



Endometriosis's Effect on Embryo Quality and perinatal outcomes in In-vitro Fertilization as well as Intracytoplasmic Sperm Injection: A Comprehensive Review and Meta-Analysis

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Abstract:

Background: Endometriosis's impact on the results of assisted reproductive technology has been the subject of numerous investigations. Nevertheless, these findings are still hotly contested.

Purpose: To assess how endometriosis affects (in vitro fertilization) IVF and (intracytoplasmic sperm injection) ICSI cycle embryo quality metrics as well as perinatal outcomes.

Methods: PubMed, Embase, Scopus, Cochrane Library, and Web of Science were searched. The specific features and information of the studies that were included were taken out. The random and fixed effects model was used for determining the risk ratio with 95% confidence intervals. High-quality embryo rate, cleavage rate, embryo formation rate, implantation rate, live birth rate, multiple pregnancy, number of oocytes retrieved, placenta prvia, ectopic pregnancy, as well as postpartum hemorrhage had been the principal result metrics.

Results: No discernible differences were found in the rates of high-quality embryos (RR=1.00, 95% CI 0.94–1.06), cleavages (RR=1.00, 95% CI 0.97–1.02), or embryo formation (RR=1.10, 95% CI 0.97–1.24). Substantially fewer retrieved oocytes, fertilization rates were decreased ($p < 0.00001$), and implantation rates were lower ($p = 0.04$) in women with endometriosis. Nonetheless, women with and without endometriosis had similar live birth rates. Endometriosis patients were more likely to experience pregnancy complications, such as placenta previa, multiple pregnancies, ectopic pregnancies, and postpartum hemorrhage. Other obstetric outcomes, like preterm birth and birth weight, did not show any significant differences.

Conclusions: From a morphological standpoint, endometriosis does not affect embryo quality. Women with endometriosis who receive IVF/ICSI do not experience a statistically significant change in the live birth rate. The fertilization rate and the quantity of oocytes recovered, nevertheless, are significantly impacted negatively.

Keywords: Embryo, Endometriosis, IVF/ICSI, Perinatal outcomes.



1. Introduction:

Endometriosis referred to existence of the endometrial glands or stroma on the outside the uterine cavity (Bulun et al., 2019). Infertility and persistent pelvic pain are typified by a localized immune along with an inflammation reaction that had been generated by the endometriotic tissue (Zeng et al., 2022).

Females that had received diagnosis of endometriosis were nearly twice more probable to experience the infertility, as well as endometriosis is frequently discovered in females that had delayed conception (Zondervan et al., 2020). Due to the ability of endometriosis mechanically damages gametes along with disrupts pelvis structures along with embryo transport, lowers oocyte along with embryo quality, reduces ovarian reserve, alters immune and endocrine processes, dysregulates hormonal and cell-mediated processes associated with endometrial receptivity, as well as prevents regular having sex, it was proposed that endometriosis seriously influence the likelihood of natural conceiving (Sanchez et al., 2017; Hodgson et al., 2020).

A lot of people who have endometriosis along with infertility need help to become pregnant. For individuals with endometriosis who are experiencing infertility, assisted reproductive technologies, more especially, in vitro fertilization (IVF/ICSI)—present the most effective method of conception. This method avoids anatomical deformation, tubal function disruption, and abnormalities in the peritoneal surroundings linked to this illness (Surrey, 2015). The existence of endometriosis alone might impact reproductive outcomes in females using assisted reproductive technologies (ART) is a contentious issue. While certain authors determined the detrimental effect of endometriosis (LinXN et al., 2012) other researchers had not (Bongioanni et al., 2011).

The aims of this systematic review and Meta analysis were to assess the way endometriosis impacts IVF/ICSI cycle embryo quality metrics like cleavage rate, high-quality embryo rate, embryo formation rate as well as perinatal outcomes.

2. Methods:

Search strategy

The databases: PubMed, Embase, Scopus, Cochrane Library, Web of Science were examined through 2 separate reviewers by utilizing: MeSH/Emtree Terms for endometriosis: "endometriosis" OR "endometrioma" OR "endometriotic cyst". "Embryo quality" OR "cleavage rate" OR "high-quality embryo" OR "embryo formation" OR "embryogenesis" are keywords for embryo quality. IVF/ICSI keywords: "in vitro fertilization" OR "IVF" OR "intracytoplasmic sperm injection" OR "ICSI". Perinatal outcomes keywords: "live birth rate", OR "pregnancy complications".

Study Choice

Abstracts as well as titles underwent acceptance screening by two separate reviewers, followed by full texts.

Inclusion criteria

Research including females receiving ICSI or IVF treatment
Research where subjects had diagnosis of endometriosis at different stages



Research that recorded outcomes linked with the embryo quality, such as cleavage rate, high-quality embryo rate, and embryo formation rate or perinatal outcomes.

Comparative research involving endometriosis-affected women and a non-endometriosis control group.

Case-control studies, cohort studies, as well as randomized controlled studies (RCTs).

Human research

Research released through December 2023.

English-language publications

Exclusion criteria

Research with no comparative data or a control group.

Research that fails to provide results associated with embryo quality.

In vitro or animal research with no clinical data from humans.

Reviews, editorials, conference abstracts without complete data, case reports, and case series with extremely small sample sizes.

Research where endometriosis-specific data cannot be extracted due to mixed infertility causes.

Publications in languages other than English.

Research released following December 2023

Data extraction

A pre-made form containing research characters, patient demographics, endometriosis stage, embryo quality outcomes, as well as statistical information had been independently retrieved by two observers.

Critical and quality assessment

By employing the proper instruments, such as the Newcastle-Ottawa Scale for Research based on observation, the risk of bias was evaluated.

Data Synthesis and reporting

Review Manager Version 5.4 was used for carrying out the statistical analysis. If relevant data wasn't shown in the original papers, it was abstracted and then calculated based on the corresponding raw data.

Pooled risk ratios (RR) with 95% confidence intervals were computed for embryo quality outcomes through meta-analyses. I^2 evaluated heterogeneity. There was a subgroup analysis based on the stage of endometriosis. A PRISMA flow diagram showed the investigation choice procedure, as well as the review adhered to the PRISMA 2020 guidelines.

3. Results:

Study Characteristics and Selection

Inclusion criteria had been satisfied via twenty-two research for embryo quality metrics as well as seventy studies for perinatal outcomes that were published up until December 2023. These research showed embryo quality consequences in comparison to endometriosis-free groups as controls and involved females undergoing IVF or ICSI with a verified endometriosis identification. Investigations differed regarding embryo quality evaluation techniques, endometriosis stages, as well as sample size.



Research indicated that endometriosis had little consequences for oocyte or embryo aneuploidy rates; in unilateral endometrioma, impacted ovaries had comparable high-quality embryo rates as contralateral ovaries.

Table (1): Meta-Analysis of Embryo Quality Outcomes

Outcome	Number of Studies	Risk Ratio (RR)	95% Confidence Interval	Heterogeneity (I ²)	Interpretation
High-quality embryo rate	18	1.00	0.94 – 1.06	36%	No difference
Cleavage rate	16	1.00	0.97 – 1.02	18%	Comparable
Embryo formation rate	12	1.10	0.97 – 1.24	42%	No significant difference

High-Quality Embryo Rate

Pooled analyses of eighteen researches utilizing data regarding rate of high-quality embryos revealed none discernible variation among women had endometriosis and controls (Risk Ratio [RR] = 1.00, 95% Confidence Interval [CI] 0.94 to 1.06). The variation had been moderate (I² = 36%).

Cleavage Rate

Sixteen researches recorded cleavage rate, with pooled RR = 1.00 (95% CI 0.97 to 1.02), indicating comparable cleavage rates between groups. Low the variation had been was detected (I² = 18%).

Embryo Formation Rate

Data from 12 research assessing embryo formation rates yielded a pooled RR = 1.10 (95% CI 0.97 to 1.24), demonstrating no statistically noteworthy variation. Heterogeneity was moderate (I² = 42%).

Table (2): Subgroup Analysis: Advanced Endometriosis (Stage III/IV)

Outcome	Risk Ratio (RR)	95% Confidence Interval	Interpretation
High-quality embryo rate	1.02	0.94 – 1.10	No significant difference
Cleavage rate	1.00	0.98 – 1.02	No significant difference
Embryo formation rate	1.05	0.97 – 1.14	No significant difference

In eight researches concentrating upon endometriosis that was mild to serious, pooled estimates for comparable outcomes remained non-significant: high-quality embryo rates RR = 1.02 (95% CI 0.94–1.10), cleavage rate RR = 1.00 and embryo formation rate RR = 1.05, all with acceptable heterogeneity

IVF/ICSI cycle results

Substantially lesser oocytes had been extracted from individuals experienced endometriosis. ($p < 0.00001$) with a decreased fertilization frequency. Implantation frequency was also substantially lesser ($p = 0.04$) in individuals experienced endometriosis group.

IVF/ICSI perinatal results after endometriosis

Endometriosis-affected and non-affected females had comparable frequency of live birth. Females with endometriosis had been probably experienced problems during pregnancy:



Placenta previa is most prevalent; multiple pregnancies are most prevalent. High rates of ectopic pregnancy and postpartum hemorrhage. There were no discernible variations in additional reproductive consequences involving birth weight and preterm birth. These results suggested that endometriosis is connected with high obstetric dangers, even though pregnancy success per IVF cycle may be similar.

Table (3): IVF/ICSI Cycle and perinatal results after endometriosis

Outcome	Risk Ratio (RR)/p-value	Significance
Number of oocytes retrieved	Significantly lower (p < 0.00001)	Significant reduction in EMS
Implantation rate	Lower (p = 0.04)	Significant reduction in EMS
Live birth rate	Similar	No significant difference
Multiple pregnancies	Higher in EMS	Increased risk
Placenta previa	Higher in EMS	Increased risk
Ectopic pregnancy	Higher in EMS	Increased risk
Postpartum hemorrhage	Higher in EMS	Increased risk

4. Discussion:

Key findings include:

The current work found none substantially distinct variance in the rates of high-quality embryos (RR=1.00, 95% CI 0.94–1.06), cleavages (RR=1.00, 95% CI 0.97–1.02), or embryo formation (RR=1.10, 95% CI 0.97–1.24).

Embryo quality variables (high-quality embryo rate RR=1.02, cleavage rate RR=1.00, embryo formation rate RR=1.05) were not significantly different from individuals without endometriosis, also in advanced stage III–IV endometriosis. In contrast to the healthy contralateral ovary, unilateral endometrioma did not result in decreased embryo quality (RR=0.99 for high-quality embryos).

Some research suggests that endometriosis may have an effect on implantation as well as live birth rates, possibly because of changes in endometrial receptivity instead of a direct reduction of embryo quality. In general, morphological analysis indicates that endometriosis in and of itself does not impair embryo development parameters. Simón et al., (1994) retrospective study comprised 192 donor oocyte cycles from 78 females had tubal infertility and 59 patients with endometriosis infertility. Receiving oocytes from endometriosis patients resulted in substantially decreased rates of implantation as well as clinical pregnancy. A total of 35 individuals undergoing 89 cycles of IVF treatment were retrospectively examined by Arici et al., (1996). It had been proposed that endometriosis hinders implantation. Women with endometriosis had an implantation rate of 3.9%, while those with tubal factor and unexplained infertility had rates of 7.2% and 8.1%, respectively. One factor contributing to endometriosis-related infertility is inappropriate implantation, which may result from endometrial dysfunction or an embryotoxic environment. According to Geber et al., (1995), women had minimal to mild endometriosis and those with moderate to severe endometriosis had comparable implantation and pregnancy rates. The number of retrieved oocytes as well as the implantation levels is affected, that is probably due to the impacts of inflammation or ovarian reserve. Crucially, females had endometriosis who use artificial conception to conceive are more likely to experience



complications while pregnant, which calls for closer observation throughout pregnancy. Heterogeneity of the research involved, the difference in endometriosis stages, as well as the predominance of retrospective designs are some of the drawbacks. Regardless of receiving higher doses of gonadotropins, Boucret et al., (2020) discovered that patients suffered from endometriosis had considerably fewer oocytes as well as mature oocytes recovered, as well as significantly fewer embryos and high-quality embryos.

Wu et al., (2021) examined how endometriosis affected IVF/ ICSI consequences. Endometriosis has negative consequences regarding the quantity as well as the oocytes state. Also, in contrast with individuals without surgery, patients had endometriosis experienced surgery before receiving IVF/ICSI experiences greater rates of oocyte maturation, fertilization, along with high-quality embryos.

Large research investigations in the future should validate ways for improving IVF/ ICSI results in these individuals and delve deeper into the mechanisms underlying reproductive risks.

5. In conclusion,

endometriosis does not affect the embryo quality. Endometriosis patients who experience IVF/ICSI do not experience a statistically significant change in the live birth rate. The fertilization rate and the quantity of oocytes recovered, nevertheless, are significantly impacted negatively

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