



Relationship between endometriosis and infertility

Relación entre endometriosis e infertilidad

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ABSTRACT

Background: Endometriosis is a chronic condition affecting a significant percentage of women of reproductive age. It is associated with various complications, including infertility. This systematic review aims to analyze the relationship between endometriosis and infertility, addressing the underlying pathophysiological mechanisms and the impact of treatments. Material and methods: Searches were conducted in scientific databases, selecting 15 studies that met predefined criteria. Observational studies, systematic reviews, and meta-analyses were included. Data were organized to facilitate the comparison of results. Results: Findings indicate a significant association between endometriosis and infertility, with a probability of infertility ranging from 30 % to 60 % in diagnosed women. Hormonal, inflammatory, and oocyte quality alterations were identified as relevant pathophysiological mechanisms. Surgical treatments showed moderate benefits, though varying by case. Conclusion: Endometriosis is clearly related to infertility, emphasizing the importance of early diagnosis and appropriate management. Further research is needed to deepen the understanding of underlying mechanisms and improve treatment strategies.

Keywords: Endometriosis; infertility; pathophysiological mechanisms; treatment; diagnosis.

RESUMEN

Introducción: La endometriosis es una enfermedad crónica que afecta a un significativo porcentaje de mujeres en edad fértil. Se ha asociado con diversas complicaciones, entre ellas la infertilidad. Esta revisión sistemática busca analizar la relación entre la endometriosis y la infertilidad, abordando los mecanismos fisiopatológicos implicados y el impacto de los tratamientos. Material y métodos: Se realizaron búsquedas en bases de datos científicas, seleccionando 15 estudios que cumplieran con criterios predefinidos. Se incluyeron estudios observacionales, revisiones sistemáticas y metaanálisis. Los datos fueron organizados para facilitar la comparación de resultados. Resultados: Los hallazgos indican una asociación significativa entre endometriosis e infertilidad, con una probabilidad de infertilidad que varía entre el 30 % y el 60 % en mujeres diagnosticadas. Se identificaron alteraciones hormonales, inflamatorias y de la calidad ovocitaria como mecanismos fisiopatológicos relevantes. Los tratamientos quirúrgicos mostraron beneficios moderados, aunque varían según el caso. Conclusión: La endometriosis se relaciona claramente con la infertilidad, destacando la importancia del diagnóstico temprano y el manejo adecuado. Se requieren más investigaciones para profundizar en los mecanismos subyacentes y mejorar las estrategias de tratamiento.

Palabras clave: Endometriosis; infertilidad; mecanismos fisiopatológicos; tratamiento; diagnóstico.

INTRODUCTION

Endometriosis is a common and often underdiagnosed gynecological condition that affects between 10 % and 20 % of women of reproductive age. This disease has been recognized as one of the leading causes of infertility, with estimates indicating that between 30 % and 50 % of women with endometriosis face difficulties conceiving.(1,2,3)

This highlights the complex and controversial relationship between endometriosis and infertility, which represents a growing challenge in reproductive health worldwide, especially in Latin America, where infertility significantly affects the quality of life of women and their families.(4,5,6) Various pathophysiological mechanisms have been proposed to explain how endometriosis may contribute to infertility, including immunological, hormonal, and anatomical alterations.(7,8,9) However, numerous questions remain about this relationship's exact magnitude and nature.(10,11,12)

This condition can compromise egg quality, embryo implantation, and fallopian tube function, but these mechanisms remain the subject of debate and lack consensus in the scientific literature.(13,14) In addition, the effectiveness of available treatments, such as laparoscopic surgery and hormonal interventions, to improve fertility in women with endometriosis has shown inconsistent and contradictory results, underscoring the urgent need for further research to obtain more robust clinical evidence.(15) The present study is motivated by the lack of consensus on the exact mechanisms linking endometriosis to infertility and the need to consolidate current knowledge to improve the diagnosis and treatment strategies for this condition in women of reproductive age. This systematic literature review aims to critically analyze the relationship between endometriosis and infertility, integrating data from recent studies to provide an updated perspective on the underlying mechanisms and possible therapeutic interventions.

The hypothesis guiding this study is that endometriosis negatively impacts fertility through multiple mechanisms that are not yet fully defined. The main objective of the research is to examine and consolidate existing knowledge about this relationship, identifying possible strategies for more effective management of infertility associated with endometriosis.

In addition, this study aims to contribute to the advancement of scientific knowledge, guide more effective clinical practices, and develop public health strategies that improve the quality of life of women affected by this disease.

METHODS

The present study was designed as a systematic literature review to analyze and synthesize the available evidence on the relationship between endometriosis and infertility in women of reproductive age. It focused on collecting, evaluating, and synthesizing relevant studies published in the last ten years.

Specific inclusion and exclusion criteria were carried out in the selection of studies. Articles that examined the relationship between endometriosis and infertility in women of reproductive age were published in Spanish and Portuguese and corresponded to systematic reviews, meta-analyses, or observational studies. Only studies published in the last ten years were considered unless they were deemed essential to the historical context. Articles that did not focus specifically on the relationship between endometriosis and infertility, those that did not meet the established quality criteria, and publications older than ten years were excluded unless they were considered fundamental to the development of the theoretical framework.

The search for articles was conducted in recognized databases such as PubMed, SciELO, and Google Scholar, using a convenience sampling strategy based on the relevance and quality of the studies identified. For data collection, keywords and MeSH terms such as "endometriosis," "infertility," "relationship," "women of reproductive age," "Endometriosis," "Infertility, Female," and "Reproductive Age" were used, combined with Boolean operators such as AND, OR, and NOT, to refine the search and obtain specific results. The review included research published globally without geographical restrictions, provided that it met the previously defined inclusion criteria.

The studies were selected through a systematic and rigorous search process in the databases above. Initially, a total of 235 potentially relevant articles were identified. Of these, 110 were retrieved from PubMed, 75 from SciELO, and 50 from Google Scholar. To refine the results, specific filters were applied, such as language (Spanish and Portuguese), publication date (last ten years), and study type (systematic reviews, meta-analyses, and observational studies). After applying these filters, the number of articles was reduced to 90.

Subsequently, a detailed review of the abstracts was conducted to assess the relevance of

each study regarding the inclusion criteria, which resulted in the exclusion of 45 articles that did not directly address the relationship between endometriosis and infertility. Of the remaining 45 studies, another 20 were excluded because they did not meet the established methodological quality standards, such as clarity in the definition of the study population, transparency in the presentation of results, and consistency in the methodology used.

Finally, a comprehensive review of the texts of the 25 articles that passed the previous stages was conducted, and 10 additional studies were excluded at this stage due to insufficient data or lack of clarity on the direct relationship between endometriosis and infertility. Thus, 15 articles that met all the inclusion and quality criteria were selected, forming the basis for elaborating the results and discussion of this study. This rigorous selection ensures that the articles included provide a representative and well-founded view of the relationship between endometriosis and infertility in women of reproductive age.

Finally, possible biases related to the selection of articles and the variable quality of the studies reviewed are acknowledged. In addition, the limitation to the last ten years and the choice of studies in specific languages may affect the comprehensiveness of the review. However, these limitations were considered and will be discussed in the interpretation of the results to provide a critical assessment and contribute to advancing knowledge on the relationship between endometriosis and infertility in women of reproductive age.

RESULTS

In this review, 15 studies that met the established selection criteria were considered. The articles analyzed include eight observational studies, four systematic reviews, and three meta-analyses. The most relevant findings are presented below, organized into subtopics for easy understanding.

Demographic Characteristics of the Studies Analyzed

The studies covered diverse populations ranging from 20 to 45 years. Most of the research focused on women diagnosed with endometriosis by laparoscopy, a diagnostic method used for those who had difficulty conceiving for more than a year. A summary of the characteristics of these studies is presented in figure 1.

Table 1. Characteristics of the included studies

Study	Population	Age (years)	Main result
Duarte AN, Righi M. (2021)	Women with endometriosis	20-45	Significant association with infertility
Torres JIL da Silva Lima et al. (2021)	Women without diagnosis	25-35	Difficulties in early diagnosis
Goyeneche AP Caicedo et al. (2022)	Infertile women	20-40	Alterations in oocyte quality
Pinargote AD Gómez et al. (2021)	Infertile women	30-45	Endometriosis as the main cause
Ramírez Moran AF et al. (2019)	Women with infertility	28-42	Causal factors of infertility
De Oliveira Campos FA et al. (2021)	Women with endometriosis	25-40	Direct relationship between endometriosis and infertility
Tomás C, Metello JL (2019)	Women with endometriosis	30-45	Benefits of surgery
López Villaverde V. (2023)	Infertile women	22-38	Update on endometriosis
Rodríguez-Purata J et al. (2016)	Women with endometriosis	25-45	Evaluation of the role of surgery
Cango M del C Guamán et al. (2023)	Infertile women	20-35	Analysis of associated infertility
Tenezaca Bermeo KM (2023)	Women with endometriosis	18-40	Causes of infertility
Díaz JA Beltrán (2020)	Infertile women	30-44	Relationship with endometriosis
Magaña MV (2024)	Women with endometriosis	25-40	Selected topics in endocrinology
Guamán Cango M del C (2023)	Women with endometriosis	20-38	Infertility analysis
Pinto LV Reis Costa et al. (2022)	Infertile women	24-42	Relationship and treatment of infertility

Table 2. Relationship between endometriosis and infertility

Study	Association (Yes/No)	Probability of infertility (%)	Notes
Duarte AN, Righi M. (2021)	Yes	30-50%	High prevalence in women with endometriosis
Torres JIL da Silva Lima et al. (2021)	Yes	40-60%	Difficulties in early diagnosis
Goyeneche AP Caicedo et al. (2022)	Yes	35-55	Alterations in oocyte quality
Pinargote AD Gómez et al. (2021)	Yes	30-50	Endometriosis identified as the main cause
Ramírez Moran AF et al. (2019)	Yes	40-60	Multiple factors contribute to infertility
De Oliveira Campos FA et al. (2021)	Yes	30-50	Significant relationship between both conditions
Tomás C, Metello JL (2019)	Yes	35-55	Benefits of surgery in some cases
López Villaverde V. (2023)	Yes	30-50	Update on prevalence
Rodríguez-Purata J et al. (2016)	Yes	30-50	Evaluation of the role of surgery
Cango M del C Guamán et al. (2023)	Yes	30-50	Analysis of associated infertility
Tenezaca Bermeo KM (2023)	Yes	40-60	Common causes of infertility
Díaz JA Beltrán (2020)	Yes	35-55	Direct relationship with endometriosis
Magaña MV (2024)	Yes	30-50	Review of endocrinological aspects
Guamán Cango M del C (2023)	Yes	30-50	Comprehensive literature review
Pinto LV Reis Costa et al. (2022)	Yes	40-60	Treatment and management approach

Effect of Treatments on Fertility

Four studies analyzed explored the impact of surgical and hormonal treatments on improving fertility in women with endometriosis. The results were mixed; some studies, such as those by Rodríguez-Purata et al.(9)and Pinto et al.(15), reported a moderate improvement in pregnancy rates after laparoscopic surgery, while others found no statistically significant differences compared to hormonal treatments. Overall, meta-analyses suggested that surgery may offer modest benefits, although these vary depending on the case.

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Identified Physiopathological Mechanisms

Several studies highlighted the relevance of immunological and hormonal alterations in infertility associated with endometriosis. In six of the studies reviewed, such as those by Cango et al.(10)and López Villaverde (8), elevated levels of inflammatory markers were identified in women with endometriosis, which negatively affects both embryo implantation and oocyte quality. Although the underlying mechanisms are still under debate, it is suggested that immune system dysfunction and oxidative stress play an essential role (figure 3).

Limitations of the included studies

Despite consistent findings on the relationship between endometriosis and infertility, eight studies reported limitations, such as small sample sizes and the lack of adequate control groups, which could influence the generalizability of the results. In addition, differences in the operational definitions of infertility and endometriosis were found between studies, which could have introduced biases in the comparisons.

In conclusion, the results of this systematic review indicate a straightforward but complex relationship between endometriosis and infertility. Treatment effects vary, and further research is needed to consolidate the pathophysiological mechanisms involved.

Table 3. Physiopathological mechanisms identified in infertility associated with endometriosis

Study	Mechanism identified	Observations
Duarte AN, Righi M. (2021)	Hormonal alterations	Affect ovulation and oocyte quality
Torres JIL da Silva Lima et al. (2021)	Chronic inflammation	Relationship with embryo quality
Goyeneche AP Caicedo et al. (2022)	Immune system dysfunction	Altered immune response
Pinargote AD Gómez et al. (2021)	Oxidative stress	Negative impact on embryo implantation
Ramírez Moran AF et al. (2019)	Alterations in the menstrual cycle	Imbalances that affect fertility
De Oliveira Campos FA et al. (2021)	Elevated inflammatory markers	Relationship with embryo quality
Tomás C, Metello JL (2019)	Changes in the ovarian microenvironment	Affect oocyte maturation
López Villaverde V. (2023)	Alterations in angiogenesis	Impact on endometrial vascularization
Rodríguez-Purata J et al. (2016)	Systemic inflammatory response	Relationship with chronic infertility
Cango M del C Guamán et al. (2023)	Altered local immunity	Difficulties in implantation
Tenezaca Bermeo KM (2023)	Changes in cellular communication	Affect synchronization in fertilization
Díaz JA Beltrán (2020)	Alterations in oocyte quality	Relationship with the ovarian cycle
Magaña MV (2024)	Proinflammatory markers	Impact on fertilization
Guamán Cango M del C (2023)	Endocrine dysfunction	Alterations in hormone levels
Pinto LV Reis Costa et al. (2022)	Negative environmental stimuli	Affect overall fertility

DISCUSSION

This systematic review covered 15 studies focused on exploring the relationship between endometriosis and infertility, revealing important advances and areas where significant gaps in knowledge still exist. Of these studies, 12 agreed on establishing a clear association between the two conditions, reinforcing the hypothesis that endometriosis plays a crucial role in women’s reproductive problems. The infertility rates observed range from 30 % to 60 %, which is consistent with previous research and underscores the consensus that endometriosis negatively impacts female fertility. Studies such as that by Duarte et al.(1)support this correlation, documenting a high prevalence of infertility among women with endometriosis. Similarly, research by Torres et al.(2) highlights the challenges associated with early detection of this condition, noting that delays in diagnosis can hinder timely intervention, which negatively influences the chances of conception.

Challenges in Diagnosis and Treatment

The diagnosis of endometriosis remains a considerable challenge. According to several studies, such as that by Torres et al.(2), the disease is often identified late, reducing the possibility of effective intervention in the early stages. Throughout the review, it was observed that differences in the definition of infertility and the diagnostic criteria used in the studies make it difficult to compare them directly, highlighting the urgent need to comply with standardized protocols for endometriosis.

The treatment of endometriosis and its impact on fertility varies considerably across the studies reviewed. For example, Rodríguez-Purata et al.(9)and Pinto et al.(15)reported that laparoscopic surgery can moderately improve pregnancy rates in women with this condition. However, other studies, such as that by Tomás et al.(2), found no significant differences between surgery and hormonal treatments, suggesting that the benefits of surgical intervention may depend on individual patient characteristics, the stage of the disease, and the type of surgery performed. This diversity in results points to the need for additional studies that directly compare the effects of both interventions to identify specific factors that better predict the success of one treatment over another.

Physiopathological Mechanisms and Their Impact on Infertility

An essential aspect of this review is the identification of the pathophysiological mechanisms linking endometriosis to infertility. According to recent studies, such as those by Cango et al.(14)and López Villaverde (8), chronic inflammation and oxidative stress play fundamental roles in reducing fertility. These processes affect ovarian function, decrease oocyte quality, and consequently reduce

the chances of pregnancy. Chronic inflammation, characterized by an imbalance in inflammatory markers, is a hallmark of endometriosis, as detailed by authors such as Pinargote et al.(4) and De Oliveira Campos et al.(6). In addition, changes in the ovarian microenvironment and hormonal alterations were pointed out by Duarte et al.(1), who mention that these imbalances directly impact ovulation, affecting pregnancy rates.

Despite advances in understanding these mechanisms, debate persists regarding their interpretation. While some studies emphasize immune dysfunction and increased inflammatory markers, others suggest that angiogenesis and hormonal alterations may play an even more critical role. What is clear is that the mechanisms involved do not affect all patients in the same way, and factors such as genetics or the severity of the disease could significantly influence how these physiological alterations translate into fertility problems. Research by Tenezaca Bermeo (11) supports this variability, arguing that the pathological processes in endometriosis are not uniform and can manifest in different ways depending on the patient.

Limitations and Future Considerations

Despite consistent findings demonstrating the relationship between endometriosis and infertility, this review has several significant limitations that should be considered. First, several of the studies reviewed had relatively small sample sizes, limiting their results' generalizability. Additionally, the absence of control groups in some studies, such as that by Cango et al.(14), makes it difficult to establish clear causal relationships between endometriosis and reproductive problems. These methodological limitations reinforce the need for larger, better-designed studies with robust control groups and more accurate diagnostic tools.

Another limiting factor is the lack of consensus on the diagnostic criteria used to define both endometriosis and infertility, which makes it difficult to compare results across studies. This lack of uniformity affects the interpretation of the data and introduces potential biases in data collection and analysis. Future research should focus on developing more consistent definitions and diagnostic criteria, allowing for more accurate and rigorous comparisons between studies. Finally, this review highlights the need for further research into the best treatment options for improving fertility in women with endometriosis. While studies on surgical interventions have shown encouraging results, the differences observed suggest that a better understanding of the conditions under which surgery is most effective than hormonal treatments is needed. The most commonly used hormonal therapies include gonadotropin-releasing hormone (GnRH) agonists, which induce a pseudo-menopausal state to reduce endometriosis lesions; combined oral contraceptives, which suppress ovulation and slow disease progression; and progestogens, which help minimize endometrial growth. Future research should focus on larger-scale clinical trials to conclusively evaluate the different therapeutic options and determine the most appropriate based on each patient's specific characteristics.

CONCLUSIONS

In conclusion, this review confirms that endometriosis is closely related to infertility through mechanisms that include hormonal alterations, chronic inflammation, and oxidative stress. Although methodological limitations and differences in diagnostic and therapeutic approaches complicate a complete understanding, the results suggest an urgency for additional studies to address these gaps in knowledge and provide more effective solutions. Future research must focus on developing personalized treatments and improving early diagnostic techniques to optimize reproductive success rates for women suffering from this complex condition.

Personal or professional relationships that could influence the objectivity and validity of the results presented.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest

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