Open Access

Pak J Med Res
Vol. 64, No. 1, 2025

Original Article

To Investigate the Effect of Endometriosis on Intracytoplasmic Sperm Injection Outcome Among Infertile Women without Previous History of Ovarian Surgery

Rohina Gul[1], Fauzia Tabbasum Cheema[2], Aliya Muzafar[3], Aisha Awais[1], Rameen Nisar[1], Saba Sardar[1]

Lahore Institute of Fertility and Endocrinology[1], Hameed Latif Hospital, Islam Medical College[2], New Life Hospital, Fatima Jinnah Medical University[3], Lahore.

Abstract

Objective: This study aimed to determine the impact of endometriosis on oocyte maturation in stimulated In-vitro Fertilization/Intra Cytoplasmic Sperm Injection (IVF/ICSI) outcomes.
Study type, settings & duration: This retrospective study was conducted at Hameed Latif Hospital, Lahore from March 2021 to March 2023.
Methodology: About 180 women were included in this study. All the study subjects were categorized into two groups in equal, where Group A presented with ovarian endometriosis and Group B presented women without endometriosis. Infertility parameters in both groups were same like age, body mass index (BMI), and infertility duration. Outcome parameters (ovarian reserve, fertilization rate, embryo quality, implantation rate and pregnancy outcomes) were compared in both groups.
Results: The mean age was 38 years in both groups. In group A, BMI and the Antral Follicle Count was lower as compared to group B. (*p*-value =0.04) The number of oocytes retrieved, matured, and fertilized was higher in group B (14±5.31, 13±4.60, 12.5±4.79) as compared to group A (5±2.52, 4.83±2.40, 3.66±1.03). All the variables were statistically significant with the *p*-value <0.05. The pregnancy rate in Group A was 30% and in Group B, it was 29%.
Conclusion: Oocyte number and quality are affected by endometriosis. However, ovarian endometrioma does not affect the embryo quality and the outcome of pregnancy.
Key words: Endometriosis, oocyte quality, implantation rate, in-vitro fertilization, pregnancy rate, EMS.

Introduction

Infertility is a rising medical issue. Many couples suffer from infertility as a result of environmental pollution, societal pressure, and variations in fertility perceptions. Infertility is predicted to afflict 8-12% of couples in their reproductive years.[1] Although assisted reproductive technologies (ARTs) have made significant developments, infertility remains a major concern for infertile couples, as well as gynecologists and embryologists.

The development of endometrial glands and stroma outside the uterus may cause endometriosis. It typically affects females throughout their reproductive age which causes pelvic discomfort and infertility. It can also be without symptoms.[2] Endometriosis is an estrogen-dependent illness characterized by active tissue located around the uterus, typically on the ovaries and peritoneal peritoneum.[3] Around 2-10% of women of reproductive age faced this problem and 30-50% of women suffering from fertility issues.[4] The antral follicle count (AFC) and oocyte retrieval decreases in endometriosis which shows the poor ovarian response but is unrelated to the pregnancy outcome, leading to the conclusion that there is no

Corresponding Author:
Rameen Nisar
Lahore Institute of Fertility and Endocrinology
Hameed Latif Hospital
Lahore.
Email: rameennisar23@gmail.com
Received: 26 November 2024, **Accepted:** 14 March 2025
Published: 15 April 2025

Authors Contribution

RG & AM conceptualized the project. SS performed the statistical analysis. RN also did the data collection. RG & AA did the literature search. Drafting, revision & writing of manuscript were done by FTC & AM.

impact on ART outcomes by endometriosis.[5] The prevalence of endometriosis is 5-16.8% [6] in Pakistan and around 5-10% all over the world in reproductive age.[7]

The American Society for Reproductive Medicine (ASRM) classification was used to describe the level of endometriosis laparoscopically. Endometriosis in these areas can cause signs of profound dyspareunia and dysphasia which also effect the lifestyle, sexual activity, and fertility status.[8] Endometriomas are endometriosis cysts filled with blood resulting from ectopic endometrial tissue when it is positioned in the ovary or between the ovary and the ovarian fossa.[9] The oocyte is critical in defining embryonic competence, which is especially important for the success of in vitro fertilization (IVF). Several publications also describe the oocyte shape may also be a non-invasive indicator of oocyte quality.[10]

To treat endometriotic infertility, there are different Assisted Reproductive Techniques used including IVF and ICSI but the effect of endometrioma on ART results is yet unknown. According to the research, these results vary; some show lower oocyte retrieval numbers and poorer embryo quality, while others show that, even with fewer oocytes retrieved following IVF treatment, live birth rates are comparable to those of women without endometrioma.[11] Prior studies have either included a single-endometrioma group without a control group for comparison, or they have primarily examined the impact of surgical endometrioma removal on ART outcomes rather than the effect of the endometrioma itself.[12]

This study aimed to check the impact of endometriosis on oocyte maturation in stimulated IVF/ICSI outcomes. In case group, women had no prior surgical treatment and in the control group women who had no ovarian surgery and had no history of endometriosis.

Methodology

This retrospective study was held at the Hameed Latif Hospital, Lahore from March 2021 to March 2023. The sample size was 180, which we calculated conveniently. All the study subjects were categorized into two groups in equal where Group A presented with ovarian endometriosis (cases) and Group B presented women without endometriosis (control). Infertility parameters in both groups were tried to keep same including age, higher body mass index (BMI), and infertility duration. Outcome parameters (ovarian reserve, fertilization rate, embryo quality, implantation rate and pregnancy outcomes) were also analyzed in both groups**.** Women aged 20 to 45 years and had endometriosis and male with normal semen parameters were included in this study. Female with any medical or surgical history and any other cause of infertility were excluded. A written consent form was used for all the patients to use their clinical, hormonal, and ultrasound records. All the data were kept confidential.

In Vitro Fertilization/ Intracytoplasmic Sperm Injection Treatment Procedure:[12,13] All ovarian stimulation cycles included in this study were the first IVF/ICSI attempts for all patients, who underwent conventional stimulation following a flexible gonadotropin-releasing hormone (GnRH) agonist or an antagonist protocol, according to the observed follicular growth by ultrasound and blood tests. Follicle growth was regularly monitored by transvaginal ultrasound, in addition to the Follicle Stimulating Hormone (FSH), Prolactin (Prol), Anti-Mullerin Hormone (AMH), Thyroid Stimulating Hormone (TSH), serum estradiol (E2), progesterone, and luteinizing hormone (LH) levels during the cycle. On ultrasonography, final oocyte maturation was induced by administering human chorionic gonadotropin (hCG) when at least one follicle exceeded 18 mm in diameter. Oocyte aspiration was performed 34–36 h after hCG administration. Fresh embryo transfers were performed on Day 5. Only one or two embryos were transferred. Micronized progesterone (600 mg/day) was delivered vaginally to support the luteal phase. A rise in blood β-hCG levels, measured 14 days after embryo transfer, was used to diagnose pregnancies.

The data was categorized according to the baseline characteristics, and oocyte retrieval cycle. As baseline characteristics: age, BMI, the duration of infertility, primary or secondary infertility, and in the hormonal profile: serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), E2, and AFC on menstrual cycle D3, and duration and dose of gonadotropin stimulation were recorded. The number of follicles larger than 14mm in diameter on the trigger day, number of oocytes retrieved, matured oocytes retrieved, fertilized oocytes, cleaved oocytes.

All the data was entered and analyzed in a Statistical Package for Social Sciences (SPSS) software version 26.0. Descriptive analysis was performed for all variables, and categorical parameters were presented as frequency and percentage. To check the association between qualitative variables, the Pearson Chi-square test was used. The level of significance was 5%.

The ethical approval was obtained from the Research Ethics Committee of Hameed Latif Hospital, Lahore vide letter no. IRB/2021/19.

Results

About 180 women were selected and divided into case (90 women with endometrioma) and control (90 women without endometrioma) groups. There were no significant differences regarding age, BMI, and infertility duration in both groups.

Patients with endometrioma had a higher percentage of irregular menstrual cycles. Most of the cases had secondary infertility 30(33.3%) as compared to controls 22 (24.4%) (Table-1).

The case group showed significantly lower AMH levels (2.29±1.64 ng/ml v/s 3.47±0.42 ng/ml, *p*-value 0.00), and TSH (3.23±3.60 v/s 5.54±4.39, *p*-value =0.02) while the levels of FSH, LH and Prolactin was significantly higher (10.52±3.42 IU/L v/s 6.10±0.04 IU/L, *p*-value =0.00), (6.79±5.39 v/s 5.60 ± 2.86, *p*-value =0.22), (13.60±5.48 v/s 12.32±3.64, *p*-value =0.03) respectively. Antral follicle count (AFC) was lower in case group as compared to the control (3.83±1.60 v/s 6.50±0.70 with a *p*-value of 0.04 (Table-2).

Regarding the stimulation protocol, in the case group, 30 (33.3%) women were selected for the Agonist protocol, 60 (66.7%)were selected for GnHR antagonist protocol while in the control group, 13 (14.4%) women were selected for Agonist protocol, 77 (85.6%) were selected for GnHR antagonist protocol (*p*-value =0.00).

Those women who had endometrioma faced the higher stimulation duration and higher doses of FSH (3128±1540 v/s 2667±1430, *p*-value =0.01), but a lower follicles number (9.50±3.56 v/s 30±14.14, *p*-value =0.00), oocytes retrieved (5.39±2.52 v/s 14±5.31, *p*-value= 0.00), mature oocytes (4.83±2.40 vs. 13.50±4.60, *p*-value= 0.00) and fertilized oocytes (3.66±1.03 vs. 12.5±4.79, *p*-value= 0.00)

In both groups there wasstatistical significance observed regarding endometrial thickness on decision day (10.61±0.81 v/s 10±0.32, *p*-value= 0.00). E2 and P4 were higher in cases [[2631.50 (3878-1385)] v/s 1336 (4205.83-538.70)] , *p*-value =0.00), (7.28±3.09 v/s 5±1.41, *p*-value =0.01). The pregnancy rate (PR) was slightly higher in the cases (20/66=30% v/s 22/74=29%) as compared to controls, but was not statistically significant (Table 3).

Discussion

Endometriosis is a major contributor to the reduction in female fertility, but because of the advancement of IVF/ICSI technology, most females may now be pregnant and deliver a baby.[11] This study showed that patients with ovarian endometrioma had significantly poorer oocyte quantity and responsiveness to ovarian stimulation for ART treatment than controls. According to our results, patients in both groups the mean of age was 38 years and BMI was 27 kg/m^2 The ovarian reserve was lower in the endometrioma group as compared to the non-endometrioma group. Women with endometrioma had a considerably lower ovarian reserve than the control group, also described in past research that endometriotic women had lower ovarian count as compared to the control group.[12] Another study also found that the mean number of oocyte retrievals was lower in patients as compared to normal. One could be tempted to think that endometriosis would reduce the number of oocytes found.[13]

Table 1: Demographic characteristics of patients.

Characteristics	*Cases (Group A)*	*Control (Group B)*
Age (years) [mean ± SD]	38±4.62	38±4.24
BMI (kg/m^2) [mean ± SD]	27.22±5.71	27.03±5.03
Infertility Duration (years) [mean ± SD]	6.93±4.25	6.65±3.92
Menstrual Cycle [n (%)]		
Irregular	26(28.9)	1(1.1)
Regular	64(71.1)	89(98.9)
Type of Infertility [n (%)]		
Primary	60(66.7)	68(75.6)
Secondary	30(33.3)	22(24.4)
Previous Investigation [n (%)]		
Laparoscopy	19(21.1)	25(27.8)
Hysteroscopy	11(12.2)	7(7.8)
Both	-	7(7.8)
No Investigation	60(66.7)	51(56.7)

Table 2: Endocrine and sonographic parameters.

Hormonal Profile	*Cases (Group A) [mean ± SD]*	*Control (Group B) [mean ± SD]*	*p-value*
FSH (IU/L)	10.52±3.42	6.10±0.04	0.00*
LH (IU/L)	6.79±5.39	5.60±2.86	0.22
Prol (ng/mL)	13.60±5.48	12.32±3.64	0.03*
AMH (ng/ml)	2.29±1.64	3.47±0.42	0.00*
TSH (mIU/L)	3.23±3.60	5.54±4.39	0.02*
AFC (mm)	3.83±1.60	6.50±0.70	0.04*
Endo (mm)	7.50±0.70	6.90±0.98	0.63

*Indicated p-value <0.05 consider as significant

Table 3: Stimulation protocol and outcome parameters.

Parameters	*Cases (Group A)*	*Control (Group B)*	*p-value*
Stimulation Protocol [n (%)]			
Agonist	30(33.3)	13(14.4)	0.00
Antagonist	60(66.7)	77(85.6)	
Follicles on decision day	9.50±3.56	30±14.14	0.00
FSH dose	3128±1540	2667±1430	0.01
Endometrial thickness on decision day	10.61±0.81	10±0.32	0.00
E2 [median(max-min)]	2631.50(3878-1385)	1336.9(4205.83-538.70)	0.00
P4 (mean ± SD)	7.28±3.09	5±1.41	0.01
Oocyte retrieved	5±2.52	14±5.31	0.00
Matured oocytes	4.83±2.40	13.50±4.60	0.00
Fertilized oocytes	3.66±1.03	12.5±4.79	0.00
No. of embryo transferred [n (%)]			
1	29(43.9)	41(55.5)	0.51
2	37(56.1)	33(44.5)	
Pregnancy outcome [n (%)]			
β-HCG positive	20(22.2)	22(24.4)	0.34
β-HCG negative	46(51.1)	52(57.8)	
No ET	24(26.7)	16(17.8)	
Pregnancy Rate (PR) (%)	20/66 (30%)	22/74 (29%)	

Numeric data presented as mean and standard deviation except E2 which is presented as median (max-min), and categorical data presented as number and frequency. P-value <0.05 consider as significant.

Especially, when analyzing the effect of endometriosis on ovarian response, various complicating indicators, including (i) previous surgical treatment, might reduce the ovarian reserve and receptivity and (ii) inadequate oocyte pick up.[14] Concerning the last point, clinicians are often worried about the danger of infection during oocyte retrieval and wish to stop the transfixion of endometriomas.[15]

Furthermore, the ovaries may be dislocated in the pelvis as a result of endometriosis, which makes retrieval difficult. Consequently, it was discovered that women with diagnoses had a prevalence of incomplete follicular aspiration that was more than three times greater.[16]

This study also found that women with endometriomas have a much-reduced rate of oocyte maturation and fertilization, as well as less embryo quantity, reliable with other findings. Despite the fewer studies included, found a lower fertilization rate per egg in endometriotic women.[17] According to another study, this conclusion is associated with treated patients. The insemination rate appears good in patients who have milder endometriosis. However, the assessment of the fertilization rate is not free from other confounders.[18]

According to previous research, the endometriosis group had significantly fewer follicles larger than 15 mm, retrieved oocytes, and mature oocytes.[19] The endometriosis group had considerably fewer embryos, less good-quality embryos, and a much lower cumulative clinical pregnancy, most likely due to a significantly lower number of mature oocytes extracted. Most studies showed that reduced number of mature oocytes and embryos in endometriosis.[20]

The clinical pregnancy and live birth rate were common outcome parameters in many studies, on the other hand, some studies also described the cumulative clinical pregnancy. There was an insignificant difference in the outcome parameters in these studies; nevertheless, several

aspects of the oocyte retrieval cycle were substantially different between cases and controls, particularly the number of oocytes retrieved.[21]

However, we did not compare the particular treatment procedures and their effectiveness for endometriosis patients in this study, which necessitates additional extensive examination in the future. However, considering the lack of clinical research on the impact of endometrioma on embryo quality, as stated in our review, we believe that further randomized controlled trials with suitably powered sample sizes will be necessary to back up our findings.[22]

The findings of this study concluded that ovarian endometrioma has a deleterious influence on ovarian reserve but not pregnancy outcomes, in women getting ART treatment. Before the ART procedures, the ovarian count and fertilization will be increased by treating the endometrioma, but it has little effect on pregnancy outcomes and may harm ovarian reserves. Endometriosis must be identified and controlled for patients to benefit from and achieve excellent clinical results with IVF/ICSI procedures.

Acknowledgement

I am grateful to Dr. Rashid Latif Khan for offering me this wonderful opportunity and for his exceptional guidance. I would also like to express my heartfelt appreciation to the entire LIFE team for their invaluable cooperation and support.

Conflict of interest: None declared.

References

1. Bala R, Singh V, Rajender S, Singh K. Environment, lifestyle, and female infertility. Reprod Sci 2021; 28(3): 617-38.
2. Saunders PT, Horne AW. Endometriosis: Etiology, pathobiology, and therapeutic prospects. Cell 2021; 184(11): 2807-24.
3. İlhan M. Experimental Animal Models in Obstetrics and Gynecology. Duzce Med J 2024; 26(1): 72-8.
4. Akalewold M, Yohannes GW, Abdo ZA, Hailu Y, Negesse A. Magnitude of infertility and associated factors among women attending selected public hospitals in Addis Ababa, Ethiopia: a cross-sectional study. BMC Women's Health 2022; 22: 1-12.
5. Li A, Zhang J, Kuang Y, Yu C. Analysis of IVF/ICSI-FET outcomes in women with advanced endometriosis: influence on ovarian response and oocyte competence. Front Endocrinol 2020; 11: 427.
6. Memon E, Sumreen M, Baloch H. Frequency of endometriosis found on laparoscopic examination among females with subfertility. Professional Med. J. 2022;29(02):206-11.
7. Moradi Y, Shams-Beyranvand M, Khateri S, Gharahjeh S, Tehrani S, Varse F, et al. A systematic review on the prevalence of endometriosis in women. Indian J Med Res 2021; 154(3): 446-54.
8. Keckstein J, Hudelist G. Classification of deep endometriosis (DE) including bowel endometriosis: From r-ASRM to Enzian-classification. Best Pract Res Clin Obstet Gynaecol 2021; 71: 27-37.
9. Garg A, Manchanda A, Batra R. 14 Benign Adnexal Disease. Comprehensive Textbook of Diagnostic Radiology: Four Volume Set 2021: 233.
10. Bartolacci A, Intra G, Coticchio G, dell'Aquila M, Patria G, Borini A. Does morphological assessment predict oocyte developmental competence? A systematic review and proposed score. J Assist Reprod Genet 2022; 1(5): 3-17.
11. Wu Y, Yang R, Lan J, Lin H, Jiao X, Zhang Q. Ovarian endometrioma negatively impacts oocyte quality and quantity but not pregnancy outcomes in women undergoing IVF/ICSI treatment: a retrospective cohort study. Front Endocrinol 2021; 12: 739228.
12. Aghajanova L, Altmäe S, Sokalska A. Uterine factors associated with fertility impairment. Front Endocrinol 2023; 14: 1307237.
13. Aghajanova L, Altmäe S, Sokalska A. Uterine factors associated with fertility impairment. Front. Endocrinol 2023; 14: 1307237.
14. Sachs MK, Makieva S, Dedes I, Kalaitzopoulos DR, El-Hadad S, Xie M, et al. Higher miscarriage rate in subfertile women with endometriosis receiving unbiopsied frozen-warmed single blastocyst transfers. Front Cell Dev Biol 2023; 11: 1092994.
15. Popoutchi P, MARQUES JUNIOR OW, Averbach P, Cardoso Filho CA, Averbach M. Surgical techniques for the treatment of rectal endometriosis: a systematic review of randomized controlled trials and observational studies. Arq Gastroenterol 2021; 58: 548-59.
16. Somigliana E, Li Piani L, Paffoni A, Salmeri N, Orsi M, Benaglia L, et al Endometriosis and IVF treatment outcomes: unpacking the process. Reprod Biol. Endocrinol 2023; 21(1): 1-11.
17. Lantsberg D, Fernando S, Cohen Y, Rombauts L. The role of fertility preservation in women with endometriosis: a systematic review. J Minim Invasive Gynecol 2020; 27(2): 362-72.
18. Nezhat C, Khoyloo F, Tsuei A, Armani E, Page B, Rduch T, et al. The prevalence of endometriosis in patients with unexplained infertility. J Clin Med 2024; 13(2): 444.
19. Robin C, Uk A, Decanter C, Behal H, Collinet P, Rubod C, et al. Impact of endometriosis on oocyte morphology in IVF-ICSI: retrospective study of a cohort of more than 6000 mature oocytes. Reprod Biol Endocrinol 2021; 19: 1-12.
20. Esmaeilzadeh S, Ghorbani M, Abdolahzadeh M, Chehrazi M, Jorsaraei SG, Mirabi P. Stages of endometriosis: Does it affect oocyte quality, embryo development and fertilization rate?. JBRA Assist Reprod 2022; 26(4): 620.

21. Huang J, Lin J, Lu X, Cai R, Song N, Kuang Y. Delayed versus immediate frozen embryo transfer after oocyte retrieval: a systematic review and meta-analysis. J Assist Reprod Genet 2020; 37: 1949-57.
22. Perrone U, Ferrero S, Gazzo I, Izzotti A, Maggiore UL, Gustavino C, et al. Endometrioma surgery: hit with your best shot (but know when to stop). Best Pract Res Clin Obstet Gynaecol 2024; 96: 102528.