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SYSTEMATIC REVIEW

Relationship between endometriosis and infertility: systematic bibliographic review

Relación entre endometriosis e infertilidad: revisión bibliográfica sistemática

Gabriela Scarcella Santos[1]

[1]Universidad Abierta Ingteramericana, Facultad de Medicina y Ciencias de la Salud Carrera de Medicina. Buenos Aires, Argentina.

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Corresponding Author: Gabriela Scarcella Santos

ABSTRACT

Introduction: 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.
Method: 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.
Conclusions: 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.
Método: se realizaron búsquedas en bases de datos científicas, seleccionando 15 estudios que cumplían 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.
Conclusiones: 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.

METHOD

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.

Estudio	Población	Edad (años)	Resultado principal
Duarte AN, Righi M. (2021)	Mujeres com endometriosis	20-45	Asociación significativa con infertilidad
Torres JIL da Silva Lima et al. (2021)	Mujeres sin diagnóstico	25-35	Dificultades en el diagnóstico temprano
Goyeneche AP Caicedo et al. (2022)	Mujeres infértiles	20-40	Alteraciones en calidad ovocitaria
Pinargote AD Gómez et al. (2021)	Mujeres infértiles	30-45	Endometriosis como causa principal
Ramirez Moran AF et al. (2019)	Mujeres com infertilidad	28-42	Factores causales de infertilidade

De Oliveira Campos FA et al. (2021)	Mujeres com endometriosis	25-40	Relación directa entre endometriosis e infertilidade
Tomás C, Metello JL (2019)	Mujeres com endometriosis	30-45	Beneficios de la cirugía
López Villaverde V. (2023)	Mujeres infértiles	22-38	Actualización sobre endometriosis
Rodríguez-Purata J et al. (2016)	Mujeres com endometriosis	25-45	Evaluación del papel de la cirugía
Cango M del C Guamán et al. (2023)	Mujeres infértiles	20-35	Análisis de la infertilidad associada
Tenezaca Bermeo KM (2023)	Mujeres com endometriosis	18-40	Causas de infertilidade
Díaz JA Beltrán (2020)	Mujeres infértiles	30-44	Relación con endometriosis
Magaña MV (2024)	Mujeres com endometriosis	25-40	Tópicos selectos en endocrinología
Guamán Cango M del C (2023)	Mujeres con endometriosis	20-38	Análisis de infertilidad
Pinto LV Reis Costa et al. (2022)	Mujeres infértiles	24-42	Relación y tratamiento de infertilidad

Figure 1. Characteristics of the included studies

Estudio	Asociación (Sí/No)	Probabilidad de infertilidade (%)	Notas
Duarte AN, Righi M. (2021)	Sí	30-50%	Alta prevalencia en mujeres con endometriosis
Torres JIL da Silva Lima et al. (2021)	Sí	40-60%	Dificultades en diagnóstico temprano
Goyeneche AP Caicedo et al. (2022)	Sí	35-55	Alteraciones en la calidad ovocitaria
Pinargote AD Gómez et al. (2021)	Sí	30-50	Endometriosis identificada como causa principal
Ramirez Moran AF et al. (2019)	Sí	40-60	Factores múltiples contribuyen a la infertilidad
De Oliveira Campos FA et al. (2021)	Sí	30-50	Relación significativa entre ambas condiciones
Tomás C, Metello JL (2019)	Sí	35-55	Beneficios de la cirugía en algunos casos

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López Villaverde V. (2023)	Sí	30-50	Actualización sobre la prevalencia
Rodríguez-Purata J et al. (2016)	Sí	30-50	Evaluación del papel de la cirugía
Cango M del C Guamán et al. (2023)	Sí	30-50	Análisis de la infertilidad asociada
Tenezaca Bermeo KM (2023)	Sí	40-60	Causas comunes de infertilidad
Díaz JA Beltrán (2020)	Sí	35-55	Relación directa con endometriosis
Magaña MV (2024)	Sí	30-50	Revisión sobre aspectos endocrinológicos
Guamán Cango M del C (2023)	Sí	30-50	Revisión bibliográfica exhaustiva
Pinto LV Reis Costa et al. (2022)	Sí	40-60	Enfoque en tratamiento y manejo

Figure 2. Relationship between endometriosis and infertility

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 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).

Gómez et al. (2021)		la implantación embrionaria
Ramirez Moran AF et al. (2019)	Alteraciones en el ciclo menstrual	Desbalance s que afectan la fertilidad
De Oliveira Campos FA et al. (2021)	Marcadores inflamatorios elevados	Relación con la calidad del embrión
Tomás C, Metello JL (2019)	Cambios en el microambiente ovárico	Afectanla maduración ovocitaria
López Villaverde V. (2023)	Alteraciones en la angiogénesis	Impacto en la vascularización del endometrio
Rodríguez-Purata J et al. (2016)	Respuesta inflamatoria sistémica	Relación con la infertilidad crónica
Cango M de C Guamán	Inmunidad local alterada	Dificultades en la implantación

Estudio	Mecanismo identificado	Observaciones
Duarte AN, Righi M. (2021)	Alteraciones hormonales	Afectan la ovulación y la calidad ovocitaria

Torres JIL da Silva Lima et al. (2021)	Inflamación crónica	Relación con la calidad del embrión
Goyenechе AP Caicedo et al. (2022)	Disfunción del sistema inmune	Respuesta inmune alterada
Pinargote AD et al. (2023)	Estrés oxidativo	Impacto negativo en
Tenezaca Bermeo KM (2023)	Cambios en la comunicación celular	Afectan la sincronización en la fecundación
Díaz JA Beltrán (2020)	Alteraciones en la calidad ovocitaria	Relación con el ciclo ovárico
Magaña MV (2024)	Marcadores proinflamatorios	Impacto en la fecundación
Guamán Cango M del C (2023)	Disfunción endocrina	Alteraciones en los niveles hormonales
Pinto LV Reis Costa et al. (2022)	Estímulos ambientales negativos	Afectan la fertilidad global

Figure 3. Physiopathological mechanisms identified in infertility associated with endometriosis

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.

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.

BIBLIOGRAPHIC REFERENCES

1. Duarte AN, Righi M. Associação entre endometriose e infertilidade feminina: uma revisão de literatura. Acta Elit Salutis. 2021;4(1).

2. Torres JIL da Silva Lima, Santos JF, Pereira MCS, et al. Endometriose, dificuldades no diagnóstico precoce e a infertilidade feminina: uma revisão. Research, Society and Development. 2021;10(6).

3. Goyeneche APC, Cárdenas AL, Fernández MG, et al. Endometriosis e infertilidad: aspectos básicos para el abordaje inicial. Arch Ginecol Obstet. 2022;60(1):19–36.

4. Pinargote AD Gómez, et al Recimundo. Endometriosis como causa de infertilidad. Recimundo. 2021;5(3):230–8.

5. Ramírez Morán AF, Rodríguez JF, Sánchez G, et al. Factores causales de infertilidad. Rev Inform Cient. 2019;98(2):283–93.

6. De Oliveira Campos FA, Silva RA, Lima CR, et al. A relação entre endometriose e infertilidade: uma revisão de literatura. Braz J Health Rev. 2021;4(6):24379–90.

7. Tomás C, Metello JL. Endometriosis and infertility – where are we? Acta Obstet Ginecol Port. 2019;13(4):235–41.

8. López Villaverde V. Endometriosis e infertilidad: una puesta al día. Rev Iberoam Fertil Reprod Hum. 2023:57–94.

9. Rodríguez-Purata J, González-Robayna I, Casillas-Rivero L, et al. ¿Cuál es el verdadero papel de la cirugía en la infertilidad asociada con endometriosis? Ginecol Obstet Mex. 2016;84(1).

10. Guamán Cango MC, Rodríguez PM, López GP, et al. Infertilidad asociada a endometriosis: revisión bibliográfica. Salud ConCiencia. 2023;2(2).

11. Tenezaca Bermeo KM. Endometriosis como causa de infertilidad: revisión bibliográfica. 2023.

12. Díaz JA Beltrán. Endometriosis: una causa de la infertilidad femenina. Rev Neuronum. 2020;6(2):238–40.

13. Magaña MV. Endometriosis e infertilidad. In: Tópicos selectos en endocrinología reproductiva. 2024:289.

14. Guamán Cango MC. Infertilidad asociada a endometriosis: revisión bibliográfica. 2023.

15. Pinto LV Reis Costa, Almeida SM, Ferreira LG, et al. Endometriose e infertilidade: relação e tratamento. Braz J Health Rev. 2022;5(2):5889–98.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORSHIP CONTRIBUTION

Conceptualization: Gabriela Scarcella Santos.
Data curation: Gabriela Scarcella Santos.
Formal analysis: Gabriela Scarcella Santos.
Research: Gabriela Scarcella Santos.
Methodology: Gabriela Scarcella Santos.
Project management: Gabriela Scarcella Santos.
Resources: Gabriela Scarcella Santos.
Software: Gabriela Scarcella Santos.
Supervision: Gabriela Scarcella Santos.
Validation: Gabriela Scarcella Santos.
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