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Oocyte Quality in Women with Endometriosis

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Abstract
Background: Endometriosis is a chronic gynecological condition that affects approximately 10% of women of reproductive age globally. It is associated with significant morbidity due to symptoms such as pelvic pain and infertility. Current knowledge suggests that endometriosis impacts oocyte quality, a critical factor for successful fertilization and pregnancy. Despite extensive research, the exact mechanisms remain unclear, and further updates are necessary to optimize treatment strategies. ***Objectives:*** This review aims to summarize current evidence regarding the impact of endometriosis on oocyte quality and its subsequent effects on fertility outcomes, particularly in the context of in vitro fertilization (IVF). ***Methods:*** A comprehensive search was conducted in PubMed using the terms "endometriosis AND oocyte quality," "endometriosis AND infertility, and "endometriosis AND IVF." The review included studies published up to July 2024. ***Outcome:*** The review findings indicate that endometriosis may be associated with decreased oocyte quality, characterized by impaired morphological features and molecular abnormalities. These defects potentially lead to lower fertilization rates, impaired embryo development, and reduced pregnancy outcomes. However, some studies suggest that with controlled factors such as age and ovarian reserve, IVF outcomes may be comparable to those without endometriosis. ***Conclusions and Outlook:*** For clinicians and scientists working in medically assisted reproduction, understanding the impact of endometriosis on oocyte quality is crucial for improving fertility treatment outcomes. Advances in assisted reproductive technologies and personalized treatment approaches may mitigate these adverse effects. The potential for using artificial intelligence to assess oocyte quality presents a promising avenue for future research, as currently there is no direct and objective measure to assess this parameter.

Introduction

Endometriosis is a chronic gynecological condition characterized by the ectopic presence of endometrial-like tissue, typically in the pelvic cavity but also potentially affecting other abdominal organs. Affecting approximately 10% of women of reproductive age globally, endometriosis is a significant health concern due to its associated symptoms and the scarce existing knowledge regarding treatment options [1]. The primary symptoms include pelvic pain, dysmenorrhea, and dyspareunia,

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which can severely impact a woman's quality of life [1]. In addition to these symptoms, endometriosis is a well-recognized cause of infertility. Studies indicate that 30–50% of women with endometriosis experience infertility, and about 20–50% of infertility patients are diagnosed with endometriosis [2].

The pathophysiology of endometriosis involves a complex interplay of genetic, hormonal, immunological, and environmental factors [3]. Despite extensive research, the exact mechanisms underlying its development and progression remain unclear. Various theories, including retrograde menstruation, genetic predisposition, and immune system dysfunction, have been proposed to explain its etiology [4]. Retrograde menstruation suggests that menstrual blood flows backward through the fallopian tubes into the pelvic cavity, allowing endometrial cells to implant and grow outside the uterus. However, additional factors, such as immune dysfunction, are believed to play a crucial role in the establishment and persistence of ectopic endometrial tissue [4].

Fertility impairment in women with endometriosis is a significant concern, with endometriosis often associated with decreased oocyte quality, which is a critical determinant of successful fertilization, embryo development, and pregnancy outcomes [5]. The ovarian environment in women with endometriosis is frequently altered, leading to compromised oocyte quality [6]. Studies have shown that oocytes from women with endometriosis exhibit impaired morphological features and molecular abnormalities, which may be indicative of lower quality and could be associated with reduced fertility outcomes [5, 6].

However, live-birth rates in women with endometriosis undergoing in vitro fertilization (IVF) have been debated, with some studies indicating reduced rates due to the combined effects of decreased oocyte quality, impaired embryo development, and altered endometrial receptivity [7]. Nonetheless, other studies suggest that when controlled for factors such as age and ovarian reserve, IVF outcomes in women with endometriosis can be comparable to those in women with other infertility diagnoses [8].

Lastly, emerging evidence suggests that endometriosis may not be a single entity but rather a collection of related conditions with different pathophysiological mechanisms and clinical manifestations. This heterogeneity can influence the impact of endometriosis on female fertility, leading to variations in disease severity, response to treatment, and reproductive outcomes [9].

Endometriosis is now understood to be a diverse condition that can appear in different forms and severities, affecting various parts of the pelvic anatomy in unique ways. This means it should not be seen as a single disease but rather one with different types, such as mild peritoneal implants, which are small surface lesions, or invasive endometriomas, which are cysts that can damage healthy ovarian tissue and affect deeper structures [1]. These variations influence symptoms, fertility, and treatment responses differently. Thus, categorizing endometriosis into subtypes is important for better understanding and personalizing treatment approaches. This approach helps explain why some patients with endometriosis may experience severe pain and infertility, while others with similar-looking lesions may have minimal symptoms [10]. Thus, women with deep-infiltrating endometriosis might require different surgical and medical approaches compared to those with superficial peritoneal endometriosis.

Such detailed classification can aid in predicting disease progression and treatment response, thereby optimizing patient care, but also help identify accurate data regarding the pathology. Bibliography regarding endometriosis and oocyte quality is scarce and most relevant papers do not address the abovementioned need to distinguish between different stages and location of endometriosis, even without discussing the complexity of diagnostic itself.

It has been described that endometriosis is a benign gynecological disease historically associated with impaired fertility and reduced IVF outcomes. This presumable effect can be explained due to a diminished ovarian reserve and/or to a lower oocyte quality in patients who suffer this condition [2]. The ovary is the most common location of endometriosis and ovarian reserve is one of the main prognostic factors concerning fertility and is closely related to a woman's age. Currently, the pathophysiological mechanism of decreased ovarian reserve in cases of endometriosis remains diffuse. However, increasing histological, molecular, and morphological evidence demonstrates that endometriomas have a detrimental effect on ovarian function [11].

In patients with endometriosis-related infertility, assisted reproduction techniques (ART) are an appropriate option to achieve a pregnancy. ART treatments can circumvent the inflammatory processes limited to the pelvic cavity, typically present in patients who present this disease [2]. However, intrauterine insemination is not considered effective for addressing the negative impact of endometriosis on tubal function and fertility, and it has been linked to a higher rate of recurrence [8]. IVF has become a key treatment for patients with infertility due to endometriosis. However, its impact on pregnancy rates

and the effectiveness of ART in these patients remain debated [12]. The evidence is mixed; some studies report lower pregnancy rates for women with endometriosis compared to those with other infertility issues, while other studies show no significant differences in live-birth rates between women with and without endometriosis undergoing assisted reproductive treatments [13].

The analysis of reproductive results in women with an endometrioma who had not undergone adnexal surgery suggested a decrease in the ovarian response as a higher cancellation rate and fewer oocytes and embryos were observed [14]. Despite this global effect, it is essential to highlight two issues concerning endometrioma such as its size and bilaterality. Women with unilateral endometriomas undergoing IVF cycles showed that the affected ovary and the healthy one had a similar number of codominant follicles and oocytes [15]. On the other hand, women with bilateral endometriomas had an even lower ovarian response; however, pregnancy rates per transfer might not be affected [16]. Thus, cumulative live-birth rate may be lower due to the poorer ovarian response, demonstrating the quantitative impact of the disease on fertility [16]. These results might be suggestive that endometriosis per se does not impair oocyte competence but impacts reproductive potential in IVF cycles as a lower oocyte yield may be obtained in endometriosic patients. A recent prospective observational cohort study examined the impact of deep-infiltrating endometriosis and endometriomas, diagnosed via transvaginal ultrasound on the cumulative live-birth rate of the first IVF cycle [17]. Despite no observed differences in the number of retrieved mature oocytes, fertilization rate, or quality of embryos between the groups, women with deep-infiltrating endometriosis had a significant lower cumulative live-birth rate.

Furthermore, other clinical studies have reported lower fertilization and pregnancy rates in women with endometriosis undergoing IVF compared to those with other causes of infertility. For instance, Harb et al. [13] conducted a systematic review and meta-analysis, finding that women with stage 3 and 4 endometriosis had lower implantation and pregnancy rates compared to women without the condition, although no differences in live-birth rates were achieved in this study. Current scientific evidence for IVF, egg donation treatments, and transcriptomic analysis of the endometrium indicates that endometrial receptivity is not affected by the presence of the disease or its clinical stage. Therefore, the presumable impaired implantation rates in patients with endometriosis are currently assumed to be due to oocyte and consequent embryo quality and not due to hampered endometrial receptivity [18, 19]. Another potential explanation for the lower reproductive outcomes observed in women with endometriosis is the presence of comorbidities, particularly adenomyosis, which can significantly affect implantation and increase the risk of miscarriage [20]. Adenomyosis involves the growth of endometrial tissue within the muscular wall of the uterus, which can lead to a thickened and enlarged uterus, reduced uterine receptivity, and altered uterine contractions [21]. These changes can impair the ability of an embryo to implant properly and maintain a pregnancy, directly affecting the success rates of ART [20, 21]. Adenomyosis often coexists with endometriosis, yet it is not consistently accounted for in registries related to ART [22]. Thus, it may be challenging to isolate the effects of endometriosis on IVF outcomes. As a result, conclusions drawn from these registries regarding the impact of endometriosis alone on IVF success rates should be approached with caution. It is essential to consider the potential confounding influence of adenomyosis and other related conditions when interpreting these data, as they may have a major contribution to reproductive failure.

Women with endometriosis often show a reduced ovarian response during controlled ovarian stimulation for IVF. This reduced response is characterized by a lower number of retrieved oocytes and a higher cancellation rate of IVF cycles [14]. Studies have reported that women with endometriomas produce fewer oocytes during IVF compared to women with other infertility causes [11]. The presence of endometriomas is believed to adversely affect ovarian function, potentially due to the inflammatory environment and altered follicular milieu [11], compromising ovarian reserve. Different ovarian stimulation protocols have been explored to optimize IVF outcomes in women with endometriosis. A recent review suggests that prolonged GnRH agonist protocols may improve ART outcomes in advanced endometriosis [23]. This could be also explained due to the treatment of undiagnosed adenomyosis meaning that the benefits might not be specific to endometriosis alone. Similarly, while GnRH antagonists are sometimes viewed as less effective for ovarian suppression, clinical experience shows they can still be effective, depending on the patient's condition due to shorter treatment durations and reduced risk of ovarian hyperstimulation syndrome [14]. Additionally, progestin-primed ovarian stimulation protocols have shown promise in improving oocyte and embryo quality in women with endometriosis, presumably due to its anti-inflammatory effects [23, 24].

Other studies have suggested that when controlled for factors such as age and ovarian reserve, the IVF outcomes

in women with endometriosis are comparable to those in women with other infertility diagnoses [8]. This conclusion is supported by the results obtained by González-Comadran [25]. This group used data from the South American IVF registry, which included results from 145 centers of 3.583 endometriosis patients versus 18.833 controls and found no differences in IVF outcomes between the two groups. Another study that analyzed 13.614 IVF cycles found that the impact of endometriosis on live-birth rates may be minimal, particularly when high-quality embryos are transferred [26].

Another systematic review and meta-analysis indicates reduced live-birth rates in this population [27], presumably due to the combined effects of decreased oocyte quality and impaired embryo development, as embryos derived from oocytes of women with endometriosis also tend to exhibit lower quality. A plausible mechanism that would explain the effect of endometriosis in oocyte quality may be explained by an altered ovarian microenvironment in endometriosic patients. Granulosa cells, which surround and nourish the oocyte, are affected by the pro-inflammatory events that occur in endometriosis. Studies have described that endometriosis induces apoptosis, inflammation, oxidative stress, disrupted steroid hormone production, and mitochondrial dysfunction in granulosa cells, leading to decreased oocyte quality [28]. This research highlights elevated levels of inflammatory cytokines and oxidative stress markers, which contribute to follicular atresia and impaired oocyte development, as represented in Figure 1. This dysfunction is believed to be a key factor contributing to the reduced oocyte quality observed in women with endometriosis, as it may impair meiosis, the supply of essential resources for oocyte development and influence ovulation [2].

Historically, oocyte quality can be assessed in vitro by the observation of different dysmorphisms present when denudating the eggs after oocyte pick-up. The presence of specific oocyte dysmorphisms, either extra or intracytoplasmic, has been associated to poor embryonic outcomes [29]. Although some authors have suggested that, these dysmorphisms render poor prognostic value in cellular competence [30]. Literature addressing if endometriosis predisposes to the presence of different structural anomalies in oocytes is scarce as most studies have inferred that this disease predisposes to a worse oocyte quality indirectly, mostly due to a suboptimal embryo development. However, Borges et al. [5] identified increased extra-cytoplasmic defects in oocytes from endometriosis patients. The authors suggest that poorer oocyte quality might be key factors in the reduced implantation rates seen in endometriosis patients. Also, a retrospective study found that endometriosis patients exhibit a higher prevalence of abnormal oocyte morphology, such as dark cytoplasm and fragmented polar bodies [31]. Also, it was reported that severe endometriosis leads to a significant reduction in the rate of morphologically normal oocytes, yet fertilization and subsequent pregnancy outcomes remained unaffected [32]. However, a retrospective study that included more than 2,000 eggs from endometriosis patients reported no significant difference in the average oocyte quality and metaphase II oocyte morphology between endometriosis and control groups [33]. Collectively, these studies underscore that while endometriosis can negatively affect oocyte morphology and quantity, it is unclear whether these dysmorphism have a detrimental impact on reproductive outcomes in IVF cycles.

Some previous works have observed higher rates of embryonic fragmentation, uneven cleavage, and cytoplasmic abnormalities in these embryos [5, 34]. These findings suggest that the negative impact of endometriosis extends beyond the oocyte to affect early embryonic development as well. Interestingly, a study by Ferrero et al. [6] identified significant transcriptomic differences between oocytes from women with endometriosis and those from healthy donors, highlighting molecular alterations that may contribute to poor embryo quality, as shown in Figure 2. These include alterations in mitochondrial function, increased DNA fragmentation, and changes in the expression of genes involved in oxidative stress response and apoptosis. Overall, the pathophysiological mechanisms of endometriosis are complex and multifactorial, involving a combination of genetic, hormonal, and immunological factors that together create an adverse environment for oocyte development. Understanding these mechanisms is crucial for developing targeted interventions to improve oocyte quality and fertility outcomes in women with endometriosis [24].

A systematic review and meta-analysis examined the impact of endometriosis on embryo quality in IVF/ICSI cycles, concluding that endometriosis does not significantly compromise embryo quality from a morphological perspective [35]. According to the authors, women with endometriosis had similar high-quality embryo rates, cleavage rates, and embryo formation rates compared to those without the condition. This consistency was observed across various stages of endometriosis and in cases with unilateral endometrioma. The study suggests that while endometriosis does not appear to affect embryo morphology, it is essential to consider other factors, which may play a significant role in fertility outcomes. Furthermore, the study highlights the need for universal criteria for

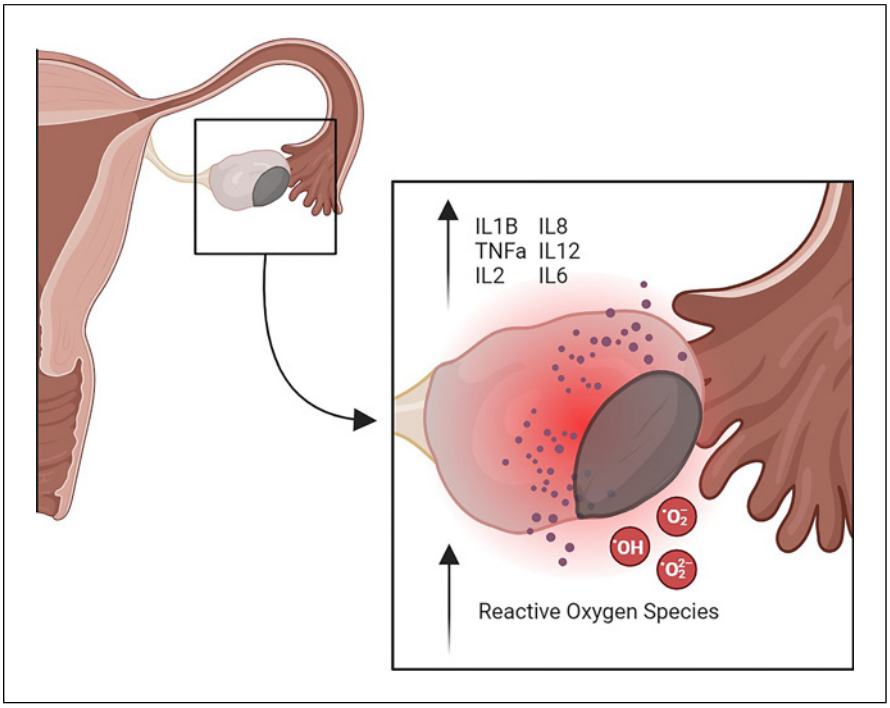

Fig. 1. Pro-inflammatory events in endometriosis. Elevated levels of inflammatory cytokines and oxidative stress markers, which can be found in follicular fluid and alter physiological environment during follicular growth.

embryo grading to ensure consistency across studies, as embryo grading according to morphologic criteria is subject to variability and may be imprecise when comparing results between different laboratories [36]. Nevertheless, embryo quality is also determined by the sperm cell and male factor should be considered when inferring that embryo quality may be an indicator of oocyte competence.

There is a key role for the use in emerging technologies, such as artificial intelligence (AI) softwares, which provide objective and reliable data that can be compared between different centers and users. Using machine learning and deep learning algorithms to assess embryonic morphologic and morphokinetic features will render consistent data regarding this intriguing issue. Interestingly, one study aimed to assess the impact of endometriosis on embryo quality using time-lapse imaging to analyze relative morphokinetics [37]. Data were collected from 168 patients undergoing IVF, with 72 having endometriosis. The study found that embryos from patients with endometriosis exhibited poorer relative kinetics compared to controls, indicating altered embryo development. Specifically, cleavage synchronicity was decreased, suggesting impaired embryonic quality. These findings support the hypothesis that endometriosis negatively affects oocyte quality, contributing to reduced fertility treatment outcomes. Also, these results obtained are in accordance with the ones observed by the group of Brizek et al. [38] nearly 30 years ago. This group studied 235 human embryos and observed nuclear and higher cytoplasmic impairment, cytoplasmic fragmentation, and uneven cleavage in embryos derived from oocytes of females with endometriosis than those derived from patients with other forms of infertility.

A recent study aimed to evaluate the impact of complete endometriosis resection on embryo quality, assessed through morphokinetic parameters using time-lapse imaging and machine learning. The retrospective analysis included 237 embryos from 128 IVF cycles [39]. The study found that embryos from patients with endometriosis without complete resection had significantly lower chances of pregnancy according to the attributed morphokinetic score, compared to those from the control group without endometriosis. In contrast, embryos from patients with complete resection of endometriosis showed a significant improvement in morphokinetic values, comparable to embryos from patients without endometriosis. The authors suggest that complete resection of endometriosis can significantly improve embryo quality, indicating a positive effect of surgical intervention on early embryo development.

Finally, embryo euploidy is considered one of the most important prognostic factors contributing to IVF treatment success [40, 41]. It could be hypothesized that aberrant ovarian microenvironment due to the presence of endometriomas may increase embryo aneuploidy by compromising the meiotic spindle, leading to poor IVF outcomes. However, a study by Juneau et al. [7] demonstrated no difference in aneuploidy rate between

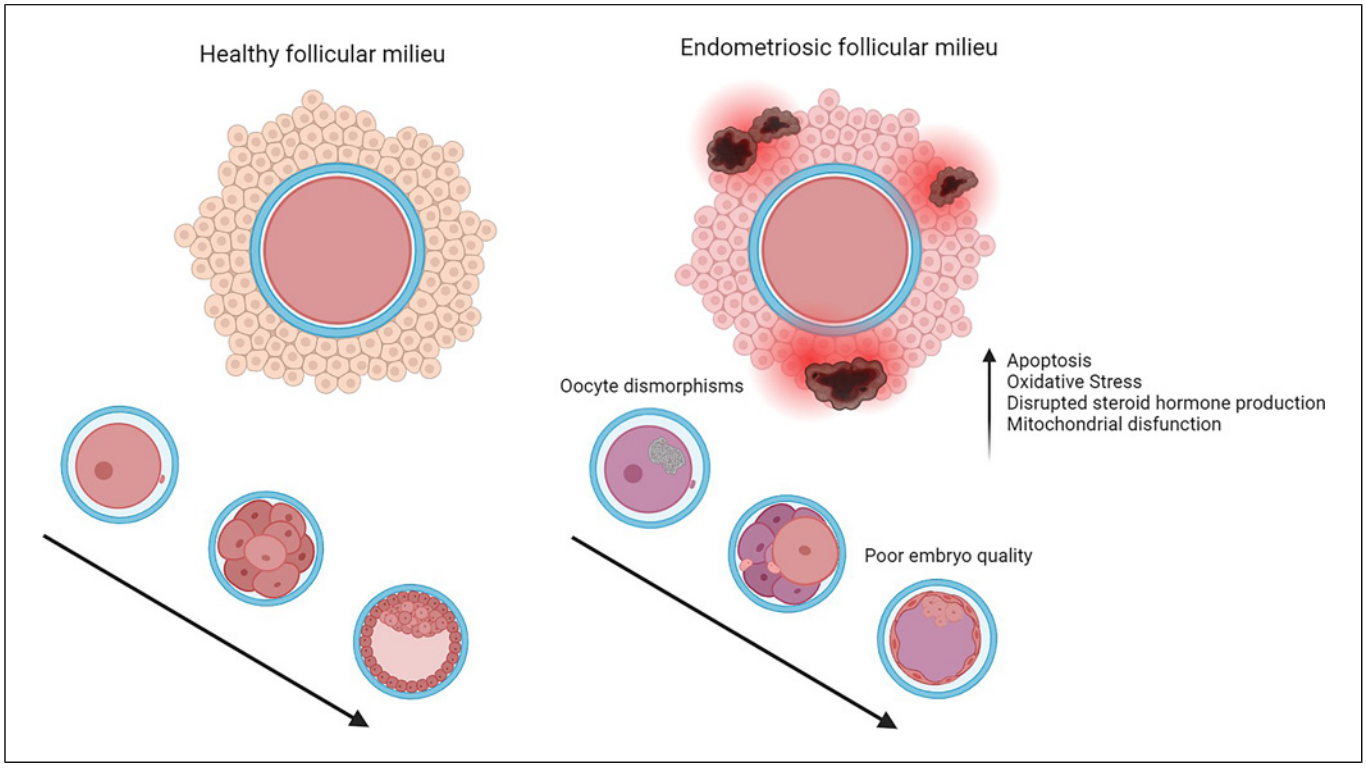

Fig. 2. Endometriosic milieu predisposes to apoptosis, oxidative stress, disrupted steroid hormone production, and mitochondrial dysfunction in granulosa cells. These changes hamper oocyte competence and posterior embryonic development.

endometriosis patients and controls after IVF cycles when adjusting for age. Nevertheless, a recent work that analyzed 308 embryos from endometriosis patients found a statistically significant increase in embryo aneuploidy in this cohort compared to controls [42]. Thus, whether ovarian endometrioma predisposes to an increase in aneuploidy remains yet to be elucidated.

On the other hand, oocyte vitrification is recommended for women with endometriosis, especially those undergoing surgical treatment for endometriomas or those planning to delay childbearing. Early intervention with fertility preservation can help mitigate the adverse effects of endometriosis on ovarian reserve and oocyte quality. Studies by Cobo et al. [43, 44] have demonstrated that egg freezing is an effective strategy for women with endometriosis who wish to delay conception.

Cobo et al.'s [44] studies offer detailed insights into the quantity of oocytes in endometriosis patients undergoing fertility preservation through vitrification. The authors observed that surgical removal of endometriomas significantly impacts ovarian reserve and cumulative live-birth rate per cycle if performed before egg freezing. The group also shows promising oocyte survival rates in endometriosis patients. These data may be read as an indicative of good quality oocytes in this cohort and that the presence of this disease may not predispose to a clinically significant lower oocyte survival rate after egg thawing. The 2021 study further emphasized these findings. It was found that the ovarian response and cumulative live-birth rates were significantly influenced by age and previous ovarian surgery. Women without prior ovarian surgery had better ovarian responses and higher cumulative live-birth rates compared to those with unilateral or bilateral surgery. The study highlighted the importance of performing fertility preservation before surgical interventions in young women with endometriosis to maximize reproductive outcomes [44]. The overall oocyte survival rate remained consistent, indicating that fertility preservation offers a viable option for women with endometriosis to safeguard their fertility, especially before significant impacts from the disease or surgical interventions.

As reviewed, criteria used to assess oocyte quality are indirect and/or offer poor prognosis (e.g., oocyte dysmorphisms, embryo quality, and/or oocyte survival rate). The use of AI in assessing oocyte quality has shown significant advancements [45]. There exist some commercial scoring systems that allow for a more objective and

consistent assessment of oocyte viability and potential, reducing the subjectivity associated with traditional methods of oocyte evaluation. By analyzing high-resolution images of oocytes, softwares can detect subtle morphological features that may not be easily discernible to the human eye, thereby improving the accuracy of quality assessments. For example, the non-invasive Magenta or Violet softwares use a convolutional neural network to analyze 2D images of denuded oocytes, assigning a quality score on a scale of 0–10. These tools standardize the assessment of oocyte viability and potential, thereby improving the selection process for predicting fertilization potential and high-quality blastocyst formation [46, 47]. By utilizing large datasets of oocyte images, AI models like Magenta can detect subtle morphological features indicative of oocyte health and developmental competence, leading to more consistent and reliable outcomes in ART [45]. This technology not only enhances the reliability of oocyte selection for assisted reproductive techniques such as in IVF but also aids in better planning and decision-making for future treatment cycles. The implementation of this technology in clinical practice may shed light on whether endometriosis compromises oocyte quality and competence, as might provide direct evaluation of the morphology and cytoplasmic features of the eggs obtained in IVF cycles of endometriosis patients.

Conclusion

In conclusion, endometriosis might be associated with poorer oocyte quality and lower quantity; however, it is not clear that this disease has a detrimental impact on IVF outcomes. Differences in diagnostic methods, lack of standardization and imprecise description of endometriosis stages may explain the lack of consistency found in the literature regarding this topic. This is in accordance with Ata and Somigliana [9], who argue that endometriosis might not be as big a factor in infertility as traditionally thought. While it can cause problems by creating adhesions that block the fallopian tubes, the exact ways it affects fertility otherwise are still unknown. Oocytes from women with endometriosis have the same potential to develop into healthy embryos as those from women without the condition, which suggests that the impact on egg quality might be overstated. Studies reviewed show that ART outcomes, like fertilization rates, embryo growth, and pregnancy rates, are not significantly worse for women with endometriosis, except when fallopian tube issues are affected. We propose that the detrimental impact of endometriosis on fertility might be overestimated and, provided ovarian reserve is preserved, medically assisted reproduction is an effective treatment from patients who present this pathology. Adenomyosis, which frequently coexists with endometriosis, can impair implantation, affect uterine function, and increase miscarriage rates. Since the effects of adenomyosis are often not separated from those of endometriosis in studies, its influence on ART success may be mistakenly attributed to endometriosis. Finally, new technologies, such as AI might shed light on whether this pathology affects oocyte quality.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

R.T. searched the bibliography included, wrote the manuscript, and elaborated the figures. J.A.G.-V. had the original idea and supervised manuscript elaboration.

References

1 Taylor HS, Kotlyar AM, Flores VA. Endometriosis is a chronic systemic disease: clinical challenges and novel innovations. The Lancet. 2021;397(10276):839–52. https://doi.org/10.1016/S0140-6736(21)00389-5

2 Bonavina G, Taylor HS. Endometriosis-associated infertility: from pathophysiology to tailored treatment. Front Endocrinol. 2022;13:1020827. https://doi.org/10.3389/fendo.2022.1020827

3 de Ziegler D, Borghese B, Chapron C. Endometriosis and infertility: pathophysiology and management. The Lancet. 2010;376(9742):730–8. https://doi.org/10.1016/S0140-6736(10)60490-4

4 Hirsch M, Begum M, Paniz É, Barker C, Davis CJ, Duffy JMN. Diagnosis and management of endometriosis: a systematic review of international and national guidelines. BJOG. 2018;125(5):556–64. https://doi.org/10.1111/1471-0528.14838

5 Borges E Jr, Braga DPAF, Setti AS, Vingris LS, Figueira RCS, Iaconelli A Jr. Endometriosis affects oocyte morphology in intracytoplasmic sperm injection cycles. JBRA Assist Reprod. 2015;19(4)235–40. https://doi.org/10.5935/1518-0557.20150046

6 Ferrero H, Corachán A, Aguilar A, Quiñonero A, Carbajo-García MC, Alamá P, et al. Single-cell RNA sequencing of oocytes from ovarian endometriosis patients reveals a differential transcriptomic profile associated with lower quality. Hum Reprod. 2019;34(7):1302–12. https://doi.org/10.1093/humrep/dez053

7 Juneau CR, Kraus E, Werner M, Franasiak J, Morin S, Patounakis G, et al. Patients with endometriosis have aneuploidy rates equivalent to their age-matched peers in the in vitro fertilization population. Fertil Steril. 2017;108(2):284–8. https://doi.org/10.1016/j.fertnstert.2017.05.038
8 Vigano P, Benaglia L, Busnelli A, Berlanda N, Vercellini P, Somigliana E. Management of endometriosis in the infertile patient. Semin Reprod Med. 2016;35(01):31–7. https://doi.org/10.1055/s-0036-1597125
9 Ata B, Somigliana E. Endometriosis, staging, infertility, and assisted reproductive technology: time for a rethink. Reprod Biomed Online. 2024;49(1):103943. https://doi.org/10.1016/j.rbmo.2024.103943
10 Vercellini P, Viganò P, Somigliana E, Fedele L. Endometriosis: pathogenesis and treatment. Nat Rev Endocrinol. 2014;10(5):261–75. https://doi.org/10.1038/nrendo.2013.255
11 Filippi F, Benaglia L, Paffoni A, Restelli L, Vercellini P, Somigliana E, et al. Ovarian endometriomas and oocyte quality: insights from in vitro fertilization cycles. Fertil Steril. 2014;101(4):988–93.e1. https://doi.org/10.1016/j.fertnstert.2014.01.008
12 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):107. https://doi.org/10.1186/s12958-023-01157-8
13 Harb H, Gallos ID, Chu J, Harb M, Coomarasamy A. The effect of endometriosis on *in vitro* fertilisation outcome: a systematic review and meta-analysis. BJOG. 2013;120(11):1308–20. https://doi.org/10.1111/1471-0528.12366
14 Yang C, Geng Y, Li Y, Chen C, Gao Y. Impact of ovarian endometrioma on ovarian responsiveness and IVF: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(1):9–19. https://doi.org/10.1016/j.rbmo.2015.03.005
15 Esinler I, Bozdag G, Arikan I, Demir B, Yarali H. Endometrioma ≤3 cm in diameter per se does not affect ovarian reserve in intracytoplasmic sperm injection cycles. Gynecol Obstet Invest. 2012;74(4):261–4. https://doi.org/10.1159/000339630
16 Karadağ C, Yoldemir T, Demircan Karadağ S, Turgut A. The effects of endometrioma size and bilaterality on ovarian reserve. J Obstet Gynaecol. 2020;40(4):531–6. https://doi.org/10.1080/01443615.2019.1633518
17 Alson S, Henic E, Jokubkiene L, Sladkevicius P. Endometriosis diagnosed by ultrasound is associated with lower live birth rates in women undergoing their first in vitro fertilization/intracytoplasmic sperm injection treatment. Fertil Steril. 2024;121(5):832–41. https://doi.org/10.1016/j.fertnstert.2024.01.023
18 Miravet-Valenciano J, Ruiz-Alonso M, Gómez E, Garcia-Velasco JA. Endometrial receptivity in eutopic endometrium in patients with endometriosis: it is not affected, and let me show you why. Fertil Steril. 2017;108(1):28–31. https://doi.org/10.1016/j.fertnstert.2017.06.002
19 Garcia-Velasco JA, Fassbender A, Ruiz-Alonso M, Blesa D, D'Hooghe T, Simon C. Is endometrial receptivity transcriptomics affected in women with endometriosis? A pilot study. Reprod Biomed Online. 2015;31(5):647–54. https://doi.org/10.1016/j.rbmo.2015.07.014
20 Horton JM, Sterrenburg M, Lane SIR, Maheshwari A, Li TC, Cheong Y. Reproductive, obstetric, and perinatal outcomes of women with adenomyosis and endometriosis: a systematic review and meta-analysis. Hum Reprod Update. 2019;25(5):592–632. https://doi.org/10.1093/humupd/dmz012
21 Harada T, Khine YM, Kaponis A, Nikellis T, Decavalas G, Taniguchi F. The impact of adenomyosis on women's fertility. Obstet Gynecol Surv. 2016;71(9):557–68. https://doi.org/10.1097/OGX.0000000000000346
22 Chapron C, Vannuccini S, Santulli P, Abrão MS, Carmona F, Fraser IS, et al. Diagnosing adenomyosis: an integrated clinical and imaging approach. Hum Reprod Update. 2020;26(3):392–411. https://doi.org/10.1093/humupd/dmz049
23 Naem A, Krentel H, Moawad G, Naem J, Venezia R, Etrusco A, et al. Hormonal Therapies before in vitro fertilization in women with endometriosis: the Minotaur's Labyrinth and the Ariadne's Thread. Best Pract Res Clin Obstet Gynaecol. 2024;95:102500. https://doi.org/10.1016/j.bpobgyn.2024.102500
24 Corachán A, Pellicer N, Pellicer A, Ferrero H. Novel therapeutic targets to improve IVF outcomes in endometriosis patients: a review and future prospects. Hum Reprod Update. 2021;27(5):923–72. https://doi.org/10.1093/humupd/dmab014
25 González-Comadran M, Schwarze JE, Zegers-Hochschild F, Souza MDCB, Carreras R, Checa MÁ. The impact of endometriosis on the outcome of Assisted Reproductive Technology. Reprod Biol Endocrinol. 2017;15(1):8. https://doi.org/10.1186/s12958-016-0217-2
26 Kamath MS, Subramanian V, Antonisamy B, Sunkara SK. Endometriosis and oocyte quality: an analysis of 13 614 donor oocyte recipient and autologous IVF cycles. Hum Reprod Open. 2022;2022(3):hoac025. https://doi.org/10.1093/hropen/hoac025
27 Hamdan M, Omar SZ, Dunselman G, Cheong Y. Influence of endometriosis on assisted reproductive technology outcomes: a systematic review and meta-analysis. Obstet Gynecol. 2015;125(1):79–88. https://doi.org/10.1097/AOG.0000000000000592
28 Fan W, Yuan Z, Li M, Zhang Y, Nan F. Decreased oocyte quality in patients with endometriosis is closely related to abnormal granulosa cells. Front Endocrinol. 2023;14:1226687. https://doi.org/10.3389/fendo.2023.1226687
29 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;39(1):3–17. https://doi.org/10.1007/s10815-021-02370-3
30 Rienzi L, Vajta G, Ubaldi F. Predictive value of oocyte morphology in human IVF: a systematic review of the literature. Hum Reprod Update. 2011;17(1):34–45. https://doi.org/10.1093/humupd/dmq029
31 Kasapoglu I, Kuspinar G, Saribal S, Turk P, Avcı B, Uncu G. Detrimental effects of endometriosis on oocyte morphology in intracytoplasmic sperm injection cycles: a retrospective cohort study. Gynecol Endocrinol. 2018;34(3):206–11. https://doi.org/10.1080/09513590.2017.1391203
32 Shebl O, Sifferlinger I, Habelsberger A, Oppelt P, Mayer RB, Petek E, et al. Oocyte competence in in vitro fertilization and intracytoplasmic sperm injection patients suffering from endometriosis and its possible association with subsequent treatment outcome: a matched case–control study. Acta Obstet Gynecol Scand. 2017;96(6):736–44. https://doi.org/10.1111/aogs.12941
33 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 6,000 mature oocytes. Reprod Biol Endocrinol. 2021;19(1):160. https://doi.org/10.1186/s12958-021-00798-x
34 Sharma S, Bathwal S, Agarwal N, Chattopadhyay R, Saha I, Chakravarty B. Does presence of adenomyosis affect reproductive outcome in IVF cycles? A retrospective analysis of 973 patients. Reprod Biomed Online. 2019;38(1):13–21. https://doi.org/10.1016/j.rbmo.2018.09.014
35 Dongye H, Ji X, Ma X, Song J, Yan L. The impact of endometriosis on embryo quality in in-vitro fertilization/intracytoplasmic sperm injection: a systematic review and meta-analysis. Front Med. 2021;8:669342. https://doi.org/10.3389/fmed.2021.669342
36 Storr A, Venetis CA, Cooke S, Kilani S, Ledger W. Inter-observer and intra-observer agreement between embryologists during selection of a single Day 5 embryo for transfer: a multicenter study. Hum Reprod. 2017;32(2):307–14. https://doi.org/10.1093/humrep/dew330
37 Freis A, Dietrich JE, Binder M, Holschbach V, Strowitzki T, Germeyer A. Relative morphokinetics assessed by time-lapse imaging are altered in embryos from patients with endometriosis. Reprod Sci. 2018;25(8):1279–85. https://doi.org/10.1177/1933719117741373
38 Brizek CL, Schlaff S, Pellegrini VA, Frank JB, Worrilow KC. Increased incidence of aberrant morphological phenotypes in human embryogenesis an association with endometriosis. J Assist Reprod Genet. 1995;12(2):106–12. https://doi.org/10.1007/BF02211378

39 Herbert SL, Staib C, Wallner T, Löb S, Curtaz C, Schwab M, et al. Morphokinetic analysis of early human embryonic development and its relationship to endometriosis resection: a retrospective time-lapse study using the KIDScore™ D3 and D5 implantation data algorithm. Arch Gynecol Obstet. 2023;308(2):587–97. https://doi.org/10.1007/s00404-023-07008-6
40 Gill P, Ata B, Arnanz A, Cimadomo D, Vaiarelli A, Fatemi HM, et al. Does recurrent implantation failure exist? Prevalence and outcomes of five consecutive euploid blastocyst transfers in 123 987 patients. Hum Reprod. 2024;39(5):974–80. https://doi.org/10.1093/humrep/deae040
41 Tiegs AW, Tao X, Zhan Y, Whitehead C, Kim J, Hanson B, et al. A multicenter, prospective, blinded, nonselection study evaluating the predictive value of an aneuploid diagnosis using a targeted next-generation sequencing–based preimplantation genetic testing for aneuploidy assay and impact of biopsy. Fertil Steril. 2021;115(3):627–37. https://doi.org/10.1016/j.fertnstert.2020.07.052
42 Yan N, Yuan X, Huang S, Jie H, Wang J, Yuan Y. Ovarian endometrioma increases the embryo aneuploid rate: an analysis of 7092 biopsied blastocysts from fertile monogenetic disease carriers. BMC Women's Health. 2023;23(1):244. https://doi.org/10.1186/s12905-023-02406-z
43 Cobo A, Giles J, Paolelli S, Pellicer A, Remohí J, García-Velasco JA. Oocyte vitrification for fertility preservation in women with endometriosis: an observational study. Fertil Steril. 2020;113(4):836–44. https://doi.org/10.1016/j.fertnstert.2019.11.017
44 Cobo A, García-Velasco JA, Remohí J, Pellicer A. Oocyte vitrification for fertility preservation for both medical and nonmedical reasons. Fertil Steril. 2021;115(5):1091–101. https://doi.org/10.1016/j.fertnstert.2021.02.006
45 Hanassab S, Abbara A, Yeung AC, Voliotis M, Tsaneva-Atanasova K, Kelsey TW, et al. The prospect of artificial intelligence to personalize assisted reproductive technology. Npj Digit Med. 2024;7(1):55. https://doi.org/10.1038/s41746-024-01006-x
46 Mercuri N, Fjeldstad J, Krivoi A, Meriano J, Nayot D. A non-invasive, 2-dimensional (2D) image analysis artificial intelligence (AI) tool scores mature oocytes and correlates with the quality of subsequent blastocyst development. Fertil Sterility. 2022;118(4):e78–9. https://doi.org/10.1016/j.fertnstert.2022.08.241
47 Fjeldstad J, Qi W, Mercuri N, Siddique N, Meriano J, Krivoi A, et al. An artificial intelligence tool predicts blastocyst development from static images of fresh mature oocytes. Reprod Biomed Online. 2024;48(6):103842. https://doi.org/10.1016/j.rbmo.2024.103842