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Endometriosis and Infertility: Treatment Strategies and Reproductive Outcomes -Literature Review

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ABSTRACT

Endometriosis is a chronic gynecological disorder characterized by the presence of endometrial-like tissue outside the uterine cavity, leading to chronic pelvic pain, dysmenorrhea, and infertility. This review explores the pathogenesis of endometriosis, mechanisms contributing to infertility, classification systems, reproductive outcomes, and current treatment strategies. Medical therapies can relieve symptoms but are unsuitable for women seeking pregnancy. Surgical management may improve spontaneous conception in selected patients, although it may adversely affect ovarian reserve. Assisted reproductive technologies (ART), including intrauterine insemination (IUI) and in vitro fertilization (IVF), remain important fertility treatment options. However, controversy persists regarding the direct impact of endometriosis on ART outcomes. Given the complex and multifactorial nature of endometriosis-associated infertility, individualized multidisciplinary management is recommended.

INTRODUCTION

Endometriosis is a chronic gynecological condition characterized by the presence of endometrial-like tissue outside the uterine cavity, commonly affecting the ovaries, fallopian tubes, and pelvic peritoneum [1,2]. The ectopic tissue induces chronic inflammation and fibrosis, resulting in pelvic pain, dysmenorrhea, dyspareunia, and infertility [2].

Endometriosis affects approximately 10–15% of reproductive-aged women and is strongly associated with infertility (1). The prevalence rises to 25–50% among infertile women, while infertility occurs in approximately 30–50% of women diagnosed with endometriosis [1]. Although the association between endometriosis and infertility is well established, the exact cause–effect relationship remains controversial.

The ESHRE Guideline Development Group recommends considering endometriosis in women presenting with cyclical or non-cyclical symptoms including dysmenorrhea, dyspareunia, dysuria, dyschezia, painful rectal bleeding, fatigue, and infertility [3].

Classification Systems for Endometriosis

Several classification systems have been developed since 1979 to stage the extent and severity of endometriosis. The American Fertility Society (AFS) classification and the revised American Society for Reproductive Medicine (rASRM) system remain the most commonly used classifications [2].

The Enzian classification was later introduced to better characterize deep infiltrating endometriosis (DIE) lesions [2]. These systems aim to standardize disease description, facilitate research, and improve patient counseling. However, current classification systems have limited ability to predict fertility outcomes [2].

Pathogenesis of Endometriosis

The exact pathogenesis of endometriosis remains unclear. Proposed theories include retrograde menstruation, coelomic metaplasia, altered immunity, metastatic spread, stem cell dysfunction, and genetic predisposition (5).

Retrograde Menstruation

Retrograde menstruation, first proposed by Sampson, is the most widely accepted theory. Menstrual blood containing viable endometrial cells refluxes through the fallopian tubes into the peritoneal cavity, where the cells implant and proliferate [5]. Women with endometriosis exhibit greater volumes of refluxed menstrual blood and endometrial tissue fragments compared with unaffected women [5].

Fecundity in Women with Endometriosis

Fecundity refers to the probability of achieving a live birth during one menstrual cycle. In healthy couples, monthly fecundity ranges from 15–20% and declines with age (5). In untreated women with endometriosis-associated infertility, monthly fecundity decreases substantially to approximately 2–10% [5].

Mechanisms Linking Endometriosis and Infertility

Several mechanisms have been proposed to explain infertility associated with endometriosis.

Distorted Pelvic Anatomy

Pelvic adhesions and anatomical distortion caused by endometriosis may impair ovulation, interfere with ovum pickup, and disrupt gamete transport [5].

Altered Peritoneal Function

Women with endometriosis demonstrate increased peritoneal fluid volume, activated macrophages, inflammatory cytokines, prostaglandins, and proteases [5]. These inflammatory changes may adversely affect sperm function, oocyte quality, embryo development, and tubal motility.

Altered Hormonal and Immune Function

Immunological abnormalities including elevated IgG, IgA antibodies, activated lymphocytes, and autoantibodies have been identified in women with endometriosis

(5). These abnormalities may impair endometrial receptivity and embryo implantation.

Endocrine and Ovulatory Dysfunction

Endometriosis has been associated with luteal phase defects, abnormal follicular development, and altered luteinizing hormone surges, although definitive evidence remains limited [5].

Impaired Implantation

Reduced expression of αvβ integrin and abnormalities in endometrial ligand synthesis may impair implantation in women with endometriosis [5].

Endometriosis Fertility Index (EFI)

The Endometriosis Fertility Index (EFI) is a validated scoring system used to predict spontaneous pregnancy rates following surgical management of endometriosis. The EFI incorporates patient age, duration of infertility, ovarian function, tubal status, and surgical findings [2,7].

Higher EFI scores (>7) are associated with improved spontaneous conception rates, whereas lower scores suggest the need for assisted reproductive technologies [2]. The ESHRE guideline recommends counseling women regarding their postoperative fertility prognosis using EFI [3].

Endometriosis and Assisted Reproductive Technology

Endometriosis has become one of the most common indications for assisted reproductive technology (ART) [8]. However, the effect of endometriosis on ART outcomes remains controversial.

Several studies report that women with endometriosis produce fewer oocytes and may have reduced implantation and pregnancy rates compared with women without endometriosis [4,6,13]. Barnhart et al. demonstrated reduced fertilization and implantation rates among women with endometriosis undergoing ART [13].

Conversely, other studies suggest that live birth rates among women with endometriosis undergoing IVF are comparable to those without the disease [4,8,11]. Women with isolated endometriosis may achieve live birth rates similar to or higher than women with other infertility diagnoses [13].

The impact of endometriosis on ART outcomes may be confounded by associated infertility factors, previous surgery, ovarian reserve, and ovarian endometriomas [12].

Ovarian Reserve and Endometrioma

Endometriosis may negatively affect ovarian reserve through inflammatory damage and altered folliculogenesis [4,12]. Endometriomas and prior ovarian surgery can reduce anti-Müllerian hormone (AMH) levels and antral follicle count (AFC) [16].

Although women with endometriosis often produce fewer oocytes during IVF cycles, oocyte quality, embryo development, aneuploidy rates, and clinical pregnancy outcomes are generally comparable to women with other infertility diagnoses [11,12].

Surgical Management and Reproductive Outcomes

Laparoscopic surgery remains the gold standard for symptomatic pelvic endometriosis and aims to remove visible lesions and restore pelvic anatomy [7,17].

Surgical treatment may improve spontaneous conception rates, particularly in minimal or mild disease [20]. However, surgery carries the risk of diminished ovarian reserve, especially after endometrioma excision [8,16].

Some studies suggest that pregnancy rates following surgery may be comparable to ART outcomes [8]. Laparoscopic treatment after failed IVF has also been associated with improved spontaneous conception and subsequent IVF success [17].

For women with deep infiltrating endometriosis (DIE), some researchers recommend first-line ART rather than surgery due to surgical complexity and risk of complications [16].

Deep Infilating Endometriosis and Pregnancy Outcomes

DIE lesions have been associated with poorer ART outcomes and increased obstetric complications including preterm birth, placenta previa, placental abruption, and gestational hypertension [16].

Women with rectovaginal endometriosis may constitute a high-risk obstetric group requiring careful antenatal management [9].

Obstetric and Neonatal Complications

Endometriosis has been associated with adverse maternal and neonatal outcomes including placenta previa, antepartum hemorrhage, preterm birth, miscarriage, ectopic pregnancy, and increased cesarean delivery rates [9,10,14,18].

The increased risk of placenta previa appears consistent in both spontaneous and ART pregnancies (10,14). Altered uterine contractility and uterine dysperistalsis may contribute to abnormal implantation and obstetric complications [1].

Despite these risks, women with endometriosis have experienced improved reproductive outcomes over recent decades due to advances in fertility treatments and ART [9].

Endometrial Injury and Implantation

Intentional endometrial injury has been investigated as a strategy to improve implantation and pregnancy rates in women with recurrent implantation failure. Studies suggest that endometrial injury may improve implantation, clinical pregnancy, and live birth rates in selected patients [15].

DISCUSSION

The relationship between endometriosis and infertility is complex and multifactorial. Current evidence suggests that endometriosis may impair fertility through anatomical distortion, inflammation, altered ovarian function, impaired implantation, and immune dysregulation.

Although some studies demonstrate poorer ART outcomes among women with severe endometriosis, overall live birth rates are often comparable to those of women without endometriosis [4,6,11,13]. The severity of disease, ovarian reserve, previous surgery, and associated infertility factors significantly influence reproductive outcomes.

Management should therefore be individualized according to patient age, ovarian reserve, symptom severity, disease extent, and reproductive goals. Minimal and mild endometriosis may be managed similarly to unexplained infertility [20], whereas advanced disease often requires multidisciplinary management and ART.

CONCLUSION

Endometriosis remains a major cause of infertility and reproductive morbidity among women of reproductive age. Its impact on fertility involves multiple biological mechanisms including anatomical distortion, inflammation, endocrine dysfunction, and impaired implantation.

Current treatment options include surgical management, superovulation with IUI, and IVF. Although surgery may improve spontaneous conception in selected cases, ART remains central to the management of moderate and severe endometriosis-associated infertility.

Future research should focus on refining classification systems, improving fertility prediction models, optimizing ART outcomes, and identifying individualized treatment strategies for women with endometriosis.

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