

ENDOMETRIOSIS-ASSOCIATED INFERTILITY IN PAKISTAN: PATHOPHYSIOLOGICAL MECHANISMS, DIAGNOSTIC CHALLENGES, AND MANAGEMENT STRATEGIES

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ABSTRACT: One of the main causes of infertility globally, including in Pakistan, is endometriosis, a chronic gynecological condition that affects women of reproductive age. Because of a lack of knowledge, a delayed diagnosis, and restricted access to specialist treatment, endometriosis is still underdiagnosed and inadequately treated while having a substantial impact on reproductive health. The pathophysiological processes that connect endometriosis to infertility are examined in this narrative review. These mechanisms include oxidative stress, hormone abnormalities, inflammatory reactions, and decreased endometrial receptivity. Timely intervention is further delayed in Pakistan due to diagnostic obstacles, including reliance on clinical symptoms, limited availability of modern imaging tools, and cost restrictions. Assisted reproductive technologies (ART) like in vitro fertilization (IVF), medicinal therapy like hormone medications, and surgical procedures like laparoscopic excision are examples of current management options. However, socioeconomic constraints and the limits of the healthcare infrastructure frequently impede these techniques. In order to improve the management of endometriosis-associated infertility in Pakistan, future directions highlight the necessity of more knowledge, better diagnostic facilities, patient-centered care, and policy reform. Improving reproductive outcomes and impacted women's quality of life requires addressing these gaps through interdisciplinary methods and research projects.

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KEYWORDS: Endometriosis, Hormone abnormalities, IVF, Laparoscopy, Infertility

INTRODUCTION

Endometriosis is a persistent gynecological illness that causes discomfort, inflammation, and infertility when tissue that resembles the endometrium—the lining of the uterus—grows outside the uterus. Worldwide, it affects 10–15% of women who are of reproductive age; in Pakistan, prevalence estimates for women having laparoscopic assessment range from 5–25%. Although the precise origin of endometriosis is still unknown, several possibilities include immunological dysfunction, coelomic metaplasia, retrograde menstruation, and lymphatic dissemination. The ovaries, fallopian tubes, peritoneum, and, in extreme situations, the intestines and bladder are the most often impacted areas. (1, 2). Chronic pelvic discomfort, excessive menstrual flow,

infertility, dyspareunia (pain during sexual activity), and dysmenorrhea (difficult periods) are among the symptoms, which can vary in intensity. Early menarche, brief menstrual cycles, elevated estrogen levels, and family history are risk factors.(3) The normalization of menstrual discomfort and a lack of awareness make diagnosis difficult and frequently result in delayed discovery.(4) Laparoscopic surgery, which enables direct imaging and biopsy of endometriotic lesions, is still the gold standard for diagnosis, even if pelvic examinations, ultrasounds, and MRIs can also raise suspicions.(5, 6).

Based on severity, endometriosis is divided into four stages: minimal (Stage I) to severe (Stage IV), at which time there are substantial adhesions and organ involvement. Serious side effects from the

illness can include infertility, persistent discomfort, bladder and bowel problems, and in rare instances, an elevated risk of ovarian cancer. The goals of treatment include symptom management and enhanced fertility. While hormonal medications such as birth control tablets, GnRH agonists, progestins, and hormonal IUDs can inhibit endometrial development, NSAIDs are frequently used to treat pain. Surgical procedures such as a hysterectomy or laparoscopic excision of lesions may be required in extreme situations. Endometriosis-related infertility may need the use of assisted reproductive methods such as in vitro fertilization (IVF), intrauterine insemination (IUI), or ovulation induction (7). In Pakistan, Because of a lack of knowledge, the social stigma associated with menstruation health, and restricted access to specialist treatment, endometriosis is still difficult to treat. Cultural taboos prevent many women from obtaining medical attention, and medical personnel frequently misdiagnose or ignore symptoms. Furthermore, public hospitals have limited access to laparoscopic surgery and cutting-edge reproductive therapies. Prioritizing public awareness efforts, early screening initiatives, and healthcare professional training is necessary to enhance results. To comprehend the frequency and genetic variables impacting endometriosis in Pakistani women, further funding for study is also required. Endometriosis is an inflammatory, estrogen-dependent disease that has a major effect on women's reproductive health and quality of life. Better treatment and results for impacted women depend on early diagnosis, efficient medical and surgical management, and increased awareness.(8)

Epidemiology and Burden of Endometriosis in Pakistan:

Because there is a lack of epidemiological data, the real frequency of endometriosis, a serious but frequently underdiagnosed illness that affects women in Pakistan who are of reproductive age, is unknown. Its development is influenced by a number of risk factors, such as lifestyle choices, environmental exposures, hormone imbalances, and genetic susceptibility. However, diagnosis and treatment are frequently delayed due to cultural taboos around menstruation and reproductive health. Before obtaining a conclusive diagnosis, many women experience years of infertility and unexplained pelvic discomfort because medical professionals may ignore or misattribute symptoms.

The burden is further increased by socioeconomic restrictions, especially in rural regions where access to specialized gynecological care is limited. Because endometriosis-related infertility can result in emotional misery, marital difficulty, and societal shame, the disorder has a significant psychological impact in addition to its medical effects. The lack of understanding among primary care physicians and the restricted availability of sophisticated diagnostic technologies like laparoscopy make it difficult for Pakistan's healthcare system to provide prompt and accurate diagnoses. Instead of using complete treatment procedures, many instances are handled symptomatically, which results in patients receiving subpar care.

Endometriosis has significant public health ramifications, impacting women's mental health, productivity, and quality of life. To successfully address this hidden

but crippling ailment, nationwide awareness efforts, better diagnostic facilities, and easily available reproductive therapies are urgently needed (9).

Pathophysiological Mechanisms of Endometriosis-Associated Infertility:

Although there are several ideas on how endometriosis develops, the most widely recognized theory is that retrograde menstrual flux through the Fallopian tubes may be the initial cause. Endometrial tissue shedding can produce epithelial progenitor cells that can implant in the rectovaginal pouch, ovaries, or peritoneum. Once formed, these cyclically active and hormone-responsive endometriotic lesions cause pelvic adhesions, discomfort, and infertility by triggering acute and then chronic inflammatory responses. Genetic, anatomical, endocrine, and environmental variables, however, all affect an individual's vulnerability to endometriosis (10, 11).

Diagnostic Challenges in the Pakistani Healthcare System:

A study found that approximately one in four women undergoing laparoscopic procedures are diagnosed with endometriosis, highlighting its prevalence and the need for increased awareness. In Pakistan, endometriosis is still difficult to diagnose due to a number of barriers within the healthcare system, the main one being a lack of awareness among patients and healthcare providers. Many women normalize menstrual pain due to cultural beliefs, delaying medical consultation, and general practitioners frequently misdiagnose the condition as irritable

bowel syndrome or pelvic inflammatory disease (12).

Furthermore, the problem is made worse by restricted access to specialized care, particularly in rural areas where there are few gynecologists and reproductive endocrinologists. Since imaging methods like ultrasound have low sensitivity in diagnosing endometriotic lesions, early diagnosis is further hampered by the dependence on clinical symptoms rather than conclusive diagnostic instruments like laparoscopy. According to a study that compared MRI and ultrasonography, MRI was better at detecting deep infiltrative lesions than ultrasound, with a higher sensitivity (91.4%) and specificity (85.0%) (13).

Furthermore, because laparoscopy and MRI are still costly and not often offered in public hospitals, many women are unable to afford modern diagnostic procedures. In addition to discouraging women from seeking prompt medical attention, the stigma associated with reproductive health adds to the already lengthy diagnostic delay, which typically lasts for several years. To overcome these obstacles and guarantee early detection and better treatment of endometriosis in Pakistan, higher medical education, easier access to diagnostic centers, and nationwide awareness campaigns are needed.

Management for Endometriosis related infertility:

For many endometriosis patients, medical therapy has been shown to improve their quality of life. Progestins, androgens, oral contraceptives, and gonadotropin-releasing hormone agonists have all been shown to be effective in symptom management.8. Unfortunately, because of their

contraceptive effects, medicinal treatments for endometriosis virtually always restrict reproductive options. While some modalities, like depot medroxyprogesterone acetate, are quite effective at treating symptoms, they may also have long-term implications on ovulation suppression.

Patients' symptoms, particularly those related to dyspareunia, dyschezia, dysmenorrhea, and persistent pelvic discomfort, have played a significant role in guiding the surgical treatment of endometriosis. Although the benefits of surgical treatment for endometriosis-related symptoms have been proven, there is considerable disagreement on the effectiveness of surgery in treating infertility caused by endometriosis (14).

Few studies directly explore the benefits of ovulation induction as a treatment for endometriosis in women. Therefore, it is necessary to extrapolate from studies that included women with either male factor infertility or unexplained infertility the efficacy of ovulation induction and superovulation for patients with endometriosis.

In vitro fertilization (IVF) is without a doubt the most successful treatment for endometriosis-related infertility. More than 1400 live births were achieved in 2009 as a result of more than 5600 IVF cycles conducted for endometriosis patients in the US.¹⁸ The best stimulation regimens and embryo culture conditions for these individuals are still mostly unknown, nevertheless. (15)

Lifestyle Modifications:

For women with endometriosis, incorporating self-care techniques can enhance their quality of life and supplement medical therapy. Symptoms may be lessened by practicing stress-

reduction strategies like talk therapy and meditation, doing low-impact activities like yoga and swimming, and changing one's diet to include more fiber and a Mediterranean diet. Supplements like curcumin and vitamins D, C, and E have also demonstrated significant advantages, but they should only be taken under a doctor's supervision. Seeking mental health treatment and establishing a support system are also essential elements of comprehensive care (16).

Managing endometriosis-associated infertility requires a multidisciplinary strategy that is customized to the patient's disease severity, symptomatology, and reproductive objectives. Women who are impacted can benefit from collaborative care that includes gynecologists, reproductive endocrinologists, pain experts, and mental health specialists (17).

Future Directions and Recommendations:

- 1. Improving Knowledge and Instruction:** There is a substantial information gap about endometriosis among Pakistani women. Early diagnosis and therapy may result from improved understanding of the problem brought about by educational activities. Important first efforts include putting in place extensive awareness campaigns and incorporating endometriosis education into programs related to reproductive health. (8)
- 2. Enhancing Data Collection and Research:** Comprehensive epidemiological investigations are desperately needed to ascertain

the incidence and consequences of endometriosis in Pakistan. Putting money into research will help create customized management plans and guide healthcare regulations.

3. **Including Psychological Assistance:** Research shows that women who experience infertility have significant psychological anguish. Reproductive results may be enhanced and stress might be reduced by integrating mental health treatments into infertility treatment programs. It is advised to create support groups and counseling programs that are attentive to cultural differences. (18, 19)

4. **Examining Alternative Medicine:** According to new research, antioxidants like silymarin may lessen the growth of endometriomas and ease endometriosis-related pelvic pain. Large-scale clinical trials including Pakistanis can confirm these results and possibly offer new, easily accessible treatment alternatives. (20)

5. **Enhancing the Infrastructure for Healthcare:** It is essential to increase access to fertility therapies and specialist diagnostic equipment. Patient results can be improved by setting up specialized endometriosis centers with state-of-the-art imaging equipment and qualified doctors on board.

6. **Participation in the Community and Support Systems:** Women can be empowered to seek

prompt medical treatment by promoting the establishment of patient advocacy groups and support networks, which can offer emotional support and information dissemination.

By using these tactics, Pakistan can raise the standard of treatment for women with infertility linked to endometriosis, ultimately improving their reproductive health and general well-being.

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