

Investigating The Effect of Endometriosis on Ovarian Follicles and Female Infertility, a review study

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Endometriosis is a chronic gynecological condition affecting 5-10% of women of reproductive age, characterized by the presence of endometrial tissue outside the uterus. It is associated with pelvic pain and infertility, and its pathogenesis is not fully understood. The primary theory for the formation of endometriosis is retrograde menstruation, where endometrial cells implant in the peritoneal cavity, but other factors such as congenital, environmental, epigenetic, autoimmune, and allergic factors may also contribute to its development.(1, 2) The pathogenesis of endometriosis-associated infertility is not entirely clear, but it is believed that anatomical disturbances in severe cases can contribute to infertility. In mild cases, the exact mechanism is not well understood.(3) Medical treatments for endometriosis, such as hormonal therapies, do not improve fertility and should not be given to women trying to conceive. Surgical ablation or excision of minimal and mild endometriosis can improve fertility chances, and assisted reproductive technology can be used in combination with hormonal treatment in women with mild endometriosis.(4) Currently, laparoscopy is the gold standard for diagnosing endometriosis, but less invasive methods are being sought to shorten the time to diagnosis. Treatment options are limited to surgery, hormonal treatment, and analgesics, which are associated with side effects. There is growing interest in the role of the gut microbiota in endometriosis, as it may be associated with the condition through estrogen, immune inflammation, and tumor characteristics, suggesting that regulating gut microbiota disorders could be a potential treatment approach in the future.

Endometriosis is a condition where endometrial-like tissue grows outside the uterus, which can negatively impact female fertility through various mechanisms, including effects on ovarian follicles. Endometriosis can lead to inflammation, adhesions, and altered hormonal environments that can disrupt the normal function of the ovaries and the follicles they contain.

Key points on the effect of endometriosis on ovarian follicles and female infertility include:

1. Endometriosis can cause inflammation and adhesions, which may impair the normal function of ovarian follicles and their ability to release eggs (ova) during ovulation.(5)
2. Endometriosis can lead to a decline in ovarian reserve, which is the number and quality of ovarian follicles available for fertilization[3].
3. Endometriosis can cause hormonal imbalances, such as increased estrogen levels, which may affect the growth and maturation of ovarian follicles.(5)
4. Endometriosis is associated with a higher risk of poor ovarian response (POR) and premature ovarian insufficiency (POI), both of which can contribute to female infertility.(6)

5. Endometriosis can lead to anatomical distortions, such as tubal blockages or ovarian cysts, which can impede the fertilization process.(5)

Ultrasound, particularly transvaginal ultrasonography, is a valuable tool in the diagnosis and management of endometriosis and other causes of female infertility, including the evaluation of ovarian follicles.(7) Additionally, treatments like autologous platelet-rich plasma (PRP) injections have shown promise in promoting ovarian rejuvenation and increasing the possibility of a successful pregnancy in women with ovarian dysfunction, including those with endometriosis.(6) Infertility due to endometriosis is a significant factor, accounting for approximately 17% of cases, and treatments like letrozole, an aromatase inhibitor, have shown promise as an alternative to clomiphene citrate in patients with unexplained infertility undergoing controlled ovarian stimulation.(8)

How Does Endometriosis Effect Ovarian Follicles

Endometriosis affects ovarian follicles through several mechanisms, as evidenced by both animal studies and clinical observations:

1. **Increased luteinized unruptured follicles (LUF)**:** Endometriosis may lead to a higher number of luteinized unruptured follicles, which are follicles that have undergone luteinization without prior rupture, potentially impairing ovulation.(9)
2. **Inflammatory reaction**:** Endometriomas, a type of endometriosis, can induce an inflammatory reaction in nearby follicles, although this is not consistently observed. In some cases, increased cytokine concentrations in the follicular fluid have been associated with diminished ovarian response.(10)
3. **Diminished ovarian reserve**:** Endometriomas and the surgical treatment of endometriosis can negatively impact ovarian reserve, which is the number and quality of follicles available for fertilization. This can be due to the destruction of normal ovarian cortex structure, affecting the dormancy of primordial follicles.(11)
4. **Altered hormonal environment**:** Endometriosis can lead to hormonal imbalances, such as increased estrogen levels, which may affect the growth and maturation of ovarian follicles.(5)
5. **Anatomical distortions**:** Endometriosis can cause adhesions and distortions in the pelvic anatomy, which may impede the normal function of the ovaries and the follicles they contain.(5)

Can Endometriosis Cause Infertility in Women with Ovarian Endometriomas

Endometriosis, particularly when it involves ovarian endometriomas, can indeed cause infertility in women through several mechanisms:

1. **Diminished ovarian reserve**:** Ovarian endometriomas can negatively impact ovarian reserve, which is the number and quality of follicles available for fertilization. The presence of an endometrioma correlates with a lower number of developing follicles, lower number of

retrieved oocytes, and a lower embryo quality and implantation rate during in vitro fertilization (IVF) cycles.(12)

2. **Surgical treatment**: Surgical treatment of ovarian endometriomas, such as cystectomy, can negatively impact post-operative ovarian reserve. Some women who undergo surgery for endometriomas suffer from poor ovarian response, which directly affects treatment results.(11)

3. **Mechanical and thermal damage**: Surgical trauma to the ovary during endometrioma removal may compromise ovarian reserve due to mechanical injury associated with the removal of adjacent healthy ovarian tissue along with the cyst wall and thermal damage generated by energy modalities used during hemostasis.(11)

4. **Endometrioma itself**: Endometriomas may be a cause of diminished ovarian reserve, as the destruction of normal histological structure in the ovarian cortex can affect the dormancy of primordial follicles.(11)

However, it is important to note that not all studies agree on the impact of ovarian endometriomas on pregnancy success following treatment with IVF. Some studies suggest that ovarian endometriomas do not adversely affect pregnancy success after IVF treatment. The conflicting results may be due to variations in study design, patient populations, and surgical techniques.(13)

In summary, while ovarian endometriomas can contribute to infertility in women with endometriosis, the impact on pregnancy success following treatment with IVF is still a topic of debate. Further research is needed to better understand the effects of endometriosis and its treatment on ovarian reserve and fertility outcomes.

Methods

The present study was conducted by reviewing related articles in Web of Science, Scopus, and PubMed databases.

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