International Journal of Medical Sciences And Clinical Research
(ISSN – 2771-2265)
VOLUME 04 ISSUE 05 PAGES: 49-54
SJIF IMPACT FACTOR (2022: 5. 893) (2023: 6. 184) (2024: 7.544)
OCLC – 1121105677
Crossref doi Google Scholar WorldCat MENDELEY
Publisher: Oscar Publishing Services

Journal Website: https://theusajournals.com/index.php/ijmscr

Research Article

MODERN VIEWS ON INFERTILITY ASSOCIATED WITH ENDOMETRIOSIS

Submission Date: May 13, 2024, Accepted Date: May 18, 2024,
Published Date: May 23, 2024
Crossref doi: https://doi.org/10.37547/ijmscr/Volume04Issue05-09

Khasanova Dilafruz Abdukhamidovna
assistant Department of Obstetrics and Gynecology №1 Samarkand State Medical University, Samarkand, Uzbekistan

ABSTRACT

Endometriosis is still a widespread and at the same time not fully studied disease, being one of the urgent problems of modern medicine. The problem becomes even more important due to functional and structural changes in the reproductive system of women with endometriosis, in whom the frequency of infertility reaches 55-75%. To date, none of the proposed strategies for the treatment of endometriosis has led to its complete cure. ideas about the etiopathogenesis and tactics of management of patients with endometriosis-associated infertility according to the data of domestic and foreign literature.

KEYWORDS

Endometriosis, infertility, assisted reproductive technologies.

INTRODUCTION

Endometriosis is a multifactorial disease, in which there is a benign growth of tissue outside the uterine cavity, with morphological and functional properties similar to the endometrium. Despite the century-old history and great attention of scientists from all countries, endometriosis remains a widespread and at the same time not fully studied disease, being one of the urgent problems of modern medicine mainly affecting women of reproductive age, manifesting themselves in menstrual irregularities, chronic pelvic pain, and infertility. According to the literature, endometriosis occurs in 5-10% of women of reproductive age, 80% of patients with chronic pelvic pain, and 20-50% of women with infertility. Women suffering from endometriosis

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have a low quality of life, due to chronic pelvic pain, as well as a combination of symptoms such as dysmenorrhea, menorrhagia, dyspareunia, dysuria, and dyschezia.

Although there are many theories regarding the development of endometriosis, the true mechanisms of occurrence are still a mystery. Existing theories of etiopathogenesis do not reveal the true essence of endometriosis-associated infertility. Possible causes of subfertility include the following: tubal-peritoneal factor infertility, dysfunctional ovarian disorders, changes in endometrial receptivity, and others. However, the true mechanisms are still unknown. It is necessary to emphasize the key pathogenetic mechanisms of infertility in endometriosis.

THE AIM OF THE RESEARCH

Study of the main issues of infertility associated with endometriosis.

The two main symptoms of endometriosis are pain and infertility. This review of the scientific literature will focus on infertility associated with endometriosis, its causes, methods of diagnosis and treatment.

A huge number of theories of infertility in endometriosis can be divided into six main groups:

1. Violation of the transport function of the fallopian tubes;

2. Functional inferiority of the endometrium and impaired endometrial receptivity;

3. Violation of functional relationships in the hypothalamus-pituitary-ovary system;

4. the development of an autoimmune reaction;

5. Pathology of stem cells in the development of endometriosis;

6. Other factors.

Violation of the transport function of the fallopian tubes occurs due to a violation of the anatomy (occlusion of their lumen) and the functional activity of the tubes.

Violation of the anatomy of the fallopian tubes (lumen occlusion) is due to:

- germination of heterotopias into the lumen of the fallopian tubes, leading to their blockage;

- obliteration of the fallopian tubes as a result of the formation of adhesions in the pelvis (peritubary adhesions).

Violation of the functional activity of the fallopian tubes is due to:

- reduced and uncoordinated contractile activity of pipes. A.N. Strizhakov used the method of kymographic perturbation to show that every second patient with normally passable fallopian tubes had

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reduced and discoordinated contractile activity; 29.8% of patients had obstructed patency of the fallopian tubes and 20.2% had spasm in the isthmic-ampullary region;

- the ratio of PGE and PGR2a (prostaglandins E and F2a; the lower this indicator, the higher the probability of uncoordinated pipe activity).

Functional inferiority of the endometrium plays a certain role in the occurrence of infertility in endometriosis. Zh.N. Belyaeva found that in patients with endometriosis, even with a biphasic menstrual cycle, there is a delay in the transformation of the endometrium from proliferative to secretory, the absence of a concomitant secretory reaction of the glands, a violation of the content and distribution of glycogen and CHIC-positive substances, and an incorrect distribution of nucleic acids and alkaline phosphatase.

According to E.A. Kogan and A.V. Kolotovkina, changes in endometrial receptivity may be one of the leading causes of infertility and lower efficiency of ART (assisted reproductive technologies) programs in patients with external genital endometriosis. Endometrial receptivity is the ability of the uterine mucosa to increase the efficiency of the embryo implantation process. The endometrium can implant a blastocyst only during a very short and strictly defined period of the luteal phase. This period is called the nidation or implantation window. In the structure of the endometrial epithelium, changes occur, characterized by the appearance of protrusions of the membrane - podia. The maximum receptivity of the endometrium is from the 20th to the 24th day of the cycle. It is manifested by the expression of peptides and proteins that can serve as biomarkers of uterine receptivity.

In patients with infertility combined with external genital endometriosis, the endometrium has a decrease in the number of pinopodium, LEAF (leukemia inhibiting factor), the level of proteins NOXA10, glycodeline A, integrin avß3, and an increase in aromatase. An imbalance of hormonal receptors is also observed and stroma. At the same time, the severity of these changes correlates with the severity of external genital endometriosis. According to supporters of the immunological concept of the pathogenesis of endometriosis2, proteins and metabolic products formed during the cyclic transformation of endometriosis are not excreted from the body, as is the case in the phase of endometrial desquamation from the uterine cavity, but are phagocytized and resorbed by the tissues surrounding the endometriosis foci, which entails an autoimmune reaction. The latter can also manifest itself in autosperm immunization, which plays a very important role in the development of infertility.

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The increased number of mast cells in endometriosis foci suggested that they may play a role in the pathogenesis of this disease. In this regard, the use of mast cell stabilizers and inhibitors may prove effective in the treatment of endometriosis and associated pain. However, these studies are still at the preclinical stage, clinical trials will help to understand this issue in more detail and clarify the role of mast cells in the occurrence of endometriosis.

CONCLUSION

This review shows that there is still no consensus on the issue of infertility in endometriosis. There are a lot of theories, and all of them have the right to exist. In our opinion, the most promising are endometrial receptivity disorders and stem cell pathology.

In studies conducted in mice, MMSCs derived from ectopic endometrial cells showed higher angiogenic potential and ability to invade after transplantation to immuno-deficient mice compared to eutopic endometrium. There is also increased proliferation, migration, and angiogenic capacity in MMSCs obtained from peritoneal endometriosis foci and ovarian endometriosis foci compared to eutopic endometrium. These studies not only showed the presence of MMSCs in both eutopic and ectopic endometrial cells but also demonstrated the characteristics of MMSCs (increased proliferative activity and angiogenic capacity) that may play an important role in the pathogenesis of endometriosis.

Changes in endometrial receptivity may be one of the leading causes of infertility and lower effectiveness of ART programs in patients with external genital endometriosis. The reason for this is the above-mentioned decrease in the number of pinopodium, LEAF, NOXA10, glycodelin A, integrin avP3, as well as an increase in aromatase and an imbalance of hormonal receptors.

Finally, it should be emphasized that the more reliably the mechanism of infertility development is known, the more chances there are to carry out effective pathogenetic therapy, establish the safest tactics for managing pregnancy and childbirth, as well as a regimen of anti-relapse treatment after childbirth and especially after abortion.

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