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# The Effect of Endometriosis on Reproductive Function

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## Abstract

In recent years, there has been more and more talk about a direct correlation between endometriosis and reproductive function. Endometriosis is considered a fairly common, chronic inflammatory disease that is associated with pain and infertility. According to statistics, 25-50% of patients undergoing infertility treatment had or have endometriosis. However, the mechanisms that underlie the violation of reproductive function caused by endometriosis, to the full extent, still remain unknown. There are several assumptions about what exactly causes infertility. Firstly, these are anatomical changes (violation of the transportation of gametes through the fallopian tubes), secondly, a decrease in ovarian reserve due to the progressive process, and finally, the violation may affect the hypothalamic-pituitary-ovarian axis. Due to widespread infertility due to endometriosis, endometriosis has been singled out as a condition in which various fertility preservation programs may be required.

**Discipline**: Medicine, therapy, obstetrics



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# 1 Introduction

Endometriosis is a common disease characterized by the proliferation of endometriodic tissue outside the uterus, causing local chronic inflammation, which often causes infertility [1]. In healthy women, the monthly fertility rate is approximately 15-20% per month and gradually decreases with age. Unlike healthy women, in women with endometriosis, this indicator decreases by 2-10% [2]. According to the meta-analysis, the incidence of endometriosis among the general population can reach 10% [3]. Endometriosis can affect fertility in several ways: changes in the function of the fallopian tubes and ovaries; impaired gamete transport; decreased susceptibility of the endometrium; the occurrence of an inflammatory process in the peritoneal fluid, which can lead to a deterioration in the quality and functioning of sperm [4-5]. There is endometriosis: with a superficial lesion of the peritoneum, ovarian endometrioma and deep endometriosis. Deep endometriosis is the most severe form, spreading under the surface of the peritoneum by more than 5 mm (utero-sacral ligaments, muscle layer of the bladder, ureter, and intestines) [6,7]. It is necessary to mention the fact that surgical treatment of endometriosis affecting the ovaries can also reduce the ovarian reserve [8]. Women with severe forms of endometriosis using Assisted Reproductive Technology (ART) procedures for pregnancy may develop high obstetric risks [9]. For example, placenta previa, premature birth, slowing of fetal development, as well as preeclampsia [10].

# 2 Etiopathogenetic Aspects of Reproductive Disorders

Speaking of etiopathogenesis, it is impossible not to mention the anatomical changes that occur in severe forms of endometriosis (stages III and IV of the AFS classification.) Most often the lesion affects the fallopian tubes, due to the occurrence of a local inflammatory process, which also provokes the formation of peritubar and /or periovarial adhesions, endometriomas. All these processes complicate the functioning and permeability of the fallopian tubes, namely, the capture and transport of eggs, and their fertilization. But with mild forms of endometriosis, the mechanisms are more complex and can manifest themselves at different stages necessary for pregnancy, for example, folliculogenesis, ovulation, fertilization, embryo implantation. According to several studies, under the influence of endometriosis, the concentration of pro-inflammatory interleukins (IL-1, IL-6, IL-12, IF, TNF), macrophages and prostaglandins increases in the peritoneal fluid [12-14]. All these biochemical changes have an adverse effect not only on the egg but also on spermatozoa, the embryo and the completeness of the functions of the fallopian tubes. TNF and IL-1 lead to a decrease in the binding of spermatozoa to the glycoprotein membrane of the oocyte [15]. Changes also occur in the local immune response, that is, the levels of lymphocytes and IgG and IgA antibodies in the endometrium increase. This will affect the sensitivity of the endometrium and the implantation of embryos [16]. Ovarian function is also subject to pathological changes: violation of the luteal phase, premature peaks of luteinizing hormone, abnormalities of follicular crossing [17,18]. The changes also affect the hypothalamic-pituitary-ovarian axis, which is manifested by abnormally high luteinizing hormone (as mentioned above)

and prolactin, which can lead to ovarian dysfunction [19,20]. Studies indicate that such changes in the pituitary-ovarian axis mediate the occurrence of an abnormal luteal phase and a longer follicular phase [21]. Naturally, this affects and affects the secretion of estrogen and progesterone [22]. The above hormones were found in the follicular fluid of patients with endometriosis [23]. All these changes directly affect a woman's fertility, because they can affect every link of follicle maturation, and also complicate the onset of the ovulation phase of the menstrual cycle in patients with endometriosis [24,25]. The function of spermatozoa is negatively affected by cytokines, macrophages, TNF-α, which are present in the peritoneal fluid in women with endometriosis. These factors can lead to defragmentation of sperm DNA, disrupt the integrity of sperm membranes, change sperm motility, worsen both the connection between the sperm and the fallopian tube epithelium and disrupt the connection of sperm with oocytes [26,27].

## 3 Complications That Occur in the Early Stages of Pregnancy, in the Perinatal Period, Childbirth

A meta-analysis by Joanne Horton et al., showed that women with adenomyosis and endometriosis during pregnancy (meaning any method of conception) had a more than 3-fold increased risk of miscarriage, which confirms the development of suboptimal implantation and early fetal development [26]. Also, to establish intrauterine and obstetric complications, a group of IVF patients with endometriosis and a control group of IVF without endometriosis were examined. The results showed an increase in the risk of complications by 50% higher than in the control group, as well as an increase in the risk of delivery by cesarean section by 73%. Interestingly, a group of patients who did not use IVF programs, but also had endometriosis, showed an increase in the risk of postpartum hospitalization by 25%, delivery by cesarean section and formation of placenta previa by more than 3 times; the risk of preeclampsia by 18%, gestational hypertension by 29%; the development of premature labor by 42%. It was noted that ovarian endometriosis is associated with a negative effect on the output of eggs and the formation of a normal number of mature eggs during the IVF/ICSI cycle.

In the literature, there is evidence of adverse events in patients with endometriosis: rupture of the uterus; ruptures of ovarian cysts requiring surgical treatment during pregnancy; development of hemoperitoneum and even intestinal perforation. [28-30]. Perineal tissues susceptible to endometriosis are characterized by pathological looseness, which increases the risk of injury to this area [31,32]. Endometriosis can lead to the development of uterine hypotension and impaired placentation, thereby increasing the risk of having a baby with low body weight. This is evidenced by meta-analysis. In the tissues subjected to the endometriodic process, there is a violation of peristalsis, which leads to a violation of implantation of the blastocyst, which in turn leads to the development of placenta previa [33]. Conti et al. based on the results of meta-analysis, a high incidence of premature delivery (up to 37 weeks of pregnancy) was noted in women with endometriosis [34], explaining this by the development of inflammatory processes in the membranes of the fetus. These changes were observed in groups of patients with endometriosis

who had both spontaneous pregnancy and pregnancy using assisted reproductive technologies (ART) [35,36]. Breintoft et al. 2021 in their studies showed that women with endometriosis were more exposed to the development of gestational hypertension. Which, accordingly, causes the development of disseminated intravascular coagulation, placental abruption and multiple organ failure. Risks to the fetus include prematurity, intrauterine growth retardation, and even intrauterine death. A study is described showing that 13.3% of women with endometriosis had a risk of developing gestational diabetes mellitus [37]. Stephansson et al. it was found that endometriosis increases the risk of placental abruption and the development of pre- and postpartum bleeding by 80% [38]. This is not surprising, given the vascular changes caused by endometriosis. Finally, several sources in their meta-analyses indicated the risks of miscarriages and stillbirths [39]. The results of the studies varied depending on [40]:

1. How pregnancy was conceived (using ART/spontaneously),
2. The stage of endometriosis (1-2 vs. 3-4, and
3. The type of endometriosis.

Women with endometriosis who used ART programs showed a greater frequency of miscarriages. Regardless of the stage (1/2 or 3/4), women suffering from endometriosis also showed increased risks of spontaneous premature delivery.

## 4 Conclusion

Endometriosis is a disease that negatively affects both the reproductive function of a woman, causing infertility, and exposes the mother and her fetus to an increased risk of developing further complications during pregnancy. Many issues remain controversial, given the complexity of the etiopathogenetic mechanisms of endometriosis, the late diagnosis of the disease, and the frequent use of IVF programs. It is necessary to conduct further research in this area, which will reveal new mechanisms of endometriosis development, improve methods of timely screening, and identify qualitative ways to solve the problem, which will undoubtedly be of great importance for improving the health of women with endometriosis and their children.

## 5 Availability of Data and Material

Data can be made available by contacting the corresponding author.

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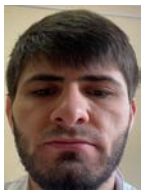

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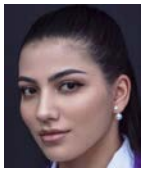

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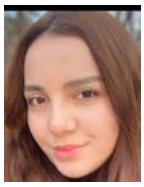

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