

**Study of infertility associated with endometriosis and its management.**

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**Abstract**

**Background:** Endometriosis is a debilitating condition characterized by high recurrence rates. The etiology and pathogenesis remain unclear. 25% to 40% of infertile women have endometriosis and 30% to 50% of women with endometriosis are infertile. Endometriosis is a state of chronic inflammation in the pelvis and is characterized by endometrial-type tissue outside of the uterus. Although exact prevalence of endometriosis is unknown, it roughly affects 2 to 10% of the female population, but 30 to 45% of females with infertility [1]. This condition leads to two main problems—pelvic pain, infertility, or both. Endometriosis also has significant impact on the quality of life of the patients and negative influence on the sexual function and interpersonal relationships. This article will deal with endometriosis-related infertility in detail.

**Method:** Total 50 cases of endometriosis with infertility were studied in the department of obstetrics and gynecology, at tertiary care, hospital was included in the study. A thorough history was taken and clinical examination, hormonal study, ultrasonography, diagnostic and therapeutic laparoscopy, artificial reproductive techniques were used.

**Results:** 13 out of 50 women had infertility with endometriosis (26%). 8 out of 13 women had mild to moderate endometriosis (61%) and 5 out of 13 had severe endometriosis (38%). 7 out of 8 women (Stage I to III) conceived by ART (IUI/IVF). 3 out of 5 women (Stage IV) conceived by ART (IVF).

**Conclusion:** According to the present study, ART treatments, such as Intrauterine Insemination (IUI) or In Vitro Fertilisation (IVF) are established treatments for endometriosis-related infertility.

**Keywords:** Endometriosis, infertility, Invitro fertilization (IVF)

### **Introduction**

Endometriosis is a disease characterized by the presence of tissue resembling endometrium (the lining of the uterus) outside the uterus. It causes a chronic inflammatory reaction that may result in the formation of scar tissue (adhesions, fibrosis) within the pelvis and other parts of the body. Several lesion types have been described:

- Superficial endometriosis found mainly on the pelvic peritoneum
- Cystic ovarian endometriosis (endometrioma) found in the ovaries
- Deep endometriosis found in the recto-vaginal septum, bladder, and bowel in rare cases, endometriosis has also been found outside the pelvis

Symptoms associated with endometriosis vary, and include a combination of:

- Dysmenorrhea
- Chronic pelvic pain
- Pain during and/or after sexual intercourse
- Painful bowel movements
- Painful urination
- Depression or anxiety

In addition to the above, endometriosis can cause infertility. Infertility occurs due to the probable effects of endometriosis on the pelvic cavity, ovaries, fallopian tubes or uterus. There is little correlation between the extent of endometrial lesions and severity or duration of symptoms, some individuals with visibly large lesions have mild symptoms, and others with few lesions have severe symptoms. Symptoms often improve after menopause, but in some cases painful symptoms can persist. Chronic pain may be due to pain centres in the

brain becoming hyper-responsive over time (central sensitisation), which can occur at any point throughout the life course of endometriosis, including treated, insufficiently treated, and untreated endometriosis, and may persist even when endometriosis lesions are no longer visible. In some cases, endometriosis can be asymptomatic.

### **What is the cause of endometriosis?**

Endometriosis is a complex disease that affects some women globally, from the onset of their first period (menarche) through menopause regardless of ethnic origin or social status. The exact origins of endometriosis are thought to be multifactorial, meaning that many different factors contribute to its development. Several hypotheses have been proposed to explain origins of endometriosis. At present endometriosis is thought to arise due to:

- Retrograde menstruation, which is when menstrual blood containing endometrial cells flows back through the fallopian tubes and into the pelvic cavity at the time that blood is flowing out of the body through the cervix and vagina during periods. Retrograde menstruation can result in endometrial-like cells being deposited outside the uterus where they can implant and grow.
- Cellular metaplasia, which is when cells change from one form to another. Cells outside the uterus change into endometrial-like cells and start to grow.
- Stem cells giving rise to the disease, which then spreads through the body via blood and lymphatic vessels.

Other factors may also contribute to the growth or persistence of ectopic endometrial tissue. For example, endometriosis is known to be dependent on estrogen, which facilitates the inflammation, growth, and pain associated with the disease. However, the relationship

between estrogen and endometriosis is complex since the absence of estrogen does not always preclude the presence of endometriosis. Several other factors are thought to promote the development, growth, and maintenance of endometriosis lesions. These include altered or impaired immunity, localized complex hormonal influences, genetics and potentially, environmental contaminants.

The American Society for Reproductive Medicine classifies endometriosis in stages, depending on location, extent, and depth of the adhesions.

- **Stage I** is a minimal form of the disease. There may be a few small adhesions or tiny lesions. These may appear on one ovary, or the tissue lining the pelvis or abdomen. There's little to no scar tissue.
- **Stage II** is a mild form, with more lesions, occurring at a deeper level. It can affect both ovaries, and there is scar tissue.
- **Stage III** refers to a moderate level of the disease. It may present small cysts on one or both ovaries, and thick adhesions. Areas like the peritoneum and cul de sac will also be affected.
- **Stage IV** is considered severe endometriosis, with deep lesions and thick adhesions. There are also large cysts on one or both ovaries and their tubes.

When talking stages, it is important to remember how the **level of the disease does not correlate with the severity of symptoms** or levels of pain suffered by a patient. This means that someone with stage III endometriosis could have fewer symptoms than someone with a stage I. This applies to endometriosis as a whole and makes it tricky to treat.

#### **Biological mechanisms that might link endometriosis infertility (according to ASRM 2012)**

- I. Distorted pelvic anatomy
- II. Altered peritoneal function

- III. altered hormonal and cell mediated function
- IV. endocrine and ovulatory abnormalities
- V. impaired implantation
- VI. abnormal uterotubal transport

#### **Causes of infertility in endometriosis:**

- Distorted adnexal anatomy that interferes with ovum pick up after ovulation.
- Abnormal folliculogenesis, anovulation, luteal insufficiency, lutenized unruptured follicle syndrome.
- Interference with early embryogenesis, recurrent miscarriage due to reduced endometrial receptivity.
- Decreased sperm survival, altered immunity and intraperitoneal inflammation.

#### **Neglected but other potentially relevant mechanism.**

- Dyspareunia
- Concomitant presence of adenomyosis or endometrial polyps
- Surgically related damage to the ovarian reserve due to excision of ovarian reserve
- Anovulation resulting from the indispensable need for hormonal therapy because of unbearable pain refractory to surgery

#### **Materials and Methods:**

Study design: experimental study design.

Study setting: the study was held at a medical college and tertiary center.

Study duration: from May 2022 to May 2023

Study population: Patients come with complaint of infertility in reproductive age group in OPD.

Sample size: 50

Expected frequency-30% to 50%, Confidence limit-6% margin of error, Confidence level-90%. Total sample 50

#### **This sample size is obtained by**

Formula:  $n \geq z^2 \frac{p \times q}{12}$

$z = 1.96$ , critical value at 95% confidence level

=1.64, critical value at 90% confidence level

p=12%, q=100-p, l= margin of error= 6%, n≥50

**Eligibility criteria**

**Inclusion criteria**

- All women in reproductive age group with infertility.

**Exclusion criteria**

- Infertility related to metabolic disorders.
- Infertility due to chromosomal abnormality our mullerian agenesis.
- Infertility due to other organic causes like fibroid.
- Infertility due to male factor.

**Methodology**

- This study was conducted in the department of obstetrics and gynaecology of medical college and tertiary care centre.
- Total 50 patients were included in this study after satisfying inclusion and exclusion criteria.
- Written informed consent was taken from all study participants. Detailed history, complete general examination was done.
- All required investigations, hormonal study, ultrasonography, diagnostic and therapeutic laparoscopy and artificial reproductive techniques were done.
- All the information was recorded in the predetermined proforma.
- Patients outcome in the form of severity of disease, confirmation of pregnancy was noted.

**Statistical analysis**

The data was coded and entered into Microsoft Excel spreadsheet. Analysis was done using SPSS version 20 windows software program. Percentage, means and standard deviations were all parts of descriptive statistics. For quantitative data comparison of all clinical parameters, the unpaired t test was utilised. When

comparing qualitative data between two or more groups, the chi square test was applied. The significance level was established at P≤0.05.

**Results**

Age group and infertility with endometriosis

Age	Endometriosis	Infertility
20-25	4	12
25-30	4	10
30-35	3	16
>35	2	12
Total	13	50

13 out of 50 women had infertility with endometriosis (26%)

Severity (Endometriosis) wise distribution

Age	Mild to moderate	Severe	Total
20-25	3	1	4
25-30	4	0	4
30-35	1	2	3
>35	0	2	2
Total	8	5	13

8 out of 13 women had mild to moderate endometriosis (61%) and 5 out of 13 had severe endometriosis (38%)

IVF treatment taken with severity of Endometriosis (Stage I to III)

Age	Mild to moderate	Conceive
20-25	3	2
25-30	4	4
30-35	1	1
>35	0	0
Total	8	7

7 out of 8 women (Stage I to III) conceived by ART (IUI/IVF)

IVF treatment taken with severe endometriosis (Stage IV)

Age	Severe	Conceived (success)
20-25	1	1
25-30	0	0
30-35	2	1
>35	2	1
Total	5	3

3 out of 5 women (Stage IV) conceived by ART (IVF)

### Discussion

Endometriosis has negative impacts on different aspects of daily life, highlighting similarities and differences between three age groups. There is a large body of quantitative studies on the psychological/ psychosocial impact of endometriosis.<sup>iii</sup> However, there were contradictory results on the psychological characteristics of patients with endometriosis.<sup>iii</sup> Quantitative studies have reported that endometriosis leads to a poor or impaired quality of life.<sup>iv</sup> A systematic literature review by Gao et al.<sup>v</sup> demonstrated that endometriosis substantially affected patients' health-related quality of life and the most often affected domains were pain, psychological functioning, and social functioning.

The relationship between endometriosis and infertility has been debated for many years. In normal couples, fecundity is in the range of 0.15 to 0.20 per month and decreases with age. Women with endometriosis tend to have a lower monthly fecundity of about 0.02–0.1 per month.<sup>vi</sup> Infertile women are 6 to 8 times more likely to have endometriosis than fertile women.<sup>vii</sup> Despite extensive research, no agreement has been reached and several mechanisms have been proposed to explain the association between endometriosis and infertility. These mechanisms include distorted pelvic anatomy, endocrine and ovulatory abnormalities, altered peritoneal function, and altered hormonal and cell-mediated functions in the

endometrium. In the study, 13 women out of 50 infertile women with endometriosis (26%). 8 out of 13 women had mild to moderate endometriosis (61%) and 5 out of 13 had severe endometriosis (38%).

According to study 10 women out of 13 endometriosis women with infertility was conceived by Assisted reproductive techniques (IUI / IVF)

### Limitation

The impact of endometriosis is worsened by a lack of understanding of the disease.<sup>viii</sup> Many participants in our study reported that they had not heard about endometriosis before their diagnosis, and that there was a lack of information among patients, families and friends, at school and workplace. The women suggested helpful actions to decrease the negative impact of endometriosis on women's lives which included: increasing GPs knowledge and understanding, more information for patients and increasing awareness and understanding in society such as earlier and more information at college life. Most women wished that society would give more importance to endometriosis and take it as seriously as other chronic diseases like diabetes, multiple sclerosis, and cancer. The need for more support groups or networks, and a better understanding and acceptance without criticizing or stigmatizing were their further suggestions. There appeared to be greater satisfaction when services were provided by a dedicated endometriosis service, especially with getting information.

### Conclusion

Assisted reproductive techniques (ART) ART treatments, such as Intrauterine Insemination (IUI) or In Vitro Fertilisation (IVF) are established treatments for endometriosis-related infertility.

Intrauterine Insemination (IUI)

Taking into account the available evidence, we tend to recommend that IUI is only suitable for milder forms of endometriosis (stage I-II) and for women that have normal fallopian tubes and whose partner's sperm is of sufficiently good quality. IUI is currently not recommended routinely by NICE, although it is still widely used throughout the world.

#### In Vitro Fertilisation (IVF)

IVF is a process of collecting eggs from a woman's ovaries, fertilising them with sperm (her partner's or donor sperm), to create embryos and then replacing the embryos in her womb. Donor eggs and sperm can also be used for IVF. IVF is mostly recommended to severe endometriosis.

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