World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(RESEARCH ARTICLE)

Check for updates

The effect of endometriosis on the fertility of women

Roshika Fernando *

Diagnostic Radiology Department, Daugavpils Regional Hospital, Latvia.

World Journal of Biology Pharmacy and Health Sciences, 2024, 19(01), 320–331

Publication history: Received on 11 June 2024; revised on 20 July 2024; accepted on 22 July 2024

Article DOI: https://doi.org/10.30574/wjbphs.2024.19.1.0441

Abstract

Endometriosis is defined by the presence of ectopic endometrial tissue outside the uterus, frequently located on pelvic organs such as the fallopian tubes and ovaries, and occasionally beyond the pelvic region. This condition manifests as dysmenorrhea, chronic pelvic pain, dyspareunia, and subfertility. Despite extensive research, the etiology and pathogenesis of endometriosis remain unclear, with laparoscopy being the definitive diagnostic method.

The association between endometriosis and infertility has been extensively debated. Endometriosis can impair fertility by disrupting embryo implantation, altering hormone levels, and compromising oocyte quality. This literature review aims to examine the effects of endometriosis on female fertility.

The review encompasses documents from clinical trials with control groups involving 196 to 22,416 reproductive-age participants (25-42 years), and case studies published over the past thirty-seven years from various regions (USA, Australia, Turkey, Africa, and Europe. Reputable databases such as BMJ, NEJM, Elsevier, AJR, Medline, and PubMed were utilized, with references compiled in the bibliography.

A risk-benefit analysis indicates that up to 50% of women with endometriosis experience infertility. Consensus on treatment options remains elusive. The relationship between endometriosis and infertility is supported by studies of both fertile and infertile women, animal studies, donor sperm studies, and in vitro fertilization outcomes. Diagnostic methodologies based on endometrial changes are providing insights into potential mechanisms of infertility, especially in women with milder disease. However, clinical management of endometriosis-related infertility has not shown conclusive success beyond in vitro fertilization.

Keywords: Endometriosis; Female fertility; Infertility; Diagnostic methodologies

1. Introduction

Endometriosis is a prevalent condition characterized by the abnormal growth of endometrial cells outside the uterus. These aberrant growths are most commonly found in pelvic organs such as the ovaries, peritoneum, uterosacral ligaments, pouch of Douglas, and rectovaginal septum. Although rare, extra pelvic endometrial abnormalities can occur in locations such as the umbilicus and stomach. The presence of endometrial tissue in these areas can cause irritation, pain, and adhesions on the affected structures [23, 5].

* Corresponding author: Roshika Nirmani

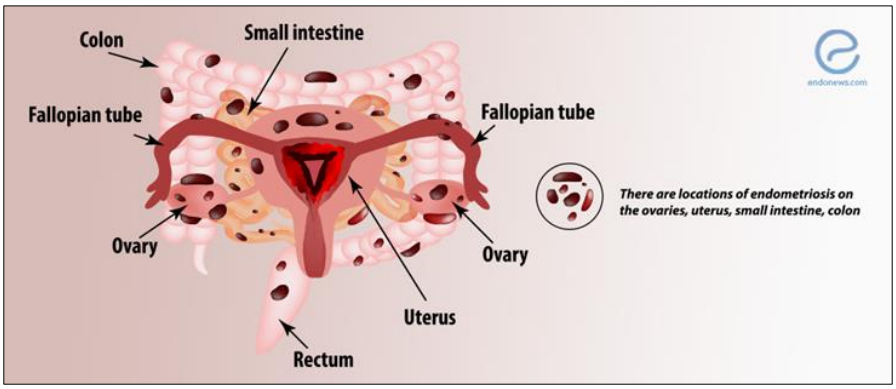


Figure 1 Endometriosis locations [10]

1.1. Aetiology and Pathogenesis

The etiology and pathogenesis of endometriosis remain largely unclear, although there is increasing evidence that it is a complex multifactorial disease with both genetic and environmental components contributing to its development [17].

- Heritability: Individuals with a family history of endometriosis, particularly among first-degree relatives, are at a higher risk of developing the condition [17, 9].
- Retrograde menstruation flow: The most widely accepted theory for the pathophysiology of endometriosis suggests that endometrial cells are transported intra-abdominally from the uterine cavity through the fallopian tubes during menstruation [6, 9]. Various risk factors may enable endometrial cells to survive in ectopic locations [6].
- Adhesions: Surgical scar implantations may attach to endometrial cells, leading to the development of endometriosis [6].
- Müllerian metaplasia: This theory posits that coelomic epithelium transforms into endometrium-like cells [6, 9].
- Lymph vascular emboli of endometrial cells: Endometrial cells may be transported to distant sites, such as the pleural cavity, through the lymphatic or circulatory systems [6].
- Increased incidence of luteinized unruptured ovarian follicle syndrome (Trapped Oocyte): Patients with severe endometriosis and distorted pelvic anatomy exhibit a high rate of infertility, potentially due to abnormalities in oocyte development and tubal transport [6].
- Early menarche or Late menopause: These complications may arise in response to hormonal changes during the menstrual cycle [1].

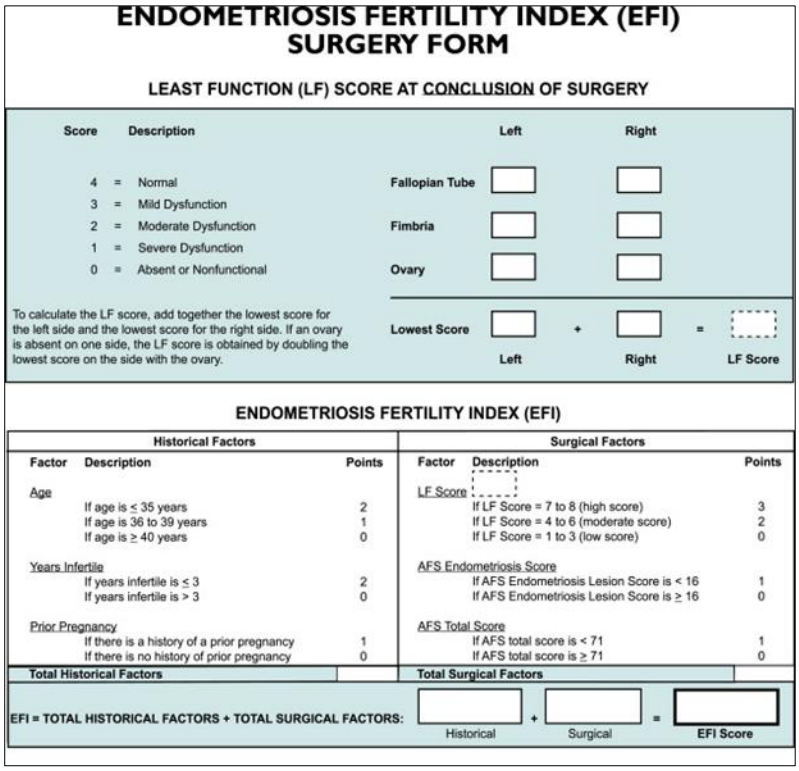
1.2. Symptoms of Endometriosis

Common signs and symptoms of endometriosis include [12, 5, 20]

- Painful periods (Dysmenorrhea): Pelvic pain and cramping may begin before and extend for several days into the menstrual period, often accompanied by lower back and abdominal pain.
- Dyspareunia: Pain during or after sexual intercourse, which is a frequent symptom.
- Pain with bowel movements or urination: These symptoms are most pronounced during menstruation.
- Excessive bleeding: Patients may experience heavy menstrual periods or intermenstrual bleeding.
- Infertility: Defined as the inability to conceive after one year (or more) of unprotected sexual intercourse.

1.3. Use of the Endometriosis Fertility Index

The Endometriosis Fertility Index (EFI) is a tool designed to predict the likelihood of achieving pregnancy following surgery. Its utility is assessed for forecasting the capacity to conceive without assisted reproductive technology (ART) after laparoscopic surgery. A study conducted in France from 2013 to 2016 involved 196 infertile patients to evaluate the effectiveness of the EFI [3].



ENDOMETRIOSIS FERTILITY INDEX (EFI) SURGERY FORM

LEAST FUNCTION (LF) SCORE AT CONCLUSION OF SURGERY

Score	Description		Left	Right
4	= Normal	Fallopian Tube		
3	= Mild Dysfunction			
2	= Moderate Dysfunction	Fimbria		
1	= Severe Dysfunction			
0	= Absent or Nonfunctional	Ovary		

To calculate the LF score, add together the lowest score for the left side and the lowest score for the right side. If an ovary is absent on one side, the LF score is obtained by doubling the lowest score on the side with the ovary.

Lowest Score: Left + Right = LF Score

ENDOMETRIOSIS FERTILITY INDEX (EFI)

Historical Factors			Surgical Factors		
Factor	Description	Points	Factor	Description	Points
Age			LF Score		
	If age is ≤ 35 years	2		If LF Score = 7 to 8 (high score)	3
	If age is 36 to 39 years	1		If LF Score = 4 to 6 (moderate score)	2
	If age is ≥ 40 years	0		If LF Score = 1 to 3 (low score)	0
Years Infertile			AFS Endometriosis Score		
	If years infertile is ≤ 3	2		If AFS Endometriosis Lesion Score is < 16	1
	If years infertile is > 3	0		If AFS Endometriosis Lesion Score is ≥ 16	0
Prior Pregnancy			AFS Total Score		
	If there is a history of a prior pregnancy	1		If AFS total score is < 71	1
	If there is no history of prior pregnancy	0		If AFS total score is ≥ 71	0
Total Historical Factors			Total Surgical Factors		

EFI = TOTAL HISTORICAL FACTORS + TOTAL SURGICAL FACTORS: Historical + Surgical = EFI Score

Figure 2 Endometriosis Fertility Index [11]

The study population met the following criteria:

1.4. Criteria for Study Inclusion

Participants in the study met the following criteria:

- Infertility persisting for over 12 months
- Presence of asymptomatic pelvic pain, dysmenorrhea, and/or deep dyspareunia
- Normal or abnormal hysterosalpingogram results
- Normo-ovulation or failure to conceive after three cycles of superovulation, with or without intrauterine insemination (IUI), used as first-line therapy for unexplained infertility
- Laparoscopic diagnosis of endometriosis
- Partner's semen classified as normal according to World Health Organisation (WHO) criteria [3]

2. Results

Among the 196 infertile women who underwent laparoscopic surgery for endometriosis-related infertility, the study yielded the following outcomes:

- 9 women (4.6%) were lost to follow-up.
- 26 women (13.2%) with an EFI score of 4 were referred directly to ART.
- 56 women (28.9%) with EFI scores of 5–6 received non-ART management for 3–6 months.
- 114 women (58.2%) with EFI scores of 7 or higher received non-ART management for up to 12 months.
- 73 women (37.2%) achieved pregnancy through non-ART management:
- 18 women (32.1%) had EFI scores of 5–6.
- 55 women (48.2%) had EFI scores of 7.

The mean time to conceive for women with EFI scores of 5–6 and 7 was 5.2 months (SD 2.8) and 3.9 months (SD 2.9), respectively [3].

In routine clinical practice, 149 women (76%) achieved pregnancy, with 37.2% after non-ART management and 38.8% after ART management. The 'baby take-home rate' was 57.1% [3].

The Endometriosis Fertility Index proved to be a valuable tool for predicting fertility outcomes in infertile patients undergoing surgery for endometriosis. Patients with a low EFI score should be promptly referred to ART to increase overall pregnancy rates [3].

2.1. Effect of Endometriosis on Infertility

2.1.1. Endometriosis-Associated Infertility

The prevalence of endometriosis is notably higher among women of Filipino, Indian, Japanese, and Korean descent [21]. Clinical manifestations of endometriosis vary based on the location of the ectopic endometrial tissue and can include dysmenorrhea, dyspareunia, chronic pelvic pain, and infertility, though some individuals may be asymptomatic. A significant challenge in the timely diagnosis and management of endometriosis is the lack of a clear correlation between symptoms and disease severity [21, 2].

Endometriosis is a leading cause of infertility through various mechanisms, although not all women with endometriosis experience difficulty conceiving [21, 2].

The primary mechanism involves altered anatomical structures. Pelvic adhesions impair oocyte release and ostial pickup, alter sperm motility, and affect myometrial contractions, leading to modified embryo transport and fertilization. Endometriosis can impact any stage of the reproductive process. Inflammatory cells in the peritoneal fluid and endometriomas have detrimental effects on oocytes, embryos, and sperm, impairing tubal function and reducing tubal mobility. This results in a lower fertilization rate in both natural and in vitro cycles [8, 14].

Endometriosis negatively affects the physiology of granulosa cells, leading to increased apoptosis and altered steroidogenesis by decreasing aromatase expression. This causes an imbalance in estrogen production, resulting in lower estradiol concentrations during the preovulatory phase and at the LH surge. The follicular phase is prolonged in these patients, as the LH surge is delayed or biphasic, leading to altered postovulatory progesterone release, which may affect oocyte maturation [8, 21].

The impact of endometriosis on the endometrium is also significant. A 2012 study demonstrated that cells could migrate from ectopic endometrial implants back to the uterine endometrium. These migrating cells exhibit upregulation of the Wnt7A gene, which affects endometrial receptivity during the implantation window. The Wnt7A gene is associated with estrogen-mediated uterine development and implantation [14, 19]. Another important gene is Hoxa10, which is involved in endometrial regeneration. Women with endometriosis have lower levels of Hoxa10, potentially explaining the reduced implantation rates. Additionally, higher levels of matrix metalloproteinases, which cause persistent endometrial breakdown, and lower levels of αβ-integrin, which impair embryo attachment, further contribute to lower implantation rates [14].

2.1.2. The Impact of Endometriosis on Early Embryo Morpho kinetics

A study conducted in Turkey evaluated 82 In Vitro Fertilisation (IVF) cycles, including 53 cycles with endometriosis and 29 cycles with tubal factor infertility. A total of 439 embryos were assessed for embryo morpho kinetics [4].

The presence of endometriosis was confirmed through laparotomy or laparoscopy in 27 patients and via transvaginal ultrasonography (TVUSG) in 26 patients, given the high diagnostic accuracy of TVUSG (Savelli 2009). Post-laparoscopic surgery, the diagnosis of endometriosis was verified by expert pathologists. The study included patients with grade 3–4 endometriosis. The control group consisted of 30 women with laparoscopically confirmed tubal factor infertility undergoing their first IVF attempt, with no evidence of endometriosis or hydrosalpinx at the time of laparoscopy. Clinical pregnancy was confirmed by the visualization of a gestational sac and foetal heartbeat using TVUSG two weeks after serum Human Chorionic Gonadotropin (βhCG) measurement [4].

In all cycles, ejaculated spermatozoa were used. Exclusion criteria included women over 40 years of age, those with partners suffering from male factor infertility, individuals requiring preimplantation genetic diagnosis due to structural or numerical chromosomal errors, and patients with uterine anomalies or polycystic ovary syndrome [4].

The study's findings indicate that endometriosis significantly influences early morpho kinetic events and cell cycles [4].

Table 1 Embryo morpho kinetics data of the study and control groups, respectively [4]

	Study Group	**Control Group**	**p-value**
No, of embryos	264	175	
tPB2	6.51 ± 9.07	3.71 ± 1.98	$p < 0.01$
tPNa	12.50 ± 7.87	11.13 ± 174	$p < 0.01$
tPNf	25.90 ± 6.31	25.30 ± 7.87	NS
t2	28.64 ± 5.24	28.25 ± 5.40	NS
t3	38.02 ± 6.87	37.67 ± 6.33	NS
t4	41.44 ± 7.35	40.19 ± 6.29	NS
t5	50.51 ± 9.86	49.76 ± 10.41	NS
t6	55.28 ± 10.14	53.77 ± 9.91	NS
t7	58.11 ± 10.14	58.33 ± 10.28	NS
t8	62.67 ± 11.80	61.45 ± 11.09	NS
t9	71.57 ± 13.37	69.62 ± 1158	NS
VP (tPNf-tPNa)	13.25 ± 6.23	14.87 ± 7.79	NS
ECC1 (tPb2-12)	22.19 ± 8.23	24.56 ± 5.66	$p < 0.01$
cc2a (t3-t2)	9.37 ± 5.08	9.42 ± 4.89	NS
ECC2	12.87 ± 5.47	12.02 ± 4.73	NS
FCC3	22.56 ± 9.4.6	22.03 ± 9.30	NS
52(t4-t3)	3.40 ± 5.31	2,53 ± 4,24	$p z 0.01$
S3(t8t5)	12.40 ± 9.20	12.59 ± 10.01	NS
GQE (%)	78 ± 41,2	93 ± 25,3	p < 0.01

Values are shown as mean±SD. Differences between means were tested by t-test for equality of means. NS = not significant GQE = Good Quality Embryos

Table 2 Differences in morpho kinetic data in control and study groups with respect to good and poor embryo quality [4]

		GOOD			**POOR**	
	Study group	**Control group**	**p-value**	**Study group**	**Control group**	**p-value**
No. of embryos	207	163		57	12	
tPB2	7.12 ± 9.91	3.69 ± 1.98	$p < 0.01$	4.27 ± 4.24	3.89 ± 1.96	NS
tPNa	12.88 ±- 8.56	11.15 ±- 3.76	$p < 0.05$	11.10 ± 4.35	10.79 ± 3.48	NS
tPNf	25.51 ± 6.46	25.99 ± 8.11	NS	27.29 ± 5.53	26.05 ± 3.36	N5
t2	27.85 ± 3.76	28.22 ± 5.49	N5	31.47 ± 8.12	28.60 ± 4.07	NS
t3	37.10 ± 6.19	37.63 ± 6.20	NS	41.31 ± 8.15	38.07 ± 8.20	N5
t4	40.40 ± 6.60	40.03 ± 5.90	NS	45.18 ± 8.66	42.35 ± 10.36	NS
t5	50.43 ± 10.04	49.23 ± 9.24	N5	50.75 ± 9.25	56.74 ± 19.83	NS
t6	55.04 ± 10.17	53.54 ± 8.82	NS	56.46 ± 10.02	56.82 ± 19.82	NS

t7	58.11 ± 10.12	58,32 ± 10.28	NS	58.25 ± 11.36	ND	
t8	62.66 ± 11.83	61.45 ± 11.09	N5	ND	ND	
t9	71.56 ± 13.37	69.62 ± 11.57	NS	ND	ND	
VP (tPNf-tPNa)	12.61 ± 6.41	14.83 ± 7.96	p < 0.05	15.69 ± 4.82	15.26 ± 5.15	NS
ECC1 (tPb2-t2)	21.18 ± 8.10	24.51 ± 5.75	p < 0.01	26.10 ± 7.60	25.15 ± 4.20	NS
cc2a (t342)	9.24 ± 5.04	9.41 ± 4.77	NS	9.84 ± 5.23	9.47 ± 6.59	NS
ECC2	12.54 ± 5.32	11.81 ± 4.45	NS	14.55 ± 6.01	15.40 ± 7.48	N5
ECC3	22.25 ± 9.46	22.02 ± 9.29	NS	ND	ND	
52(t4-t3)	3.28 ± 5.18	2.40 ± 4.05	NS	3.87 ± 5.78	4.28 ± 6.20	NS
53(t8-15)	12.47 ± 9.17	12.58 ± 10.09	NS	ND	ND	
tPB2	7.12 ± 9.91	3.69 ± 1.98	*p* < 0.01	4.27 ± 4.24	3.89 ± 1.96	NS
tPNa	12.88 ±- 8.56	11.15 ±- 3.76	*p* < 0.05	11.10 ± 4.35	10.79 ± 3.48	NS
tPNf	25.51 ± 6.46	25.99 ± 8.11	NS	27.29 ± 5.53	26.05 ± 3.36	N5
t2	27.85 ± 3.76	28.22 ± 5.49	N5	31.47 ± 8.12	28.60 ± 4.07	NS
t3	37.10 ± 6.19	37.63 ± 6.20	NS	41.31 ± 8.15	38.07 ± 8.20	N5
t4	40.40 ± 6.60	40.03 ± 5.90	NS	45.18 ± 8.66	42.35 ± 10.36	NS
t5	50.43 ± 10.04	49.23 ± 9.24	N5	50.75 ± 9.25	56.74 ± 19.83	NS
t6	55.04 ± 10.17	53.54 ± 8.82	NS	56.46 ± 10.02	56.82 ± 19.82	NS
t7	58.11 ± 10.12	58,32 ± 10.28	NS	58.25 ± 11.36	ND	
t8	62.66 ± 11.83	61.45 ± 11.09	N5	ND	ND	
t9	71.56 ± 13.37	69.62 ± 11.57	NS	ND	ND	
VP (tPNf-tPNa)	12.61 ± 6.41	14.83 ± 7.96	p < 0.05	15.69 ± 4.82	15.26 ± 5.15	NS
ECC1 (tPb2-t2)	21.18 ± 8.10	24.51 ± 5.75	p < 0.01	26.10 ± 7.60	25.15 ± 4.20	NS
cc2a (t342)	9.24 ± 5.04	9.41 ± 4.77	NS	9.84 ± 5.23	9.47 ± 6.59	NS
ECC2	12.54 ± 5.32	11.81 ± 4.45	NS	14.55 ± 6.01	15.40 ± 7.48	N5
ECC3	22.25 ± 9.46	22.02 ± 9.29	NS	ND	ND	
52(t4-t3)	3.28 ± 5.18	2.40 ± 4.05	NS	3.87 ± 5.78	4.28 ± 6.20	NS
53(t8-15)	12.47 ± 9.17	12.58 ± 10.09	NS	ND	ND	

With these discoveries, it is clear that endometriosis dominatingly influences the term of the early morpho kinetic occasions and cell cycles.

2.1.3. Oocyte Quality in Women with Endometriosis-Associated Infertility

Endometriosis significantly impacts clinical markers of oocyte quality, which is a critical factor in reproduction. This study aims to evaluate the quality of oocytes in women with infertility related to endometriosis. The investigation involved infertile women of reproductive age, ranging from 29 to 40 years, who underwent IVF and Intra-Cytoplasmic Sperm Injection (ICSI) procedures. Participants were divided into three groups:

- Group I: 50 patients with recurrent unilateral endometriomas

- Group II: 50 patients with unilateral endometriomas after surgical treatment
- Control Group: 30 patients with tubal factor infertility

Clinical and morphological assessments of oocyte quality were performed in all IVF/ICSI cycles [16, 18, 20,22, 24].

Table 3 Baseline Characteristics of Women with Infertility [16]

Characteristics	**Group I in = 501**	**Group II (n=50)**	**Control group (n = 30)**
Age, years	3336 ± 45	32.64±4,2	31.73 ± 421
Infertility duration	4.6 ± 2_4	4.2 ± 2.1	33±2.6
AMH	2.2 ± 13	2.1 ± 1,8	3.0±1.8
The number of antral follicles in the affected ovary	4.1 ± 15	5.4± 13	125±2.9 (at both sides)
The number of antral follicles in the intact ovary	*72*±2.6	7.8 ± 23	
Total number of nocytes recovered	8.8 ± 3.9	9.2±3.2	10.1 ±6.8
The number of high-quality oocytes obtained (oocyte in metaphase II)	4.1 ± 2_0	5.2 ± 2.6	9.6 ±3..5

Table 4 Characteristic of patients with endometriomas [16]

Size of endometriomas	**Group I *(n = SO)***		**Group II *(n =* 50)**	
>10mm	18	(36%)	24	(48%)
10-20 mm	20	(40%)	18	(36%)
20-30 mm	8	(16%)	6	(12%)
30-40 mm	4	(8%)	1	(2%)

The findings of the investigation indicate a statistically significant increase in the number of immature oocytes at metaphase I (MI) and the germinal vesicle (GV) stage in patients with endometriosis-associated infertility compared to the control group ($p < 0.005$). Additionally, there was notable degeneration of oocytes in patients with endometriomas exceeding 3 cm in diameter. These results suggest that endometriomas negatively impact oocyte quality, and that even after cystectomy, endometriomas continue to have a detrimental effect on the ovaries [16, 18, 20, 22, 24].

Therefore, it can be concluded that endometriomas, both before and after surgical intervention, adversely affect ovarian quality [16, 18, 20, 22, 24].

2.2. Chronic Niche Inflammation in Endometriosis Development

Chronic inflammation within the tissue niche, particularly in the peritoneal cavity, ovaries, and uterus, plays a crucial role in the development of endometriosis [13].

2.3. Peritoneal Cavity

The presence of peritoneal fluid in the peritoneal cavity results from the exudation of developing follicles and the corpus luteum. This fluid contains electrolytes, urea, steroidal hormones such as estrogen and progesterone, and other components like endometrial cells, macrophages, lymphocytes, and erythrocytes. Some of these components have secretory functions; for instance, endometrial cells secrete glycodelin, and macrophages secrete cytokines and angiogenic factors [13].

Infertility in most cases of endometriosis is primarily due to chronic inflammation induced by the abnormal environment, such as the increased volume of peritoneal fluid. Significant changes in the immune system include the

inhibition of T-cell-mediated cytotoxicity, decreased natural killer cell activity, and a rapid increase in pro-inflammatory cytokines and activated macrophages. These sudden changes create an oxidative and immunotolerant microenvironment conducive to endometriotic implantations [13].

Endometriotic implants secrete various substances, including estradiol, progesterone, monocyte chemoattractant protein (MCP)-1, transforming growth factor (TGF)-β, and vascular endothelial growth factor (VEGF). Additionally, pro-inflammatory cytokines such as interleukins (IL)-1, IL-6, and IL-8, and tumour necrosis factor alpha (TNF-α) are secreted. This mixture of secretions in the peritoneal fluid stimulates proliferative and angiogenic processes, contributing to the development and rapid progression of endometriosis [13].

The formation of endometriomas in the ovaries disrupts organ functionality and induces localized effects. The cystic fluid within endometriomas contains pro-inflammatory cytokines (IL-6 and IL-8), reactive oxygen species (ROS), TGF-β, and matrix metalloproteinases (MMPs). These components of cystic fluid alter the surrounding tissue of nearby endometriomas, leading to decreased follicular density, increased fibrosis, and loss of cortical stroma. Caspase-3 immunostaining has revealed signs of atresia in early follicles in tissue biopsies from ovaries containing endometriomas [13].

TGF-β1 and ROS contribute to fibrosis and adhesion formation through the differentiation of myofibroblasts and the expression of profibrotic genes mediated by plasminogen activator inhibitor-1. The loss of ovarian stroma has a detrimental effect on follicle formation. Pathogenesis is marked by a reduced blood supply and depletion of specific growth factors that would normally be secreted by healthy stromal cells [13].

2.4. Deep Infiltrating Endometriosis

A retrospective cohort study was conducted to investigate the impact of previous surgery for endometriosis on assisted reproductive technology (ART) cumulative live-birth rates in patients with deep infiltrating endometriosis (DE). The study included 222 DE patients who underwent ART [7].

The diagnosis of DE was established based on strict imaging criteria and histological confirmation of the disease. Women with a prior history of surgery for endometriosis were included, and their ART outcomes were compared with those of patients without a history of such surgery [7].

The cohort selection process is detailed in Figure 3. From January 2008 to December 2016, a total of 222 DE patients underwent 440 ART cycles [7].

The patient characteristics are summarized in Table 4. It is noteworthy that in 149 cases (67.1%), DE was associated with ovarian endometrioma (OMA) lesions [7].

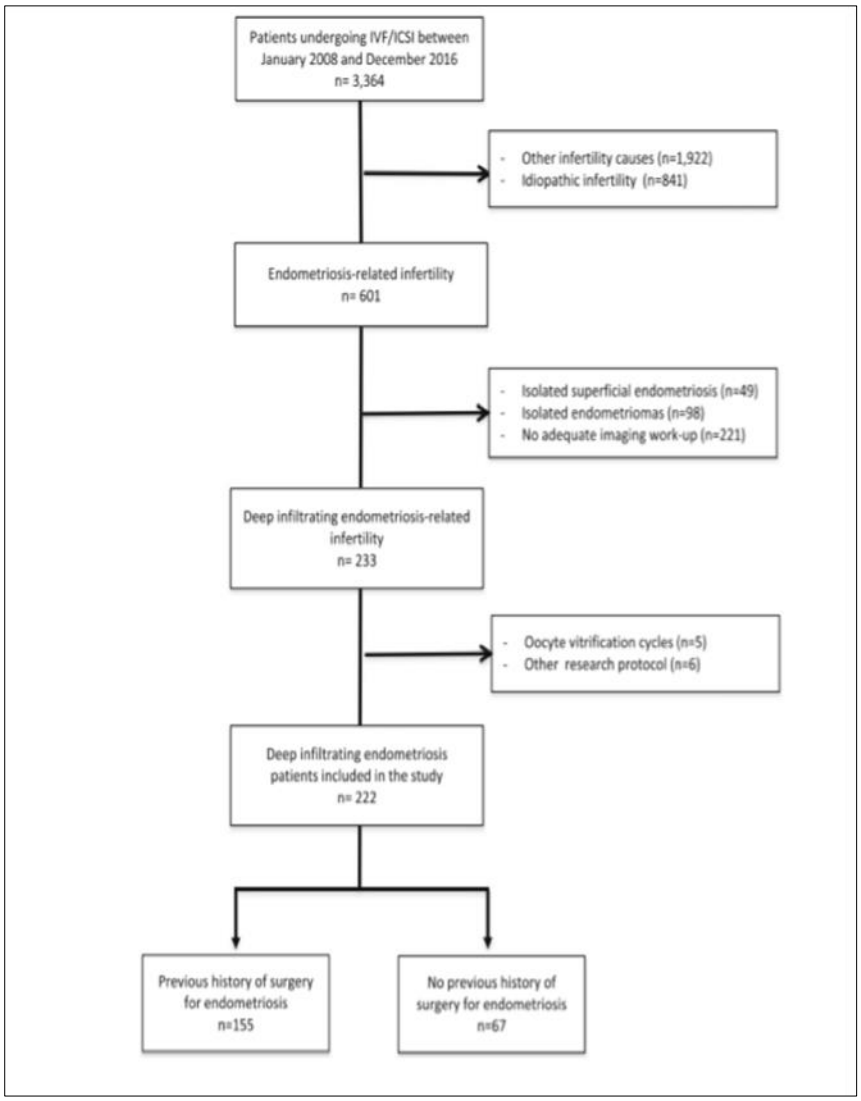


Figure 3 The process of the cohort selection [7]

Table 4 provides detailed information on the patient characteristics and their ART outcomes. Figure 3 illustrates the cohort selection process, ensuring a comprehensive understanding of the study design and its findings [7].

Table 5 Patients' characteristics in the general population (n = 222) [7]

Characteristics	Values*
Age (years)	33.0 13.9
Body mass index (cg/m²)	22.9 13.7
Infertility duration (years)	4.012.2
Gravidity	
0	163 (73.4%)
1	44 (19.8%)
2	10 (4.5%)
>3	5 (23%)
Parity	
0	193 (86.9%)
1	25 (11.3%)
>2	4 (1.8%)
Type of infertility	
Primary	163 (73.4%)
Secondary	59 (26.6%)
Associated infertility factors	
Male factor	33 (14.9%)
Tubal factor	27 (12.2%)
Associated OMA	149 (67.1%)
Unilateral	86 (57.7%)
Bilateral	63 (42.3%)
Anatomical distribution of DE lesions	
Uterosarral ligament(s)	67 (30.2%)
Vagina	9 (4%)
Bladder	12 (5.4%)
Intestine	124 (55.9%)
Ureter(s)	10 (4.5%)
Previous surgery for OSIS	155 (69.8%)
Number of previous surgeries	1.34 4 0.9
Previous surgery for OMA	96 (61.9%)
Number of previous surgeries	1.22 + 0.76
Unilateral OMA	59 (61.5%)
Bilateral OMA	37 (38.5%)
Ovarian reserve	
Day 3 FSH (LWL)	7.414.2
Day 3 AFC	10.9 16.4
Day 3 AMH (nginiL)	2.8 12.5
Associated adenomyosis	126 (56.8%)

DE, deep infiltrating endometriosis; OSIS, endometriosis; OMA, endometrioma; FSH, follicle-stimulating hormone; AFC, antral follicle count; AMH, anti- Müllerian hormone a Continuous data are presented as mean ± standard deviation; categorical data are presented as number (percentages).

Abbreviation

ART - Assisted Reproductive Technology
DE - Deep infiltrating Endometriosis
EFI - Endometriosis Fertility Index
GV - Germinal Vesicle
ICSI - Intra-Cytoplasmic Sperm Injection
IL - Iinterleukins
IUI - Intra-Uterine Insemination
IVF - In Vitro Fertilisation
LH - Luteinizing Hormone
MCP - Monocyte Chemoattractant Protein
MMPs - Matrix MetalloProteinases
OMA - Ovarian Endometrioma
ROS - Reactive Oxygen Species
TGF - Transforming Growth Factor
TNF-α - Tumor Necrosis Factor alpha
TVUSG - Trans-Vaginal UltraSonography
VEGF - Vascular Endothelial Growth Factor
WHO - World Health Organisation

βhCG - Human Chorionic Gonadotropin

3. Conclusion

- Heterogeneity of Endometriosis: Endometriosis is a complex and heterogeneous disorder that affects various aspects of the reproductive cycle, including mechanical, molecular, and genetic factors.
- Pathophysiological Factors Affecting Infertility: Several key pathophysiological factors contribute to infertility associated with endometrioma. Inflammatory changes in the peritoneal cavity can alter sperm-oocyte interaction. Distorted pelvic anatomy may impair oocyte release and utero-tubal transport. Additionally, ovarian endometriomas can adversely affect ovarian reserve and oocyte quality.
- Impact of Pro-inflammatory Microenvironment: The pro-inflammatory microenvironment in the ectopic endometrium can alter endometrial responsiveness, further contributing to infertility.
- Predictors of Reproductive Outcomes: While endometrioma is significantly associated with infertility, ovarian reserve status and response to ovarian stimulation are more critical predictors of reproductive outcomes than the mere presence of endometrioma.
- Individualized Treatment Approaches: In vitro fertilization (IVF) is the most effective treatment for infertility in endometriosis patients. However, treatment decisions should be individualized, considering the patient's age, ovarian reserve, other causes of infertility, duration of infertility, and male factors.
- Multidisciplinary Management: The management of patients with endometriosis-related infertility should involve a multidisciplinary team to address the complex and multifaceted nature of the disorder

Compliance with ethical standards

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] Ashrafi M, Sadatmahalleh SJ, Akhoond MR, Talebi M. Evaluation of Risk Factors Associated with Endometriosis in Infertile Women. Int J Fertil Steril. 2016 Apr-Jun;10(1):11-21. doi: 10.22074/ijfs.2016.4763. Epub 2016 Apr 5. PMID: 27123195; PMCID: PMC4845520.

[2] Bodean O, Voicu D, Munteanu O, Brătilă E, Bohâlţea R, Davitoiu D, Cîrstoiu M. Chronic Pelvic Pain And Endometriosis. Research and Science Today, No 2 (10)/2015: 206-214.

[3] Boujenah J, Cedrin-Durnerin I, Herbemont C, Bricou A, Sifer C, Poncelet C. Use of the endometriosis fertility index in daily practice: A prospective evaluation. Eur J Obstet Gynecol Reprod Biol. 2017 Dec;219:28-34. doi: 10.1016/j.ejogrb.2017.10.001. Epub 2017 Oct 10. PMID: 29035799.

[4] Boynukalin FK, Serdarogullari M, Gultomruk M, Coban O, Findikli N, Bahceci M. The impact of endometriosis on early embryo morphokinetics: a case-control study. Syst Biol Reprod Med. 2019 Jun;65(3):250-257. doi: 10.1080/19396368.2019.1573275. Epub 2019 Feb 11. PMID: 30741013.

[5] Bulletti, C., Coccia, M.E., Battistoni, S. et al. Endometriosis and infertility. J Assist Reprod Genet 27, 441–447 (2010). https://doi.org/10.1007/s10815-010-9436-1

[6] Chapron C, Marcellin L, Borghese B, Santulli P. Rethinking mechanisms, diagnosis and management of endometriosis. Nat Rev Endocrinol. 2019 Nov;15(11):666-682. doi: 10.1038/s41574-019-0245-z. Epub 2019 Sep 5. PMID: 31488888.

[7] Chloé Maignien & Pietro Santulli & Mathilde Bourdon & Diane Korb & Louis Marcellin & Marie-Charlotte Lamau1 & Charles Chapron - Deep Infiltrating Endometriosis: a Previous History of Surgery for Endometriosis May Negatively Affect Assisted Reproductive Technology Outcomes.

[8] Elena-Silvia Nada, Lacramioara Brinduse, Ovidiu Bratu, Dragos Marcu, Elvira Bratila Endometriosis-Associated Infertility.

[9] Environmental factors and endometriosis PATRICK BELLELIS, SERGIO PODGAEC, MAURÍCIO SIMÕES ABRÃO

[10] https://www.endonews.com/atypical-sites-of-deeply-infiltrative-endometriosis

[11] https://www.fertstert.org/article/S0015-0282%2809%2903714-5/fulltext

[12] https://www.nhs.uk/conditions/endometriosis/

[13] Lin YH, Chen YH, Chang HY, Au HK, Tzeng CR, Huang YH. Chronic Niche Inflammation in Endometriosis-Associated Infertility: Current Understanding and Future Therapeutic Strategies. Int J Mol Sci. 2018 Aug 13;19(8):2385. doi: 10.3390/ijms19082385. PMID: 30104541; PMCID: PMC6121292. https://doi.org/10.3390/ijms19082385

[14] Macer ML, Taylor HS. Endometriosis and infertility: a review of the pathogenesis and treatment of endometriosis-associated infertility. Obstet Gynecol Clin North Am. 2012 Dec;39(4):535-49. doi: 10.1016/j.ogc.2012.10.002. PMID: 23182559; PMCID: PMC3538128.

[15] Márcia Mendonça Carneiro, Ana Luiza Lunardi Rocha, Ivete de Ávila, Marcia Cristina França Ferreira. Fertility Preservation in Women with Endometriosis.

[16] Orazov MR, Radzinsky VY, Ivanov II, Khamoshina MB, Shustova VB. Oocyte quality in women with infertility associated endometriosis. Gynecol Endocrinol. 2019;35(sup1):24-26. doi: 10.1080/09513590.2019.1632088. PMID: 31532315.

[17] Rama Saha, M.D. , Hans Järnbert Pettersson, Ph.D., Pia Svedberg, Ph.D., Lena, Marions, Ph.D., Per Tornvall, Ph.D., Ralf Kuja-Halkola, Ph.D. Published:July 22, 2015DOI:https://doi.org/10.1016/j.fertnstert.2015.06.035 https://www.fertstert.org/article/S0015-0282(15)00462-8/fulltext#back-bib2 VOLUME 104, ISSUE 4, P947-952, OCTOBER 01, 2015 Heritability of endometriosis.

[18] Sallam HN, Garcia-Velasco JA, Dias S, Arici A. Long-term pituitary down-regulation before in vitro fertilization (IVF) for women with endometriosis. Cochrane Database Syst Rev. 2006 Jan 25;2006(1):CD004635. doi: 10.1002/14651858.CD004635.pub2. PMID: 16437491; PMCID: PMC8195082.

[19] Santamaria X, Massasa EE, Taylor HS. Migration of cells from experimental endometriosis to the uterine endometrium. Endocrinology. 2012 Nov;153(11):5566-74. doi: 10.1210/en.2012-1202. Epub 2012 Sep 11. PMID: 22968642; PMCID: PMC3473215.

[20] Senapati S, Sammel MD, Morse C, Barnhart KT. Impact of endometriosis on in vitro fertilization outcomes: an evaluation of the Society for Assisted Reproductive Technologies Database. Fertil Steril. 2016 Jul;106(1):164-171.e1. doi: 10.1016/j.fertnstert.2016.03.037. Epub 2016 Apr 7. PMID: 27060727; PMCID: PMC5173290.

[21] Vassilopoulou L, Matalliotakis M, Zervou MI, Matalliotaki C, Spandidos DA, Matalliotakis I, Goulielimos GN. Endometriosis and in vitro fertilisation Exp. Ther. Med. 2018 Aug; 16 (2): 1043- 1051.

[22] Vercellini P, Viganò P, Somigliana E, Fedele L. Endometriosis: pathogenesis and treatment. Nat Rev Endocrinol. 2014 May;10(5):261-75. doi: 10.1038/nrendo.2013.255. Epub 2013 Dec 24. PMID: 24366116.

[23] Vercellini, P., Viganò, P., Somigliana, E. et al. Endometriosis: pathogenesis and treatment. Nat Rev Endocrinol 10, 261–275 (2014). https://doi.org/10.1038/nrendo.2013.255

[24] . Xu B, Guo N, Zhang XM, Shi W, Tong XH, Iqbal F, Liu YS. Oocyte quality is decreased in women with minimal or mild endometriosis. Sci Rep. 2015 May 29;5:10779. doi: 10.1038/srep10779. PMID: 26022105; PMCID: PMC4448226

Authors short Biography

Roshika Nirmani Habarawa Batuwattage Fernando graduated from Riga Stradins University with a Doctor of Medicine (MD) degree in 2020. Currently working in the Diagnostics Radiology Department at Daugavpils Regional Hospital in Latvia.