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AN INVESTIGATION INTO THE RELATIONSHIP BETWEEN ENDOMETRIOSIS AND THE OUTCOMES EXPERIENCED BY INFERTILE PATIENTS

Sunita Dhankhar [1]

[1] Research Scholar, Department of Nursing, Mangalayatan University, Aligarh, India

Corresponding Author

Sunita Dhankhar,
khushi17dhankhar@gmail.com

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ABSTRACT

Introduction: Females of reproductive age have a 6–10% prevalence of endometriosis. About 25–35% of women who are infertile may have endometriosis. Treatment options for infertile patients vary according to the disease's stage. It begins with an ovulation-inducing medication a8ch ogresses to sophisticated ART. The purpose of the current research was to appraise the outcomes of surgical intervention on endometriosis subjects who are otherwise infertile.

Materials and methods: The research was undertaken in selected government hospitals in Delhi. This study included 150 patients in all, ranging in age from 20 to 40. Every demographic factor, clinical and sonographic result, and hormonal evaluation was completed. Following that, staging was completed using ultrasonographic results and a clinical pelvic evaluation. For laparoscopic surgery, patients with ovarian endometriomas larger than 4 cm were chosen. Patients who did not have an ovarian endometrioma or whose endometrioma measured less than 4 cm were selected for ovulation induction, whether or not they had previously had GnRH agonist therapy.

Results: The patients' mean age was 29.64 years and 70.52% had pry. infertility. Dysmenorrhea (76.24%) followed by Menorrhagia (54.61%) and chronic pelvic (40.51%) were the most important clinical symptoms. Decreased serum AMH was linked to bilateral endometrioma. The primary treatment was laparoscopic surgery. The remaining patients received conservative care. IUI and controlled ovarian stimulation were employed after ovulation-inducing drugs like letrozole and GnRH agonists were used to boost fertility. In 25 patients (33.33%), IVF was recommended for fertility management. In conclusion, endometriosis causes a reduced response to ovarian stimulation in addition to being linked to a decreased ovarian reserve. Therefore, obtaining effective reproductive treatment for this patient population is quite difficult.

1. INTRODUCTION

One risk factor for natural conception is endometriosis. The existence of endometrial glands outside the uterus is a hallmark of endometriosis, a persistent inflammatory illness. It typically causes pelvic discomfort, reduced fertility, or both, and 5–10% women are affected by endometriosis especially of reproductive age (Giudiice, 2010). A major concern is that up to 30–50% of women with endometriosis are infertile (Somigliana et al., 2017). Additionally, endometriosis is ten times more common in infertile people—up to 25–50%—(Ozkaen et al., 2008; Kocch et al., 2012); it also accounts for 10% of referrals for IVF therapies (Somiglana et al., 2017). According to Somigliiana et al. (2017) and Llareena et al. (2019), these include endometrioma-induced damage to the ovarian parenchyma, pelvic anatomy distortion from adhesion formation, chronic inflammation and peritoneal fluid linked to peritoneal lesions, any associated adenomyosis, altered hormone functions in the endo-metrium, dyspareunia, and iatrogenic damage during ovarian parenchyma surgery. These problems may result in decreased tubal function, poor folliculo-genesis, and/or alterations to the uterine milieu that impair embryo implantation and sperm motility (Somiglana et al., 2017; Llareena et al., 2019).

In 17–44% of cases, endometriosis manifests as an ovarian endometrioma. The relationship between endometrioma and altered ovarian endocrine function has received special attention in the scientific literature. The fluid of endometriomas contains high levels of ROS, chemicals, etc. These chemicals gradually limit the pool of primordial follicles with fibrous tissue (Sanchez et al., 2014; Llarena et al., 2019). A recent comprehensive study found that endometriosis decreases AMH levels in comparison to controls. Furthermore, the affected ovary's antral follicle count (AFC) was less than before surgery, according to a subgroup study that examined the AFC.

This confirms that the majority of ovarian reserve loss happens before surgery (Tian et al., 2021). Additionally, the ovary may be subjected to mechanical stress due to large endometriomas (Llarena et al., 2019). Additionally, endometriosis is often linked to a lowered ovulation rate. Although these findings are still debatable, it has also been proposed that women with endometriomas have lower-quality oocytes (Hareb et al., 2013; Sancheez et al., 2017).

However, patients with endometriosis appear to have similar rates of embryo aneuploidy compared to unaffected age-matched controls, and IVF patients for various reasons appear to have comparable rates of pregnancy, live birth, and miscarriage (Gonz et al., 2017). Even though there is strong evidence linking endometriosis to infertility, only 30 to 50% of endometriosis-affected women are infertile, and many of them are able to conceive naturally (Somiglana et al., 2017).

2. THE CONTRIBUTION OF SURGERY TO INCREASED FERTILITY

A contentious issue is the surgical management of infertility brought on by endometriosis. Specifically, there is disagreement on whether surgery or IVF should be used as the initial treatment for these patients (Calgna et al., 2020). The choice-making is complicated because the likelihood of enhancing fertility by surgery is depending on a number of variables, like the age of patients, previous surgeries, EFI, and rigorousness of pain. This staging technique predicts the rates of non-IVF pregnancies following surgical intervention for endometriosis.

The identification of deep infiltrated endometriosis (DIE) prior to surgery can potentially be a useful indicator of the severity of the procedure. Furthermore, DIE is a significant factor in deciding whether to use ARTs or move on with a surgical intervention, especially when paired with prognostic tools such as the EFI (Condus et al., 2024). For individuals with endometriosis, the initial indication for surgery is the presence of symptoms that are not adequately controlled with medication (Dunselman et al., 2014).

The 3-year projected cumulative pregnancy rate following laparoscopic surgery was 62%, according to a study by Adamsonn and Pastta (1994). According to other research, patients who had surgery to correct DIE prior to IVF operations had higher post-IVF conception rates than patients who did not have surgery (Ferrero et al., 2009). According to Lianng et al. (2024), surgery, whether total or partial, increased the likelihood of getting pregnant. This emphasizes how important surgical procedures are as a treatment for DIE; even if they don't completely eradicate the condition, they can still have a significant positive impact on fertility outcomes. Nevertheless, patients should always carefully consider the risks associated with surgery before deciding to have it done.

However, according to some other research, surgery has no effect on fertility outcomes (Vercellini et al., 2006). Laparoscopy may be recommended to restore normal pelvic architecture in women with DIE (Dunselmanmn et al., 2014). Some doctors advise IVF as the initial line of treatment rather than surgery for women with DIE who primarily want children (Falcone and Flyckt, 2018). Effects of surgical methods on fertility preservation and ovarian reserve in the treatment of endometriosis. As several writers have argued, the potential advantage of removing an endometrioma to increase fertility must be balanced taking into consideration the risk of damaging the ovary (Dunselman et al., 2014).

AMH levels really drop following the removal of an endometrioma, according to numerous studies and meta-analyses (Somiglana et al., 2012; Seyhann et al., 2015; Godman et al., 2016). Furthermore, within a year after laparoscopic cystectomy, AMH levels continued to drop (Zhang et al., 2024). Numerous factors have been suggested as causes of surgery-induced damage to the ovarian parenchyma, such as the overremoval of healthy ovarian tissue (Muzi et al., 2002), electrocoagulation-induced vascular damage, and autoimmune reactions brought on by severe local inflammation (Lii et al., 2009). A variety of treatments, including ethanol-based sclerotherapy, ablative operations (such as lasers), and stripping cystectomy, as well as a combination of these techniques, are typically included in the conservative surgical care of ovarian endometriomas.

In India, endometriosis is very common, particularly in infertile individuals. In a government tertiary hospital with inadequate IVF resources, the purpose of this research was to evaluate the outcome of surgical treatment for patients with endometriosis.

3. METHODOLOGY

3.1. STUDY DESIGN

This study is designed as an experimental examination to evaluate the impact of surgical intervention on uterine receptivity and pregnancy outcomes in women with endometriosis.

There will be two groups in the study:

3.2. INTERVENTION GROUP (GROUP A)

Women receiving laparoscopic surgery for endometriosis are having endometriotic adhesions and lesions removed.

3.3. GROUP B, THE CONTROL GROUP

Women undergoing conservative medical treatment, such hormone therapy or painkillers.

3.4. AREA OF STUDY

The study will be carried out at several government hospitals in Delhi, guaranteeing access to a range of patient demographics and making use of the cutting-edge surgical and diagnostic capabilities offered by these establishments. In order to guarantee that participants receive top-notch care, these facilities were chosen for their proficiency in gynecology and reproductive health.

3.5. SAMPLE SIZE

There will be 150 participants in total, split equally between two groups (75 in Group A and 75 in Group B). The sample size was established through statistical power calculations to guarantee sufficient representation and validity of the results.

Every demographic factor, clinical characteristic, sonographic characteristic, and hormonal evaluation was completed. Following that, staging was carried out based on the results of the laparoscopic and ultrasonographic procedures as well as the clinical pelvic assessment. A verbal scale that was associated with the VAS was used to score pain. where the worst discomfort is represented by 0. However, this was classified as no discomfort, moderate pain, severe pain, and intolerable pain on a verbal scale. Patients were chosen for laparoscopic surgery if their ovarian endometrioma measured more than 4 cm by USG. Patients who had no ovarian endometrioma or whose endometrioma measured less than 4 cm were chosen for ovulation induction, whether or not they had previously taken a GnRH agonist. A number of points like Ovarian reserve, tubal patency, etc., and other related comorbidities were taken into consideration while planning further infertility treatment.

4. RESULTS

Through pelvic assessment and USG evaluation, 150 individuals were chosen. Measurements were made of S. FSH, S. TSH, and S. AMH. Surgery was chosen for those with endometriomas larger than 4 cm. Three months after surgery, S. FSH and S. AMH levels were assessed. SPSS v20.0 was used to analyze the results.

Table1 Shows the Demographic Variables of the Study Participants.

Most of the Patients were >30 Years and Mean Age was 29.64 Years and 70.52% Had Primary Infertility.

Demographic variables (n=150)	
Age (mean+-)	29.64+-6.22
Type of inferility	70.52%
Primary	29.48%
Secondary	6.54+-3.98
Duration of Marriage	

Parity (%)	
Nullipara	75.64%
Multiparra	24.36%
BMI	24.76+-3.98

Table 2 Shows the Pain Score by Verbal Scale.

The Majority of Endometrioma Patients (68%), Reported Moderate To Severe Pelvic Pain, While 21% Did Not Have Persistent Pelvic Discomfort.

Pain score (n=150)	No of patients	Percentage
No pain	32	21.33333
Moderate pain	58	38.66667
Severe pan	46	30.66667
Unbearable pain	14	9.333333

Figure 1 Patients' Clinical Presentations.

The Most Significant Clinical Symptom was Dysmenorrhea (76.24%), Which was Followed by Menorrhagia (54.61%) and Persistent Pelvic Pain (40.51%).

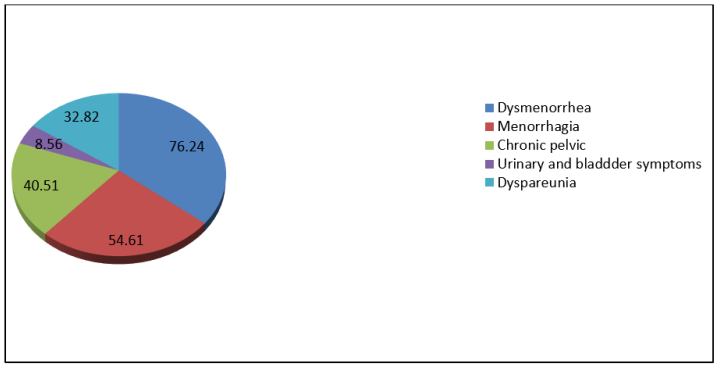


Figure 2 Shows the Data on Associated Pathology of the Patients

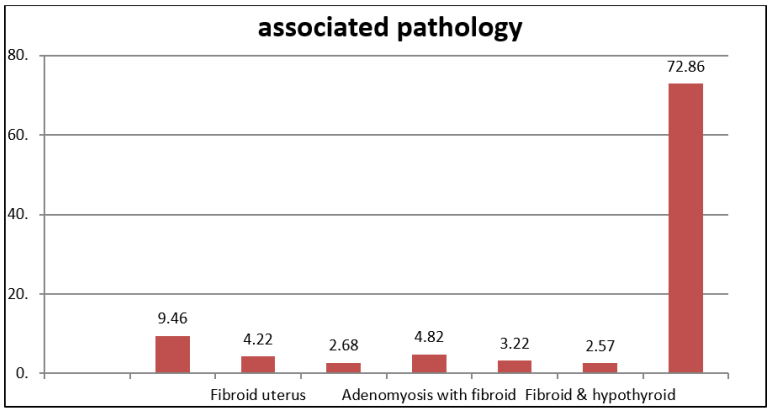
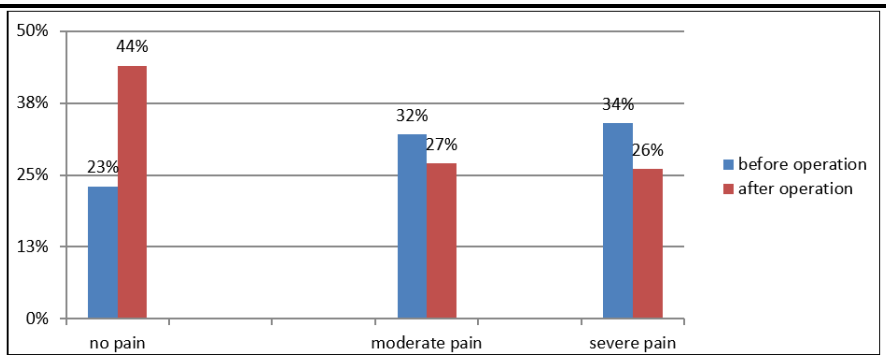


Figure 3 Shows Pain Comparison Before and After Surgery



Following surgery, patients with endometrioma and chronic pelvic discomfort did not have a substantial improvement in pain reduction. The two-tailed P value of 1.000 at the 95% CI is regarded as not statistically significant.

Table 3 Shows the Data of USG Findings.

62.66% endometrioma were unilateral and 28% were bilateral.

Size of tumour(%)	2-4cm	4-6cm	>6cm	No tumour	
laterality	18.36% Unilateral 94 62.66%	51.24% Bilateral 42 28%	24.48% No tumour 14 9.33%	3.82%	100%
Adhesion with	Superficial 90 60%	Deep 42 28%	Pouch of douglass obliteration 8 5.33%	No tumor 10 6.66%	surroundings

Table 4 Shows the Data on Baseline Hormone Levels.

The AMH level was 2.72±1.23 (mean±SD), FSH was 5.49±1.76, TSH was 3.52±1.49 and prolactin was 18.29±6.57, respectively.

Hormone levels	Mean+-SD
AMH (ng/ml)	2.72±1.23
FSH(IU/ml)	5.49±1.76
TSH (mIU/l)	3.52±1.49
Prolactin(ng/ml)	18.29±6.57

Table 5 Presents Data on Management of Fertility Without Surgery

Fertility management	n=75	%age
GnRHa Gonadotrophins	9	12%
GnRHa, Gonadotrophins & IUI	14	18.66%
OID	12	16%
OID & Gonadotrophins	13	17.33%
OID, Gonadotrophins & IUI	2	2.66%
Planned for IVF	25	33.33%

Table 6 Shows Fertility Management with Surgery

Types of surgery	N=75	percentage
Coagulation and adhesiolysis	41	54.66%
Excision of endometrioma	19	25.33%
Aspiration of cyst	5	3.33%

lapraomy	10	6.66%

Table 7 Show Outcome of Fertility Treatment.

20% of patients experienced a difficult miscarriage, and just 5.33% of patients had a live delivery with a pregnancy test result.

Outcome	N=150	%age
Pregnancy +	30	20%
Take home baby	8	5.33%
Continuing management	46	30.66%
Waiting for IVF	24	16%
Drop out due to various reasons	42	28%

5. DISCUSSION

Six to ten percent of women in their reproductive years have endometriosis. Endometriosis may affect 25–50% of infertile women. Undiagnosed endometriosis may be present in 50–60% of women who experience pain or infertility (Giudice IC., 2010). Women with obstructive Müllerian abnormalities are more likely to have it (Burney RO, Giudice IC., 2012). The disease's potential causes include direct transplantation, lymphatic vascular spread, coelomic metaplasia, retrograde menstruation, weakened immunity, and, most recently, a genetic foundation (Moridi I et al., 2017). According to recent data, stem cells produced from bone marrow move to the ectopic and utopic endometrium and develop into endometrial cells. They promote tissue development, angiogenesis, and the recruitment of stem cells (Moridi I et al., 2017). Aside from promoting the formation of the ectopic endometrium, the site's activated macrophages release VEGF, TNF, and interleukins 1, 6, and 8. (Bruner-Tran KI, et al., 2013).

Endometriosis is exacerbated by changes in estrogen metabolism and synthesis. Chronic inflammation caused by excessive prostaglandin, metalloproteinase, and chemokine production disrupts endometrial function and leads to disrupted implantation. Infertility affects between 30 and 50 percent of women with endometriosis. When gonadotropin and IUI were administered to women with modest and mild endometriosis, their monthly fecundity was lower than that of women without the condition.

Additionally, surgery lowers the ovarian reserve. The most recent version of the ASRM updated classification system, which is based laparotomy surgical findings, is the most popular classification method for managing fertility despite having a number of disadvantages (Guzick DS, et al., 2005).

A 2009 examination of 697 patients' surgical and clinical results led to the proposal of a new staging technique called the EFI, which includes the factors that best predict conception without IVF (Adamson GD, Pasta DJ. 2010). According to the ESHRE 2021-GDG (Guideline Group), infertile patients with endometriosis should get fertility treatment prior to deciding to have surgery. A patient's age and preferences, prior surgical history, ovarian reserve, other reasons of infertility, tumor size (>4 cm), presence or absence of pain complaints, and an expected EFI score of 10 should all be taken into account.

The present study included 150 patients from different backgrounds. Most of the patients were >30 years and mean age was 29.64 years and 70.52% had primary infertility. Surgery was the primary treatment for 50% of patients in this series, which is much higher than in other comparable studies. But according to a study in Canada that used laparoscopy to analyze 341 infertile women with mild to modest endometriosis, the treatment group had a significantly higher conception rate (30% vs. 17%), suggesting that surgical therapy increased fecundity. Because we are a government-run tertiary care hospital, most of the patients who came in from all over the country were in a more advanced stage of their illness and had severe adhesions, large endometriomas, or severe symptoms.

Therefore, these people need surgery to regulate their fertility as well as to relieve their symptoms. The mean serum AMH level was 2.72±1.23, FSH was 5.49±1.76, TSH was 3.52±1.49 and prolactin was 18.29±6.57, respectively.

It's unclear if surgery raises serum FSH or lowers serum AMH. if surgery should be postponed as long as feasible. For patients with a healthy ovarian reserve, letrozole or clomiphene citrate was used to induce ovulation for at least six cycles. If OID did not respond, gonadotropin was then added for three additional cycles. GnRH agonist was utilized prior to ovulation induction for one to three cycles in certain patients with endometrioma <4 cm. 16% of patients had IUI.

Therefore, every stage of fertility management in our study was hindered. Three recurring endometrioma patients with extremely low AMH were included. They are awaiting embryo transfer and have their embryos cryopreserved. Therefore, the outcome cannot be presumed. Nonetheless, we have made every effort to provide these individuals with the finest care possible.

Endometriosis-related discomfort, infertility, or both are the two main issues that women with endometriosis face. ESHRE 202110 Recommendations for hormone treatment state that ovarian suppression therapy may not be suggested to increase fertility in endometriosis-affected infertile women. In order to increase future pregnancy rates, postoperative hormone suppression with a GnRh analogue should not be recommended to women. Hormonal therapy should be made available to women who are unable or choose not to become pregnant right after surgery because it does not impair fertility and enhances the immediate results of pain management surgery. According to ESHRE10 guidelines, surgical laparoscopy may be suggested as a therapeutic option in rASRM stage I/II endometriosis since it raises the chance of a subsequent pregnancy.

Despite the lack of comparison study data, clinicians may think about using operational laparoscopy to treat endometrioma-associated infertility because it may improve the patient's chances of a spontaneous conception. 10. Operative laparoscopy for deep infiltrating endometriosis may be a therapy option for symptomatic people who wish to become pregnant, even if there is no tough proof that it increases fertility.

6. CONCLUSION

In addition to being linked to a decresed ovarian reserve, endometriosis is also the cause of a decreased ovarian stimulation response. Therefore, obtaining effective reproductive treatment for this patient population is quite difficult. We intend to overcome our treatment challenges and get the best outcome by increasing awareness, detecting patients early, enhancing surgical procedures, and maximizing ART facilities.

CONFLICT OF INTERESTS

None.

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