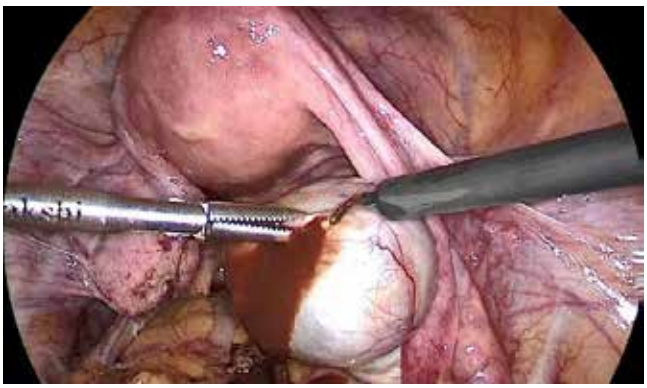


Figure 6: Use of Monopolar to make a nick on the cyst

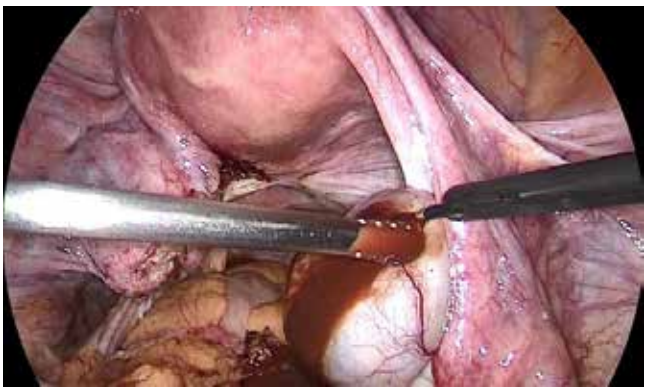


Figure 7: Suction and irrigation of the cyst

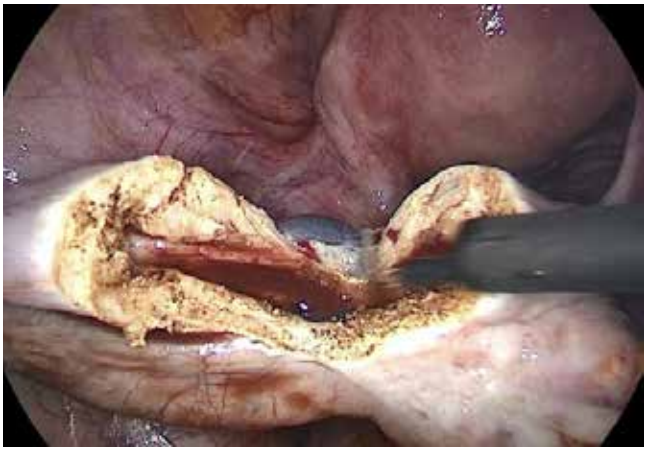


Figure 8: Identifying the cleavage plane

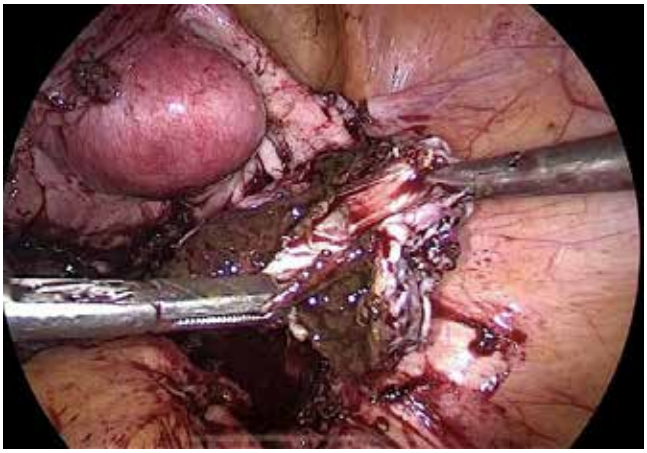


Figure 9: Stripping of the cyst wall

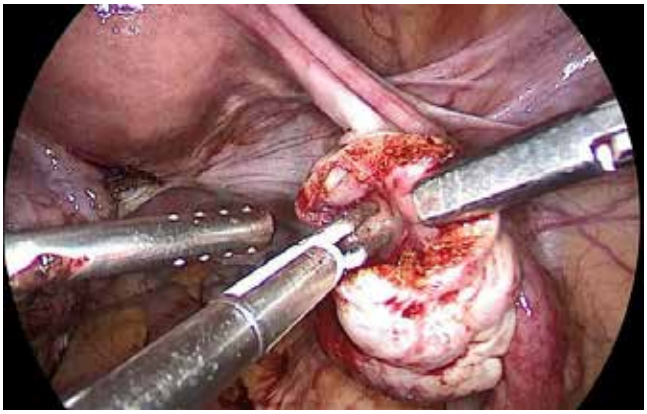


Figure 10: Use of Bipolar on bleeding points for hemostasis

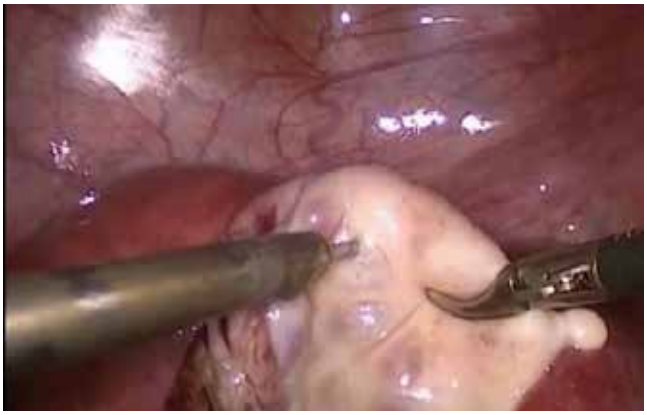


Figure 11: Intracapsular Vasopressin Injection before Cystectomy

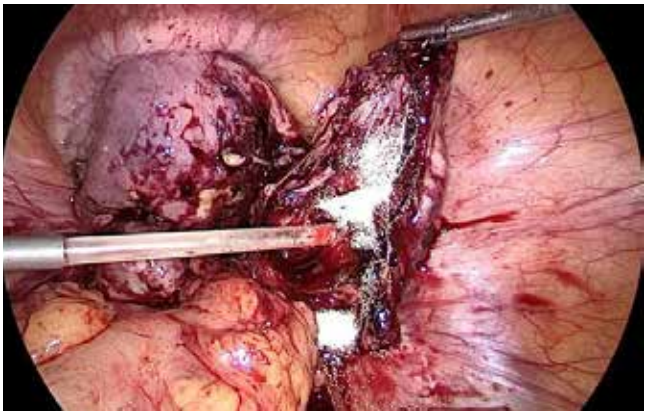


Figure 12: Surgicel Powder (Oxidized Regenerated Cellulose)

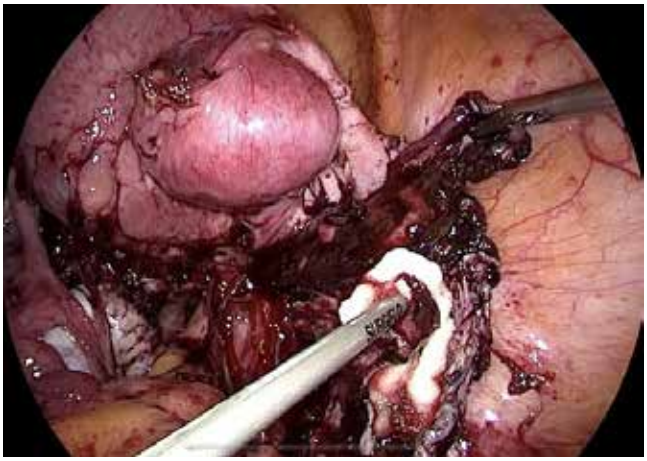


Figure 13: Floseal Hemostatic Matrix

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Ultrasound Approach to Endometriosis

INTRODUCTION

Endometriosis is defined as 'the deposition of tissue which looks and acts like endometrium at places other than the inner lining of the uterus'.

This tissue cyclically responds to hormonal changes, resulting in the collection of menstrual products in ectopic locations, leading to inflammation and scar tissue formation.

It is an '*estrogen- dependent disorder*'. Development of endometriosis may be due to a combination of genetic, hormonal, and immunological factors.

Endometriosis affects 6 to 10% women of the reproductive age group, and affects nearly 50% amongst the group of infertile women[1].

Common clinical presentation is pain- pertinent to affected organs (pelvic deposits, vaginal vault, bladder and rectum) and infertility[2].

Diagnosis of endometriosis is accomplished through surgical visualization of endometriotic deposits with histological confirmation.

It's ideal to have a non-invasive method to identify endometriosis[5]. Non-invasive diagnostic tools are biomarkers and imaging techniques.

Evidence-based biomarkers are not available in the diagnosis of endometriosis[5].

Imaging modalities that help in identifying and staging endometriosis are '*high resolution transvaginal ultrasound examinations' and 'high resolution contrast enhanced MRI*'.

PRESENTATION OF ENDOMETRIOSIS (PHENOTYPES) VARIES[3]:

- Superficial peritoneal lesion
- Endometriomas
- Deep endometriosis - depth of penetrating nodules exceeding 5mm,
- Scarring and adhesions
- Extra-pelvic lesions

Imaging is of little use in the identification of common presentations. Superficial peritoneal lesions[3], transvaginal ultrasound and MRI have 90% sensitivity and specificity in identifying endomeriomas[3].

Detection of deep infiltrating endometriosis and adhesions require skilled experts trained in transvaginal ultrasound and MRI[3]. Diagnosis of endometriosis is a complex challenge because of non-specific symptoms, lack of specific biomarkers and lack of awareness[3]

ESHRE GUIDELINES STRONGLY RECOMMENDS[5]:

- Measurement of biomarkers - should not be used.
- Imaging modalities such as transvaginal ultrasonography and MRI need to be used with the

awareness that negative findings do not rule out endometriosis. ults and unsuccessful empirical treatment.

- Laparoscopy is recommended in patients with negative imaging results and unsuccessful empirical treatment.
- Lesions identified on laparoscopic examination need to be histologically confirmed.
- Long term monitoring is not strongly recommended. Type and frequency of long-term monitoring should be individualized.

ENDO-CAVITY ULTRASOUND ASSESSMENT OF ENDOMETRIOSIS:

Pre-operative ultrasound mapping of all endometriotic lesions (location & extent) is necessary before surgery, hence helps in triaging the patient to appropriate laparoscopic surgeon.

"High quality ultrasound" is the need of the hour.

Transvaginal ultrasound evaluation of site-specific tenderness and organ mobility (soft markers) help in dynamic examination of endometriotic lesions of pelvic viscera.[6]

The IDEA (International Deep Endometriosis Analysis) Group has proposed a four-domain approach in the transvaginal ultrasound examination of patients suspected to have endometriosis[7].

Step I:

Examination of uterus & adnexa - sonographic signs of adenomyosis and endometriomas.

Step II:

Transvaginal evaluation of 'soft markers' - such as Sight Specific Tenderness (SST) and mobility of pelvic viscera.

Step III:

Assessment of Pouch of Douglas (POD) - based on 'sliding sign' (Negative sliding sign - obliterated POD, positive sliding sign -No involvement of POD).

Step IV:

Assessment of Deep Infiltrating Endometriotic nodules in the anterior and posterior compartments.

These steps can be adopted in the above order or in any order, but all the steps need to be performed.

UTERUS:

- Asymmetric enlargement of the uterus quite often with increased thickening of the posterior wall.
- Ill- defined non-homogenous myometrial lesions.
- Presence of myometrial cysts and echogenic islands.
- Interrupted endo-myometrial junction (Junctional zone).
- Color Doppler reveals intralesional vascularity.
- Uterus retroflexed with fundus adherent posteriorly to the rectum and/or sigmoid colon - "Question mark sign"[8] (Fig 1)
- Step III - involvement of Pouch of Douglas is assessed by eliciting the 'sliding sign'[9]
- Independent movement (sliding) of uterus and cervix over the anterior wall of Rectum indicated 'positive sliding sign' non-obliteration of POD
- Movement of uterus and cervix in unison with anterior rectum and sigmoid, test is 'negative sliding sign' - indicating obliterated POD.

ADNEXA:

- Presence of a well circumscribed unilocular ground glass cysts in the adnexa is suggestive of endometrioma[10] (Fig 2)
- Involvement of the fallopian tube results in a sausage shaped, incomplete septate cyst - hydrosalpinx or hematosalpinx. (Fig 3)

ANTERIOR COMPARTMENT[11]:

- Urinary bladder, Uterovesical region, ureters, anterior vaginal vault constitute the anterior compartment. Base of the urinary bladder is the common site of deep infiltrating endometriosis (Fig 4), adjacent to it is the involvement of the uterovesical region.
- Infiltrations are usually hypoechoic linear or spherical lesions.
- Involvement of the uterovesical region presents as obliteration of uterovesical space with hypoechoic lesions.
- Status of the ureters need to be assessed pre-operatively - either by demonstrating dilated distal ureters or ureteric involvement can be ruled out by dynamic demonstration of urine jet into the bladder.
- Transabdominal scan of kidneys is essential to rule out hydroureteronephrosis.

POSTERIOR COMPARTMENT:

- Anterior rectum, anterior rectosigmoid, sigmoid, rectovaginal septum, uterosacral ligaments (USL), and posterior vaginal fornix constitute the posterior compartment.
- Infiltration of posterior vaginal fornix is confirmed by demonstration of hypoechoic endometriotic nodules in the posterior vagina vault.

- Rectovaginal nodule and involvement of anterior rectum is difficult to identify by laparoscopy.
- Ultrasound can demonstrate these lesions11as thickening of the hypoechoic muscularis propria or as hypoechoic nodules (Fig5).
- Need of bowel preparation is debatable.

Ultrasound is not very effective in the demonstration of uterosacral ligament involvement, ultrasound examination of USL is achieved by taking the midline sagittal section of the cervix and then sweeping the transducer inferolateral to the cervix.

CONCLUSION:

- This article outlines the practical approach in the evaluation of Endometriosis using ultrasound as an appropriate diagnostic tool.
- The four-step approach optimizes effective assessment of endometriosis.
- Expertise in ultrasound examination of endometriosis need to be emphasized.
- Mapping of size, exact location and severity of lesions triage management strategies.
- **Disclosure statement:**

  - nothing to disclose.

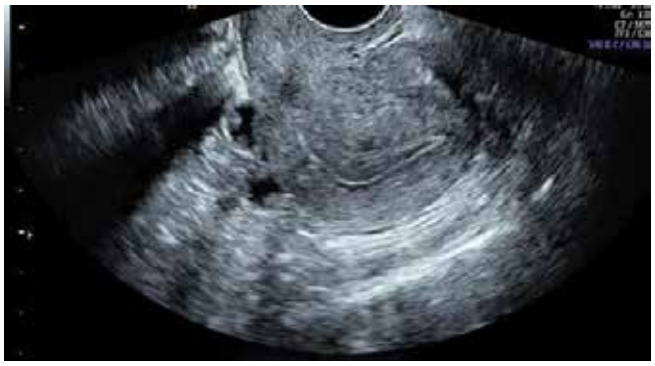

Figure 1: Question mark sign

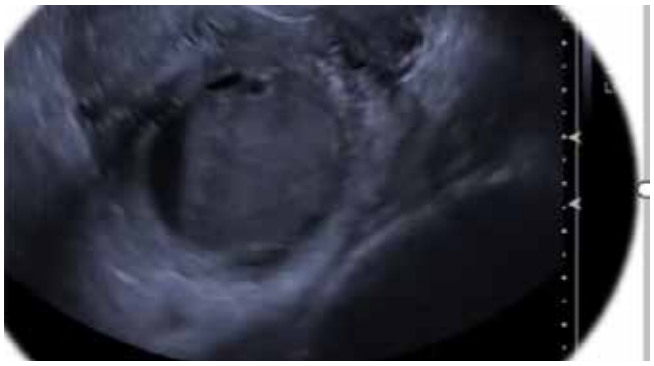

Figure 2: Well circumscribed unilocular ground glass cyst with fluid in fluid levels- endometrioma fixed to the posterior wall of the uterus

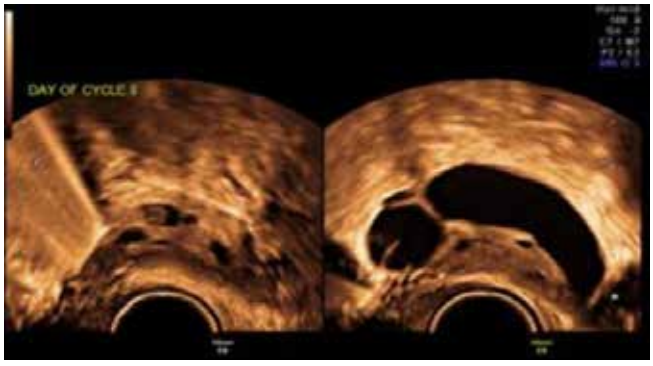

Figure 3: Hydrosalpinx

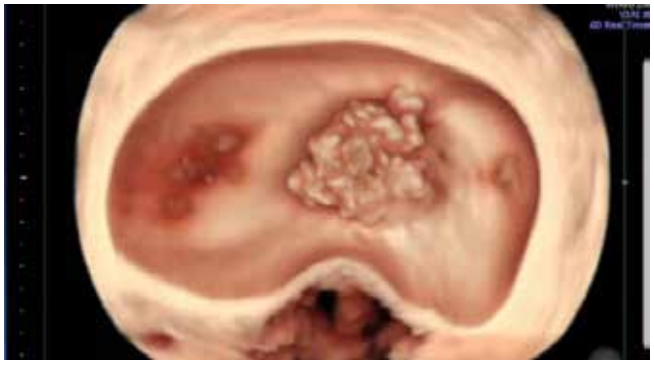

Figure 4: Deep infiltrating bladder wall endometriotic deposits

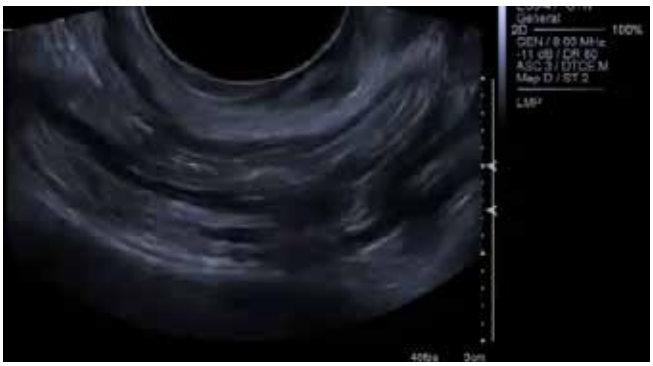

Figure 5: Anterior rectal wall endometriotic nodule

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Radical Robotic Hysterectomy for Advanced Endometriosis

Link to the video:
https://youtu.be/aAYjBxU43GQ

In this video, we describe a technique of tailored radical robotic hysterectomy for advanced endometriosis. Surgery in endometriosis is difficult because of adhesive nature of the disease. Class 2 modified radical hysterectomy reduces the pain recurrences differs from class 3 hysterectomy as the uterine artery is transacted at the level of internal os and not at its origin. We describe five steps of this surgery:

1. Sigmoid mobilisation from the lateral wall specially to identify the left ureter
2. Lateral transaction of Endo pelvic fascia beyond the IP ligament
3. Follow the ureters into the pelvis by bilateral ureterolysis
4. Rectal adhesiolysis & development of paramedical spaces
5. Anterior & posterior Colpotomy followed by ligation of the uterine arteries in the end.

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Psychological and Mind-Body Interventions for Endometriosis

Pain is a universal experience but very subjective and relative to an individual. It is the most common reason that people seek medical intervention. Pain serves an important purpose by alerting an individual/organism to discomfort/ injury. People think of pain as a purely physical sensation. Rather pain has biological, psychological and emotional factors. Chronic pain is often more complex. It is frequently experienced in the absence of any detectable tissue damage.

Furthermore, chronic pain can cause feelings such as anger, hopelessness, sadness and anxiety. Unfortunately, alleviating pain isn't always straightforward all the time. To treat pain effectively, health professionals should ad-dress the physical, emotional and psychological aspects.

In the context of Endometriosis, it is a painful disorder for some women. According to WHO, Endometriosis affects roughly 10% (190 million) of reproductive age women and girls globally[1]. In Endometriosis many women sometimes endure severe pain – especially during menstrual periods. Fertility problems may also develop. The social stereotypes of a women's identity fulfillment through mother-hood are also challenged in a condition like endometriosis.

Many women who suffer from this condition also face the stigma in families and social systems of 'not being useful/barren/sterile.' A woman with this condition may have other symptoms as fatigue, diarrhoea, constipation, bloating or nausea, especially during menstrual periods. Chronic pain may aggravate stress, anxiety, and depression.

Having a painful condition like endometriosis is stressful. Unfortunately, stress can contribute to a range of health problems, including high blood pressure, heart disease, obesity, diabetes, depression and anxiety. Stress can trigger muscle tension/spasms that may increase pain. Treatment modalities are medication, surgery, rehabilitation and physical therapy. Psychological treatments are also equally an important part of pain management. Understanding and managing the thoughts, emotions and behaviors that accompany the discomfort can help clients/patients cope more effectively with the pain—and can actually reduce the intensity of pain, resulting in an improved quality of life.

Stress is an unavoidable part of life, but an adequate know-how of: how to manage stress will help the body and the mind to lessen pain. Psychologists can help manage the stresses in a patient's life related to chronic pain. Psychologists can help one to learn relaxation techniques, such as meditation or breathing exercises to keep stress levels under control.

Some psychologists use an approach called biofeedback, which teaches how to control certain body functions. In biofeedback, sensors attached to skin measure stress response by tracking processes like heart rate, blood pressure and even brain waves. As one learns strategies to relax the muscles and the mind, one can watch on a computer screen as the body's stress response decreases. Through this method, one can determine which relaxation strategies are most effective, and practice using them to control the body's response to tension.

For patients dealing with chronic pain as in endometriosis, treatment plans are customized /designed as per the patient's socio-cultural system. The remedial plan often involves teaching relaxation techniques, changing old beliefs about pain, building new coping skills and addressing any anxiety or depression that may accompany pain. It is helping to learn to challenge any unhelpful thoughts one has about pain. A psychologist can help develop new ways to think about problems and to find solutions. In some cases, distracting from pain, itself is helpful. In other cases, a psychologist can help develop new ways to think about the pain. A psychologist can also help clients make lifestyle changes that will allow one to continue participating in work and recreational activities.

Because pain often contributes to insomnia, a psychologist may also help learn new ways to sleep better. Research into psychological and behavioral treatment for pain, now has evidence-based techniques[2,3].

Psychologists are experts in helping people cope with the thoughts, feelings and behaviors that accompany chronic pain. Managing emotions can directly affect the intensity of any pain. Patients with chronic pain should be referred to psychologists by other health care

providers to address both the physical and emotional aspects of the patient's pain.

The most common psychological treatment for pain is cognitive-behavioral therapy (CBT). Through CBT-based programs, patients can learn to steer the thoughts away from "awfulizing" pain and retrain thinking about pain as a manageable problem that one can address through treatment and self-care. CBT-based programs provide education about pain, self-management skills and psychological tools to help patients manage symptoms, become more active and live better within the context of pain. Other psychological and behavioral treatments include acceptance and commitment therapy (ACT), hypnosis and mindfulness-based stress reduction (MBSR), and Biofeedback.

Pain Reprocessing Therapy[4], (PRT) is an evidence-based approach for treating chronic pain. Rooted in neuroscience, PRT aims to rewire neural pathways in the brain. It is from the family of psychological and behavioural treatments that the brain sensitizes and constructs pain experience in part, it's not all about the body. It attempts to unwind the cycle of fear, avoidance and increased pain. This happens in two ways and first part is conceptual.

When the fear of pain becomes threatening, it becomes attended. And when it's attended, it becomes amplified. And over time pain gives rise to threat signals in the brain, which give rise to more pain. So, there's a feedback cycle where pain is ramped up over time. This is known as the sensitization process. So part of the antidote to that is simply realizing that pain is not a sign of damage.

Studies have found that some psychotherapy can be as effective as surgery for relieving chronic pain because psychological treatments for pain can alter the brain's processing feature for pain sensations. It has a process of activating the endogenous opioid receptors in the brain neural pathways. Another important method is psychoeducation to secondary school children about pain management like sensitizing young girls and women not to assume that menstrual periods are synonymous to bad pain and cramps. In many subsystems of societies periods are a still taboo topic so females are silenced through social conditioning to keep bearing agonizing pains, which can be severe dysmenorrhea in case of Endometriosis.

TIPS FOR COPING WITH PAIN:

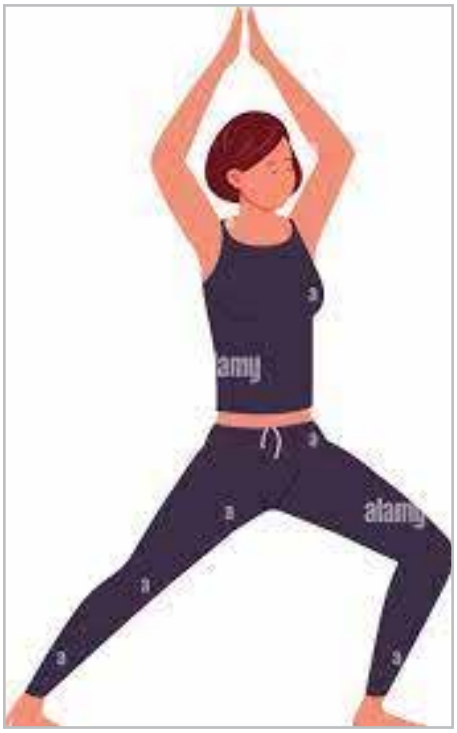
The following steps can be helpful in changing habits and improving pain management in endometriosis

Staying active:

Pain—or the fear of pain—can lead people to stop doing the things they enjoy. It's important NOT TO let pain take over your life. Make a plan about how to manage your pain, and don't push yourself to do more than you can handle.

Exercise:

Stay healthy with low-impact exercise such as stretching, yoga, walking and swimming.



Make social connections:

Call a family member, invite a friend to lunch or make a date for coffee/tea (NO alcohol) with a buddy you haven't seen in a while. Research shows that people with greater social support are more resilient and experience less

depression and anxiety. Ask for help when you need it.

Distract yourself:

When pain flares, find ways to distract your mind from it. Watch a movie, take a walk, engage in a hobby or visit a museum. Pleasant experiences can help you cope with pain.

Follow prescriptions carefully:

If medications are part of a treatment plan, be sure to use them as prescribed by the doctor to avoid possible dangerous side effects. With the right kind of psychological treatments, many people learn to manage their pain and think of it in a different way. Psychologists can help develop a routine to stay on track with the treatment.

THIS LIST CONSISTS OF A FEW SMALL, NICE THINGS TO DO FOR THE PATIENT/ CLIENT TO KEEP THE PAIN PERSPECTIVE IN RANGE OF MANAGEABILITY

1. Go for a walk in nature.
2. Stretch for at least 20 minutes every morning. Breathe long and slow. Spend at least 20 minutes in natural sunlight.
3. Actually, take some stretch breaks during the day, too.
4. Call a good friend whom you haven't spoken to in a while.
5. Create a playlist of all the songs you loved when you were younger but haven't heard in a while. Listen to them.
6. Develop a go-to method to help you unwind when you're feeling angry or stressed out.
7. Talk about your feelings with someone. But be more open about your inner world.
8. Take a minute and think about how you talk to yourself. Work on your inner dialogue. Self-compassion is crucial.
9. Get some food you love –your favourite snack, sandwich, coffee, or treat – and savour it. Like, really focus on every sip and bite.
10. Learn to press "pause" during an argument if you feel yourself getting worked up. Tell the person you're speaking to that you need a few minutes. Compose yourself. Return calmer.
11. Take a power nap.
12. Plant something in the garden, terrace, balcony. Or just get some cool houseplants. It's amazing what seeing more-green can do.
13. Write (by hand) the angriest letter you can to a person who is causing you the most stress. Take a deep breath. Throw it away.
14. Play like a kid, with kids. Have fun. Go all in on imagination. Take the journey. You'll feel much better afterwards.
15. At the end of each day, make a list of things for which you're grateful. Positive affirmations are a strong antidote against anxiety and depression, but they're incredibly helpful for changing the outlook.
16. Rearrange a room where you spend a good deal of time. A lot of mental benefit comes from a little adjustment of the scenery – especially when it's scenery you see often.
17. From swimming, to walking/ jogging, strolling, even dancing, even yoga. Whatever you do, make a pact to move your body consistently for at least 25 minutes during the day. Get those endorphins flowing.
18. Turn off push notifications on your phone. Why? The less you're forced to look at something, the more you'll intentionally look at the things you want to see and win back yourself from the pull of social media.
19. Speaking of phones, don't look at yours first thing in the morning. Give yourself an hour. Wake up. Drink some water. Mediate, relax. Whatever. Checking the news and Twitter can wait.
20. Give yourself an hour of screen-free time a day.
21. Unfollow ten accounts on social media that don't bring you joy.
22. Do you walk every day? Promise to take a different route than you normally do.
23. Write an email – or send an actual letter – to a friend or family member just to check in and say hi.
24. Seek the help you need but have been putting off. That is: sign up for that therapist, go to the doctor, make that dental appointment.
25. Spend time in prayer or meditation.
26. Dedicate ten minutes more a day to your hobby. Even if that means you're only dedicating ten minutes, that's a start.
27. Pledge to drink more water. While you're at it, eat more fruits and vegetables.

28. Prioritize a good wind-down routine at the end of the day to prepare your body for sleep.
29. While we're at it: prioritize good sleep in general.
30. Add "Time to laugh" on your calendar. Spend this five- or ten-minute chunk of time telling jokes with kids or watching videos that make you giggle. It does wonders for your state of mind.
31. Forgive yourself. Pledge to do better next time.

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Affiliated Hospital or Company: (1) _____

(2) _____

Qualification:

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1.		
2.		
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4.		
5.		
6.		

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Registration No.	Registering Body	Year
1.		
2.		
3.		

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Organisation	Type of Membership	Since
1.		
2.		
3.		
4.		
5.		

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Amount Paid: Rs. _____ (In words) _____ only

Cheque /Draft Number: _____ Date of Issue: _____

Name of Bank and branch: _____

Details for Bank Transfer:

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Account Holder: Endometriosis Society India
Account Number: 0673010072605 **IFS Code**: PUNB0067320
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