



ENDOMETRIOSIS AND EFFECTS ON WOMEN FERTILITY-A REVIEW

Shelly Khurana¹, Dhirender Kaushik², Garima Golandaz³

^{1&3}Assistant Professor, Dept. of Pharmaceutical Sciences, Gurugram University, Gurugram,122018

²Professor, Dept. of Pharmaceutical Sciences, Gurugram University, Gurugram,122018

Corresponding author: Shelly Khurana

Abstract

Endometriosis is a gynaecological disorder which can be identified by the presence of ectopic endometrial tissue outside the uterus. This disease mainly affects reproductive-aged women and having major effect on the fertility of the women. Clinical indicators of endometriosis can be dyspareunia, cyclic menstrual pain and chronic pelvic pain. All of these symptoms can affect the patient's quality of life and health conditions severely; therefore, proper medical attention and is required as soon as endometriosis is identified clinically. In this article, the prevalence, cure and management of endometriosis will be discussed.¹

Keywords: endometriosis, pelvic pain, dysmenorrhea, diagnosis, management

Discussion

Endometriosis is defined as the presence of endometrial-like tissue or glands outside the uterine cavity. It is a gynaecological disorder and most commonly identified in reproductively active women. These endometrial tissues are responding to hormonal stimulation and undergoes cyclic growth and shedding. This can further lead to internal accumulation of blood. General clinical symptoms of endometriosis are menstrual pain, and severe pelvic pain. These symptoms can have a negative effect on the quality of life of patients. Endometriosis can be present with or without symptoms. If it is present without symptoms generally missed in diagnosis. It can be one of the major causes of infertility in premenopausal women.

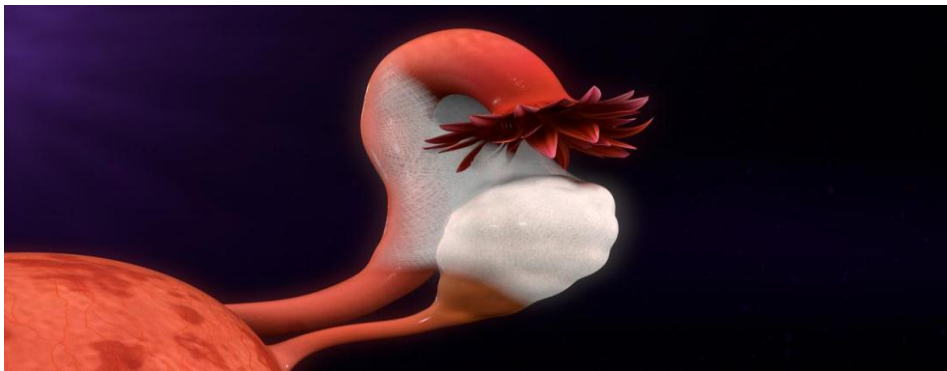
The most common sites of endometriosis are the ovaries, uterine ligaments, pouch of Douglas, and fallopian tubes. It can be identified in gastrointestinal tract, lungs, diaphragm, abdomen, and pericardium which is rare.^{2&3}

The endometriotic lesions can be divided into three types:

Red Lesions:The red lesions represent a high level of vascularization activity.

White Lesions:Whitish lesions are later phases of red lesions that have undergone a process of inflammation and fibrosis.

Black lesions: Representative of cyclic tissue decomposition and healing with the formation of scar tissue.



The presence of endometriotic lesions is presented above¹²

Signs and Symptoms

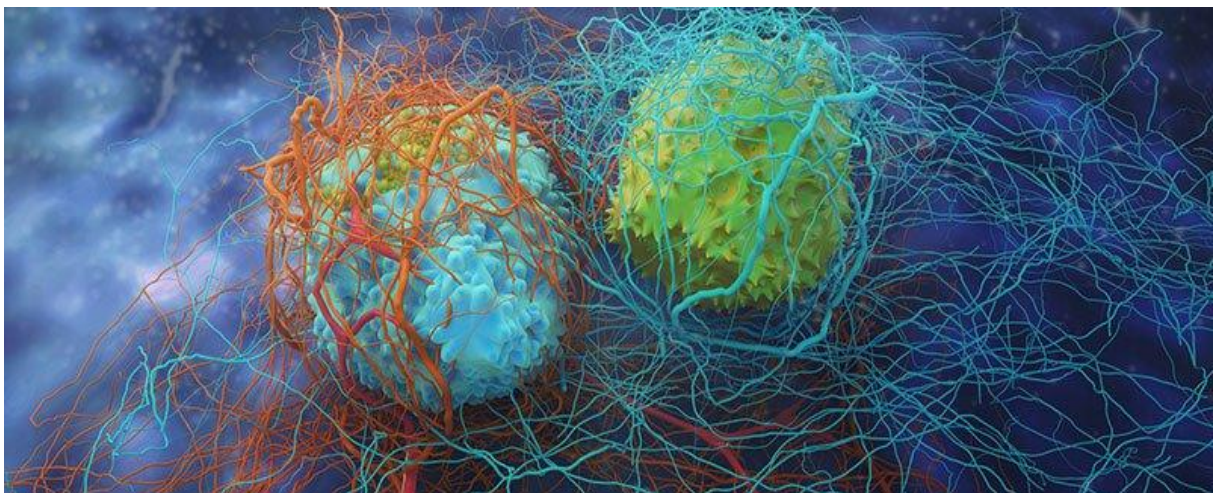
- **Painful periods (dysmenorrhea).** Pelvic pain and cramping may begin before and after menstrual period. Sometimes lower back and abdominal pain also may occur.
- **Pain with intercourse.**Pain during or after intercourse is common with endometriosis.
- **Pain with bowel movements or urination.**Patient can experience these symptoms during a menstrual period.
- **Excessive bleeding.**Patient can complain for heavy menstrual periods or bleeding between periods.
- **Infertility.**Endometriosis is generally diagnosed in those seeking treatment for infertility.

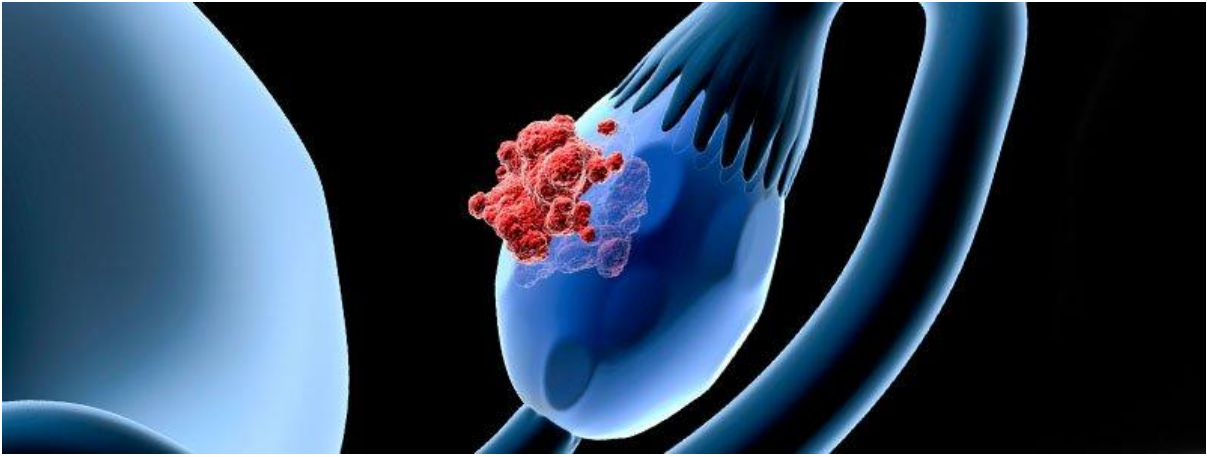
- **Other signs and symptoms** fatigue, diarrhoea, constipation, bloating or nausea, especially during menstrual periods.³

Infertility in Endometriosis

Infertility is a common complication that is known to occur in women who are suffering from any type of endometriosis. The women less than 35 years of age with endometriosis is on high risk of infertility, Women with endometriosis also have been shown to have an increase in macrophages and specific cytokines in the peritoneal fluid. The macrophages present try to maintain a state of chronic inflammation and the formation of adhesions. The increased macrophages and scarring interfere with normal sperm motility and ciliary function of the fallopian tubes. The development of adhesions also might obstruct the normal tubal transport, thereby causing infertility. In the absence of any of the above, other mechanisms may cause of decreased fertility in women with endometriosis include perturbed folliculogenesis, luteal phase defects, progesterone resistance, and anti-endometrial antibodies.^{4,5&6}

In condition of endometriosis, displaced endometrial tissue continues to behave as normal tissue. Generally, it will thicken, breaks down and bleeds with each menstrual cycle. As this displaced tissue does not find a way to exit the body, it becomes trapped. When endometriosis involves the ovaries, cysts are formed and called as endometriomas. Surrounding tissue can become irritated, scar may develop and further can lead to adhesions of fibrous tissue that can cause pelvic tissues and organs to stick to each other.^{4,5&6}





The presence of endometriotic tissue is presented above ¹³

The Cause of the Disease

The exact cause of endometriosis is not known, the possible explanations include:

- **Retrograde Menstruation.** In retrograde menstruation, menstrual blood containing endometrial cells flows back through the fallopian tubes and into the pelvic cavity instead of out of the body. These displaced endometrial cells stick to the pelvic walls and surfaces of pelvic organs, where they grow and continue to thicken and bleed over the course of each menstrual cycle.
- **Embryonic Cell Transformation.** Hormones such as estrogen may transform embryonic cells which are in the earliest stages of development and may convert into endometrial cell implants during puberty.
- **Surgical Scar Implantation:** After a surgery, such as a hysterectomy or C-section, endometrial cells may attach to a surgical incision.
- **Endometrial Cell Transport:** The blood vessels or tissue fluid (lymphatic) system may transport endometrial cells to other parts of the body.
- **Immune System Disorder:** A problem with the immune system may make the body unable to recognize and destroy endometrial tissue that's growing outside the uterus.^{7&8}

Risk Factors Associated with Endometriosis

- Never giving birth
- Starting of period at an early age
- Going through menopause at an older age
- Short menstrual cycles generally less than 27 days
- Heavy menstrual periods that last longer than seven days
- Having higher levels of estrogen in the body
- Low body mass index
- Genetic
- Any medical condition that prevents the normal passage of menstrual flow out of the body
- Reproductive tract abnormalities
- Ovarian cancer risks are higher than expected rates in those with endometriosis.^{8&9}

Diagnosis

Endometriosis can be identified by following ways:

- **Pelvic examination:** During a pelvic exam, the doctor manually feels the areas in the pelvis for abnormalities such as cysts on the reproductive organs or scars behind the uterus. Generally, it's not possible to feel scars of endometriosis unless they've caused a cyst to form.
- **Ultrasound:** High-frequency sound waves are used to create images of the interior body. The device used to capture the images is called a transducer which can be pressed against the abdomen or inserted into patient's vagina. Both types of ultrasound may be done to get the best view of the reproductive organs. A standard ultrasound imaging test won't make possible for doctor to identify endometriosis, but it can identify cysts associated with endometriosis.

- **Magnetic Resonance Imaging (MRI):** An examination that uses a magnetic field and radio waves to create images of the organs and tissues within the body. MRI assist in capturing detailed information about the location and size of endometrial implants.
- **Laparoscopy:** In some cases, laparoscopy is recommended where more clear idea of condition is required. The patient remains under the effect of general anaesthesia, the surgeon makes a tiny incision near the navel and inserts a laparoscope, which gives clear signs of endometrial tissue outside the uterus.

A laparoscopy can provide information about the location, extent and size of the endometrial implants. The surgeon can take a tissue sample (biopsy) for further testing. Often, with proper surgical planning, the surgeon can treat endometriosis during the laparoscopy so that the patient need not to undergo multiple surgeries.^{10&11}

Disease management and Treatment^{12,13 & 14}

Treatment for endometriosis usually involves medication or surgery. The doctor will choose the treatment strategy on the basis of signs and symptoms. Generally, doctors follow traditional treatment approaches i.e. first line treatment is medicines. Surgery is opted if initial treatment fails.

- **Pain Treatment**

An over-the-counter pain reliever, such as the nonsteroidal anti-inflammatory drugs (NSAIDs) ibuprofen or naproxen sodium to help ease painful menstrual cramps. Hormone therapy in combination with pain relievers if patient is not pregnant.

- **Hormone Therapy**

Hormones are sometimes beneficial in minimizing or eliminating the pain of endometriosis. The increase or decrease in levels of hormones during the menstrual cycle causes thickening of endometrial implants, collapse and bleed. Hormone therapy may slow down the endometrial tissue growth and prevent the occurrence of new implants of endometrial tissue. Hormone therapy is not beneficial as a permanent treatment. There will be recurrence of symptoms after stopping hormone therapy.

Therapies used to treat endometriosis include:

- **Hormonal Contraceptives:** Birth control pills, patches and vaginal rings help control the hormones responsible for the build-up of endometrial tissue each month. Using hormonal contraceptives especially continuous-cycle regimens may reduce or eliminate pain in some cases.
- **Gonadotropin-Releasing Hormone (Gn-RH) Agonists and Antagonists:** These drugs block the production of ovarian-stimulating hormones, lowering estrogen levels and preventing menstruation. This causes endometrial tissue to shrink. These drugs create an artificial menopause, taking a low dose of estrogen or progestin along with Gn-RH agonists and antagonists may decrease menopausal side effects, such as hot flashes, vaginal dryness and bone loss. Cycle turns normal as the use of therapy discontinued.
- **Progestin Therapy:** A variety of progestin therapies, including an intrauterine device with levonorgestrel, contraceptive implant, contraceptive injection or progestin pill, can halt menstrual periods and the growth of endometrial implants, which may relieve, signs and symptoms.
- **Aromatase Inhibitors:** Aromatase inhibitors are a class of medicines that reduce the amount of estrogen in the body. Generally, doctor may recommend an aromatase inhibitor along with a progestin or combination hormonal contraceptive to treat endometriosis.
- **Conservative Surgery:** When surgery is performed to remove the endometriosis implants while preserving the uterus and ovaries called conservative surgery. pain from endometriosis can also be treated by surgery however, endometriosis and pain may return. General procedure followed by surgeons is laparoscopy or, less commonly, through traditional abdominal surgery in more-extensive cases.
- **Fertility Treatment**
Endometriosis can lead to trouble in conceiving. The doctor may recommend fertility treatment supervised by a fertility specialist. Fertility treatment ranges from stimulating the ovaries to make more eggs to in vitro fertilization. The suitability of treatment will depend on the patient's conditions.

➤ **Hysterectomy with Removal of the Ovaries**

Surgery to remove the uterus (hysterectomy) and ovaries (oophorectomy) was considered the most effective treatment for endometriosis. But endometriosis experts are moving away from this approach, instead focusing on the careful and thorough removal of all endometriosis tissue.

The removal of ovaries results in menopause. The lack of hormones produced by the ovaries may improve endometriosis pain in some patients, while for others, endometriosis continues to cause symptoms. Early menopause also carries a risk of cardiovascular diseases, certain metabolic conditions and early death.

Conclusion

Endometriosis is an enervating disease that impacts the quality of life of the patients. Diagnostic delays are very common and can decrease the reproductive potential and fertility. An early diagnose is the best key to successful treatment. Introduction of hormone therapy and Laparoscopy can assist in controlling the situation for long time. Still, more research is needed in the area of medicine for effective treatment. More emphasis is required on awareness programmes among the young ladies who are less than 35 years i.e. child bearing stage.

References

1. Alimi Y, Iwanaga J, Loukas M, Tubbs RS. The Clinical Anatomy of Endometriosis: A Review. *Cureus*. 2018 Sep 25;10(9): e3361. doi: 10.7759/cureus.3361. PMID: 30510871; PMCID: PMC6257623.
2. Klemmt PAB, Starzinski-Powitz A. Molecular and Cellular Pathogenesis of Endometriosis. *Curr Womens Health Reviews*. 2018 Jun; 14(2): 106–116. doi: 10.2174/1573404813666170306163448.
3. Vercellini P, Viganò P, Somigliana E, Fedele L. Endometriosis: Pathogenesis and Treatment. *Nat Rev Endocrinol*. 2014 May; 10(5):261–275.
4. Prescott J, Farland LV, Tobias DK, Gaskins AJ, Spiegelman D, Chavarro JE, Rich-Edwards JW, Barbieri RL, Missmer SA. A Prospective Cohort Study of Endometriosis and Subsequent Risk of Infertility. *Hum Reprod*. 2016 Jul;31(7):1475-82. doi: 10.1093/humrep/dew085. Epub 2016 May 1.
5. Tanbo T, Fedorcsak P. Endometriosis-Associated Infertility: Aspects of Pathophysiological Mechanisms and Treatment Options. *Acta Obstet Gynecol Scand*. 2017 Jun;96(6):659-667. doi: 10.1111/aogs.13082. Epub 2017 Jan 30.
6. Harris-Glocker M, McLaren JF. Role of female pelvic anatomy in infertility. *Clin Anat*. 2013 Jan;26(1):89-96. doi: 10.1002/ca.22188. Epub 2012 Nov 30.
7. Causes of Endometriosis assessed from <https://www.endometriosis-uk.org/causes-endometriosis>.
8. Darrow SL, Vena JE, Batt RE, Zielesny MA, Michalek AM, Selman S. Menstrual Cycle Characteristics and the Risk of Endometriosis. *Epidemiology*. 1993 Mar;4(2):135-42.
9. Hemmings R, Rivard M, Olive DL, Poliquin-Fleury J, Gagné D, Hugo P, Gosselin D. Evaluation of Risk Factors Associated with Endometriosis. *Fertil Steril*. 2004 Jun; 81(6):1513-1521.
10. Kennedy S, Bergqvist A, Chapron C, D'Hooghe T, Dunselman G, Greb R, Hummelshoj L, Prentice A, Saridogan E. ESHRE Special Interest Group for Endometriosis and Endometrium Guideline Development Group. ESHRE Guideline for the Diagnosis and Treatment of Endometriosis. *Hum Reprod*. 2005;20(10):2698-704.
11. Dunselman GA, Vermeulen N, Becker C, Calhaz-Jorge C, D'Hooghe T, De Bie B, Heikinheimo O, Horne AW, Kiesel L, Nap A, Prentice A, Saridogan E, Soriano D, Nelen W. European Society of Human Reproduction and Embryology ESHRE Guideline: Management of Women with Endometriosis. *Hum Reprod*. 2014;29(3):400-12

12. Parveen Parasar, Pinar Ozcan, Kathryn L. Terry Curr; Endometriosis: Epidemiology, Diagnosis and Clinical Management *ObstetGynecol Rep.* 2017 Mar; 6(1): 34–41. Published online 2017 Jan 27. doi: 10.1007/s13669-017-0187-1

13. Casper RF; Introduction: A Focus on the Medical Management of Endometriosis. *FertilSteril.* 2017 Mar;107(3):521-522. doi: 10.1016/j.fertnstert.2017.01.008.

14. Flyckt R, Kim S, Falcone T.; Surgical Management of Endometriosis in Patients with Chronic Pelvic Pain. *SeminReprod Med.* 2017 Jan;35(1):54-64. doi: 10.1055/s-0036-1597306. Epub 2017 Jan 3.