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Factors Affecting IVF Success after Laparoscopic Surgery in Women with Endometriosis

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Abstract

Background: Considering low-quality evidence regarding the impact of laparoscopic surgery on in vitro fertilization (IVF) success rates in women with endometriosis, our research aimed to evaluate IVF success rates and their influential factors in women with endometriosis-related infertility who underwent laparoscopic surgery.

Methods: In a retrospective cohort study, we included women aged 15 to 40 years diagnosed with endometriosis-related infertility who underwent laparoscopic surgery in a university hospital. Women with severe male factor infertility, adenomyosis, uterine myomas, premature ovarian insufficiency, incomplete information, or inaccessible data from infertility centers were excluded. Data were collected from the Endometriosis Data Registry approved by the Iran University of Medical Sciences under code number 1400-2-65-21233, including age, body mass index, infertility duration, endometriosis severity, and Anti-Müllerian hormone levels before IVF. IVF success was considered by an embryonic heartbeat identification during an ultrasound exam, that is, a clinical pregnancy. Independent sample t test, Mann-Whitney, and chi-square tests were applied for single-variable analysis, and logistic regression was used for multivariable analysis.

Results: Of 55 eligible patients, IVF was successful in 23 (41.81%). The mean age of participants was 34.98 years, with a standard deviation of 5.93 years. Endometriomas were observed in 42 (76%) of the participants; unilateral endometriomas were more common than bilateral (25 [45.5%] vs 17 [30.9%]). No significant differences were identified between the IVF-positive and IVF-negative groups regarding clinical and demographic characteristics.

Conclusion: Laparoscopic surgery in women with deep infiltrating endometriosis enhances IVF success and increases pregnancy rate.

Keywords: Endometriosis, Laparoscopy, Assisted Reproductive Technique, In Vitro Fertilization, Infertility

Conflicts of Interest: *None declared*
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↑What is "already known" in this topic:
Endometriosis is a major cause of infertility, and laparoscopic surgery is widely used to improve reproductive outcomes. However, its impact on in vitro fertilization (IVF) success remains unclear. While some studies suggest improved pregnancy rates through enhanced pelvic anatomy, others highlight concerns about ovarian reserve depletion, especially in severe cases.

→What this article adds:
This study shows that laparoscopic surgery may improve IVF success, particularly in deep infiltrating endometriosis cases, by reducing inflammation and restoring pelvic anatomy. However, ovarian reserve concerns emphasize the need for individualized treatment. Larger studies are required to refine clinical guidelines and optimize fertility outcomes in endometriosis patients.

Introduction

Endometriosis is a complex, multifactorial disease with intricate interplays between genetic, immunological, hormonal, and environmental factors characterized by the presence of endometrial-like tissue outside the uterine cavity, leading to chronic pelvic pain and Infertility (1, 2). It remains a prevalent and debilitating condition affecting approximately 6% to 10% of reproductive-aged women (3). Endometriosis is not only a prevalent condition but also a debilitating one that requires comprehensive management strategies to improve both pain relief and fertility outcomes for affected women.

Laparoscopic surgery is considered the most accepted modality in treating endometriosis due to its minimally invasive nature and ability to address the pathological lesions causing symptoms and infertility directly; however, while laparoscopy is extensively used for the treatment of endometriosis, its impact on assisted reproductive technology (ART) remains contentious (4). While some studies suggest that laparoscopic surgery can enhance pregnancy rates by improving pelvic anatomy and removing endometriotic lesions (5, 6), other research indicates that surgical intervention may inadvertently harm ovarian reserve and fertility potential, particularly in cases of severe endometriosis (7).

Despite the widespread use of laparoscopic surgery in endometriosis treatment, its effectiveness in improving ART outcomes remains controversial. The available evidence on its impact on in vitro fertilization (IVF) success is inconsistent due to heterogeneous study populations, variable surgical techniques, and the lack of randomized controlled trials (8, 9). Some studies suggest a positive effect of laparoscopic surgery, particularly in cases of deep infiltrating endometriosis (DIE), by reducing inflammation and improving implantation rates (10). However, the risk of ovarian reserve depletion following surgical excision of ovarian endometriomas remains a major concern, particularly in women with already compromised ovarian function (11).

Given these discrepancies and the moderate-to-low quality of available evidence, further research is needed to clarify the role of laparoscopic surgery in enhancing ART outcomes in women with endometriosis. Therefore, in this study, we aimed to evaluate IVF success rates in women with endometriosis-related infertility who underwent laparoscopic surgery, while addressing potential confounders that may influence reproductive outcomes.

Methods

Study Design and Setting

In this cross-sectional study, we retrospectively examined all women diagnosed with endometriosis and infertility who underwent laparoscopic surgery at Rasoul Akram Hospital, affiliated with Iran University of Medical Sciences in Tehran, Iran, from June 2017 to May 2021 (Figure 1).

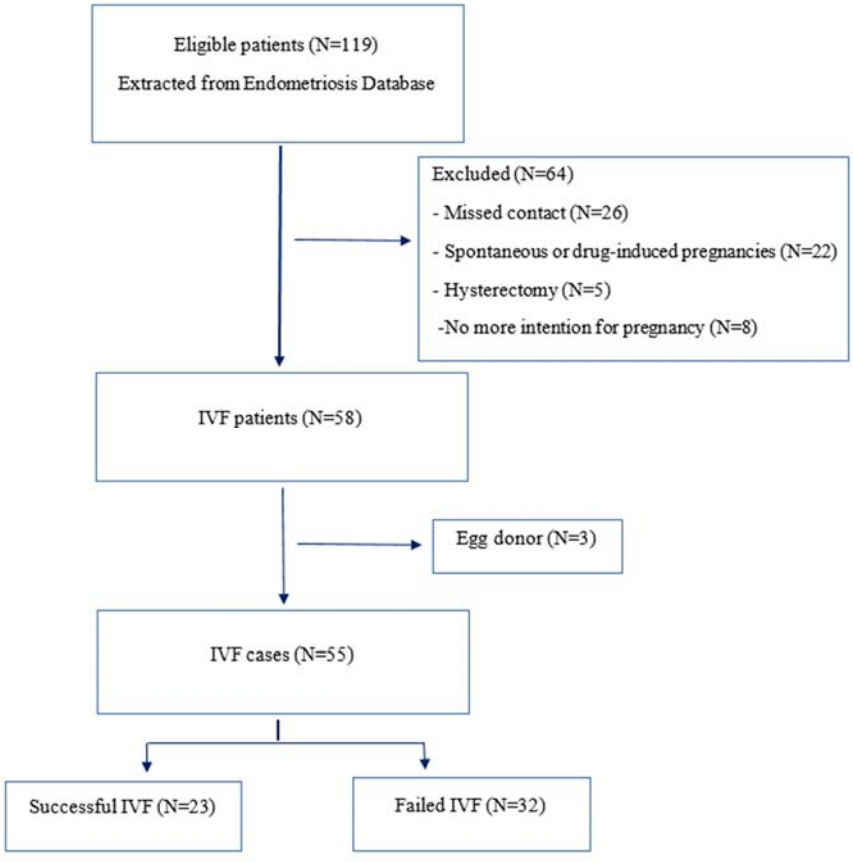

Figure 1. Study participants

Participants

Participants were women aged over 15 and under 40 years diagnosed with infertility due to endometriosis, with a normal spermogram or mild oligospermia. All participants had undergone laparoscopic surgery to treat endometriosis and underwent IVF after the surgery if pregnancy had not occurred within 6 months or so after laparoscopy. Women were excluded from the study if they had severe male factor infertility (< 5 million sperm per mL, < 5% progressive motility, < 1% normal morphology), adenomyosis, uterine myomatosis, postsurgical or premature ovarian failure (AMH <0.5 ng/mL), incomplete patient information, unclear details regarding the ART center, or if it was impossible to access information from infertility centers.

Data Sources and Measurements

Data were collected from the Endometriosis Data Registry approved by the Iran University of Medical Sciences under the code 1400-2-65-21233. They included variables such as age, body mass index (BMI), years since endometriosis diagnosis, duration of infertility, anti-Müllerian hormone (AMH) levels before IVF, an education level (high school diploma/bachelor/doctorate), employment status (employed, housewife), other medical conditions, surgical history, cause of infertility, the severity of endometriosis (including the presence of endometriomas, deep endometriosis [DE], and superficial endometriosis), and the number of IVF cycles. For missing data, efforts were made to retrieve information through patient follow-up and IVF center records. If data remained unavailable, cases were excluded from the analysis without imputation.

Outcome

The study outcome was the clinical pregnancy after IVF, which was determined by the identification of a gestational sac along with a fetal heartbeat in ultrasound.

Bias

In our study, data were collected through a combination of health information systems, paper files, and phone interviews, which might be the source of selection bias regarding the withdrawal of patients with negative results.

Statistical Analysis

Categorical variables were reported as frequencies and percentages, while quantitative variables were expressed as means and standard deviations. The comparison between successful and failed IVF results was implemented using the chi-square test and the Student t test for categorical and quantitative variables. Univariate and multivariate logistic regression analyses were conducted to identify factors influencing the success of IVF. Before conducting the logistic regression analysis, we checked for the presence of multicollinearity using the variance inflation factor (VIF), considering a threshold of VIF >5 as indicative of high collinearity. All included variables had VIF values <2, indicating no significant multicollinearity issues. The multiple binary logistic regression model included variables (age, BMI, AMH levels, duration of infertility, and endometriosis severity) based on clinical relevance and potential confounding effects rather than statistical significance in univariate analysis. Although some variables did not reach statistical significance in univariate analysis, they were retained in the final model to ensure a comprehensive assessment of potential interactions and confounders.

The significance level was set at 0.05, although in the regression model, we adjusted the effects for the potential influencing factors, even though the univariate analysis P value was higher.

Results

Out of 55 eligible patients, 41.81% (95% CI, 28.65%-54.09%) achieved a successful IVF. The mean age of the study participants was 34.98 years, with a standard deviation of 5.93 years. Endometriomas were observed in 76% of the participants, with 45.5% having unilateral endometriomas and 30.9% having bilateral endometriomas. There were no significant differences between the IVF-positive and IVF-negative groups regarding age, BMI, postdiagnosis interval, duration of infertility, AMH levels before IVF, education level, presence of other diseases, surgical history, infertility causes, endometriosis severity, and superficial endometriosis. However, patients with DE were significantly higher in the IVF-positive group. The clinical characteristics of patients with endometriosis with positive and negative IVF outcomes are summarized in Table 1.

Logistic regression analysis indicated a direct correlation between pre-IVF serum AMH levels and IVF outcomes. In contrast, both the duration of infertility and the time lag between the disease diagnosis and IVF were found to impact IVF results negatively. Furthermore, surgery improved IVF outcomes for patients with DIE (odds ratio [OR] = 4), although the statistical analysis resulted in a borderline *P* value (Table 2).

Discussion

The outcomes of this study provide insights into the role of laparoscopic surgery in enhancing IVF success rates for women with endometriosis-related infertility. Our findings indicate that DIE was more prevalent among patients with successful IVF outcomes, suggesting that specific endometriosis characteristics may support fertility restoration after surgery. This finding aligns with studies suggesting that DIE may respond well to laparoscopic surgery by reducing inflammation and improving pelvic anatomy, which can facilitate embryo implantation. Holoch and Lessey (2010) highlighted that precise lesion excision can benefit fertility, supporting our observation that anatomical improvements from surgery may aid pregnancy outcomes in advanced endometriosis (12).

Our findings align with existing research on laparoscopic surgery's potential to improve IVF outcomes, although results seem influenced by disease characteristics, particularly DIE. Hodgson et al (2020) noted that surgical intervention increased clinical pregnancy rates in endometriosis patients, suggesting surgery may counter endometriosis's fertility challenges when precisely staged. In a review,

Table 1. Baseline demographic and clinical characteristics of women with endometriosis undergoing IVF, stratified by IVF success

Variable		Total (N=55)	Successful (N=23)	Failed (N=32)	*P*-value
Age		34.9818(5.93)	35.13(5.93)	35.13(5.91)	0.990
		20-46	24-46	20-48	
BMI		25.1456(3.93)	24.82(3.07)	25.38(4.14)	0.580
		19-35	19.47-31.24	19.68-35.86	
Post-Diagnosis Interval		5.8455(3.93)	6.39(4.19)	5.45(3.19)	0.350
		1-15	1.00-15.00	1.00-13.00	
Infertility Duration (Yrs)		5.3818(3.93)	4.43(2.19)	6.06(3.85)	0.074
		1-15	1.00-9.00	1.00-15.00	
AMH (Before IVF)		1.80(1.71)	2.22(2.41)	1.5(0.87)	0.127
		0.5-9	0.7-9	0.5-4.8	
Education	Diploma	30(54.5)	12(52.2)	18(56.3)	0.920
	Bachelor	21(38.2)	9(39.1)	12(37.5)	
	Master/Doctorate	4(7.3)	2(8.7)	2(6.3)	
Job	Housewife	35(63.6)	15(65.2)	20(62.5)	0.830
	Employed	20(34.6)	8(34.8)	12(37.5)	
Other disease		19(34.5)	10(43.5)	9(28.1)	0.240
Surgical History		22(40)	10(43.5)	12(37.5)	0.650
Infertility Causes	Unexplained	25(45.5)	9(39.1)	16(50.0)	0.710
	Female factor	22(40.0)	10(43.5)	12(37.5)	
	Male factor (mild to moderate)	8(14.5)	4(17.4)	4(12.5)	
Endometriosis severity	Mild	2(3.6)	0	2(6.3)	0.220
	Moderate	14(25.5)	8(34.8)	6(18.8)	
	Severe	39(70.9)	15(65.2)	24(75.0)	
Endometrioma	No	13(23.6)	8(34.8)	5(15.6)	0.100
	Unilateral	25(45.5)	11(47.8)	14(43.8)	
	Bilateral	17(30.9)	4(17.4)	13(40.6)	
DIE (DE)		30(54.5)	14(60.9)	11(34.4)	0.052
Superficial Endometriosis		3(5.5)	22(95.7)	30(93.8)	0.760
IVF Cycle		45(81.8)	17(73.95)	28(62.2)	0.200
		10(18.2)	6(21.1)	4(12.5)	

Table 2. Univariate and Multivariate Logistic Regression Analysis of factors affecting IVF success rate in patients with Endometriosis

Variable		Univariate		Multiple regression	
		OR(95%CI)	P-Value	Adj OR(95%CI)	*P*-Value
Age		1(0.91-1.10)	0.99		
BMI		1.04(0.9-1.21)	0.57		
Years after Diagnosis		0.93(0.8-1.08)	0.345	0.76(0.58-0.99)	0.048
Years of infertility		1.18(0.98-1.41)	0.081	1.43(1.05-1)	0.022
AMH (Before IVF)		0.72(0.45-1.17)	0.19	0.46(0.20-1)	0.067
Education (Ref: Diploma)			0.92		
Job	Housewife	0.89(0.29-2.77)			
	Employed	Ref			
Other disease		1.97(0.63-6.07)	0.24	3.46(0.72-16)	0.122
Surgical History		1.28(0.43-3.82)	0.66	1.18(0.21-6)	0.853
Cause of infertility	Unexplained	Ref			
	Female factor	1.78(0.36-8.88)	0.48		
	Male factor	1.2(0.24-6.06)	0.82		
Endometriosis severity	Mild and Moderate	Ref		Ref	
	Sever	0.43(0.13-1.49)	0.433	0.245(0.42-1.43)	0.118
Endometrioma	No	Ref		Ref	
	Unilateral	0.3(0.0.058-163)	0.16	0.22(0.02-2.32)	0.200
	Bilateral	0.44(0.12-1.58)	0.21	0.26 (0.044-1.56)	0.140
DIE (DE)		2.4(0.8-7.26)	0.122	4.01(0.68-23)	0.124
Superficial Endometriosis		0.69(0.13-3.77)	0.66	5.12(0.25-105)	0.291
IVF Type Ref: Agonist		0.4(0.1-1.64)	0.21	0.18(0.02-1)	0.092

Hodgson et al reported an OR of 1.63 for clinical pregnancy after surgery, underscoring that removing endometriotic tissue may improve IVF success (8).

Our study categorized ovarian endometrioma (OMA) as no OMA, unilateral OMA, and bilateral OMA. Although endometriomas were not significantly associated with IVF outcomes, a trend showed that patients without OMAs had higher IVF success rates (34.8%) than those with unilateral (47.8%) or bilateral OMAs (17.4%). This trend reflects findings in other studies suggesting that endometriomas, especially bilateral ones, may reduce ovarian reserve, affecting fertility. Surgical excision of endometriomas is often recommended to improve pelvic anatomy, potentially benefiting IVF outcomes, although it may also lower ovarian reserve, particularly in cases with large or bilateral OMAs (Muzii et al, 2017). Our findings support individualized approaches, considering endometrioma presence and laterality in IVF and surgical planning (9).

AMH levels, a marker of ovarian reserve, were also evaluated for their influence on IVF outcomes. Although AMH levels showed a trend toward predicting IVF success, this association did not reach statistical significance (P = 0.127). This finding suggests that while AMH is an important marker of ovarian reserve, its predictive value for IVF success in endometriosis patients remains uncertain. Larger studies are needed to clarify the role of AMH in this context. Endometriosis, especially involving ovarian endometriomas, may reduce ovarian reserve, translating to lower AMH levels, but AMH alone may not fully capture ovarian function in endometriosis. Factors such as lesion location, severity, and surgical history play crucial roles in endometriosis-related infertility (13).

Our study highlighted that age and BMI did not significantly impact IVF outcomes, contrasting with broader infertility research, where these factors often predict IVF success. This discrepancy may stem from our study's low sample size, limiting statistical power. In addition, endometriosis's distinct pathophysiology may reduce the relevance of common predictors like BMI and AMH. Some studies suggest that endometriosis-related infertility is mainly independent of BMI. For example, Sarais et al (2016) found that BMI did not predict IVF outcomes in women with endometriosis, unlike other infertility causes. This observation reinforces the significance of endometriosis-specific factors, like DIE presence and severity, over traditional predictors (13).

Disease severity, assessed through the American Society for Reproductive Medicine (ASRM) classification, emerged as a significant predictor of IVF success. Our results align with the literature showing that patients with severe ASRM stages typically experience varied outcomes. Although we did not use the Endometriosis Fertility Index (EFI), the ASRM classification's predictive value aligns with Adamson (1997) and Muzii et al (2017), who found that greater disease severity correlates with a lower likelihood of pregnancy. Muzii et al, for example, reported that patients with low EFI scores had a 3-fold higher infertility odds (OR = 3.17), underscoring the importance of individualized treatment planning based on disease severity (14).

Hormonal treatments after surgery, particularly GnRH agonists, also appear crucial for fertility outcomes in moderate to severe endometriosis. Our study observed favorable effects of GnRH agonists, especially with incomplete excisions, indicating hormonal modulation may enhance IVF outcomes by suppressing residual endometriotic activity. Sallam et al (2006) demonstrated that GnRH agonists increased clinical pregnancy rates (OR = 4.28) in endometriosis patients in a Cochrane review, showing that these treatments may enhance uterine receptivity after surgery (11). Zhang et al (2022) further showed that postoperative GnRH agonist therapy mitigated adverse fertility outcomes in patients with DIE, highlighting the benefits of combining surgical and hormonal approaches for optimal IVF success (10).

However, our study and the existing literature are limited by variability in design, population demographics, and outcome measures, especially regarding live births and miscarriage rates. Retrospective cohort designs restrict generalizability. Hodgson et al noted variability in outcome measures across studies, underscoring the need for standardized protocols and robust randomized trials to clarify the long-term effects of laparoscopic surgery and hormonal therapies on fertility outcomes (8).

Limitations

This study is subject to several limitations. First, the cross-sectional design prevents the establishment of causality between laparoscopic surgery and IVF success. Second, the relatively small sample size reduces statistical power and may contribute to the lack of significant associations for some variables. Although some variables, such as AMH levels, showed a trend toward significance, the limited number of participants may have contributed to the lack of statistical significance in some analyses. Third, selection bias is possibly due to the retrospective nature of the data collection. Future prospective studies with larger cohorts and randomized controlled trials are needed to confirm these findings and establish evidence-based guidelines for endometriosis management in IVF patients.

Conclusion

Our findings underscore that specific lesion types, hormonal treatments, and pre-surgical AMH levels influence successful post-laparoscopic IVF outcomes in endometriosis patients. These factors work synergistically, especially in DIE, which may benefit most from excision and adjunctive hormonal therapy. When tailoring IVF protocols, clinicians should consider each patient's unique profile, particularly endometriosis type and extent. Individualized management protocols based on these prognostic factors are essential to improving pregnancy prospects for endometriosis patients. Further larger research with standardized, prospective designs will be critical to refining these recommendations and enhancing evidence for endometriosis-related infertility management.

Authors' Contributions

A.M.K.: study conceptualization, supervision, and manuscript revision; Sh.Ch.: study design and manuscript revision; R.D. and F.F.: primary draft; A.G.: data gathering

A.M.: statistical analysis; B.N.: manuscript preparation and Y.K.: data acquisition.

Ethical Considerations

This study was obtained from the Research Ethics Committee of Iran University of Medical Sciences (IR.IUMS.FMD.REC.1400.144).

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Conflict of Interests

The authors declare that they have no competing interests.

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