International Journal of **Health Science**

ENDOMETRIOSIS: RECENT DIAGNOSTIC STRATEGIES

Ryan Rafael Barros de Macedo
Medical student at Centro Universitário do Planalto Central Apparecido dos Santos (UNICEPLAC)

Nicoly Peres Lacerda
Medical student at the Federal University of Mato Grosso (UFMT)

Dalila Ribeiro Maia Gomes
Bachelor - Medicine at the State University of Piauí (UESPI)

Maria Luiza Pereira de Oliveira
Student - Medicine at Centro Universitário do Norte de Minas (UNINORTE)

Rafael Machado de Souza
Student - Medicine at Castelo Branco University (UCB)

Vinicius Coimbra Lima
Bachelor - Medicine at the University Center of Maranhão (UNICEUMA)
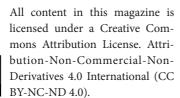
Richardson Oliveira Silva
Bachelor - Medicine at Athens College (UniAtenas)

Carlos Ademar Dias Arruda Filho
Student - Medicine at Christus University (UNICHRISTUS)

Antonio Alcides Janja Melo
Student - Medicine at Christus University (UNICHRISTUS)

Tiê Barbosa Arruda
Student - Medicine at Christus University
(UNICHRISTUS)

Tales Gemaque Matos
Student - Medicine at Centro Universitário
da Amazônia (UNIESAMAZ)

Thiago Andrade Vieira
Bachelor - Medicine - Nova Esperança
Medical School (FAMENE)

Abstract: Endometriosis is a chronic gynaecological disease characterized by the presence of endometrial tissue outside the uterine cavity, mainly affecting the ovaries and peritoneum. Its prevalence is 6% to 10% among women of reproductive age and it is one of the main causes of pelvic pain and infertility. Diagnosis is challenging, often leading to a delay of up to 10 years. Laparoscopy remains the gold standard, although methods such as ultrasound and MRI are also used to detect deep lesions. New approaches, such as the analysis of peritoneal microbiota and epigenetic biomarkers, show potential for less invasive and more accurate diagnoses. In addition, the application of technologies such as artificial intelligence and nanotechnology can speed up diagnosis and improve treatment. However, more clinical validation is needed to integrate these innovations into clinical practice.

Keywords: Endometriosis; Early diagnosis; Laparoscopy; Epigenetic biomarkers; Artificial intelligence.

INTRODUCTION

Endometriosis is a chronic gynaecological condition characterized by the presence of endometrial tissue outside the uterine cavity, predominantly affecting the peritoneum, ovaries and rectovaginal septum. Its prevalence is estimated at between 6% and 10% of women of reproductive age, and it is one of the main causes of chronic pelvic pain and female infertility. (PAŠALIĆ; TAMBUWALA; HROMIĆ-JAHJEFENDIĆ, 2023) The pathogenesis of endometriosis is still not fully understood, but different theories attempt to explain its origin and development, including retrograde menstruation, coelomic metaplasia and, more recently, the genetic-epigenetic (GE) theory. (AMRO et al., 2022; KONINCKX et al., 2021)

For decades, the prevailing hypothesis was that viable eutopic endometrial cells, transported via retrograde menstruation, implan-

ted themselves in the peritoneum and formed endometriotic lesions. However, this theory does not fully explain the heterogeneity of the disease, especially in cases of extrapelvic endometriosis. The GE theory proposes that endometriosis results from a sequence of cumulative epigenetic alterations that affect pluripotent cells, giving them endometrial characteristics even in ectopic locations. This model suggests that the risk of the disease is higher in genetically predisposed women and that its progression depends on the interaction between epigenetic and environmental factors, such as oxidative stress and the peritoneal microbiota (AMRO et al., 2022; KONINCKX et al., 2021).

The pathophysiology of endometriosis involves complex processes such as angiogenesis, neuroinflammation and immunological alterations. Endometriotic lesions show resistance to progesterone and overexpression of aromatase, which favors local estrogen synthesis and perpetuates the inflammatory process. The resulting chronic inflammation contributes to pelvic pain, which can occur even in the absence of large lesions, due to sensitization of peripheral nerve fibres and distant neuroinflammation (KONINCKX et al., 2021).

The diagnosis of endometriosis remains a challenge, as the variability in clinical presentation can lead to a significant delay in the recognition of the disease caused partly by the normalization of debilitating menstrual pain and patients' reluctance to seek medical attention, and partly due to gynaecologists' reliance on diagnostic methods that do not adequately address all patients' concerns. Studies indicate an average interval of up to 10 years between the onset of symptoms and definitive diagnosis, often carried out using laparoscopy, which is considered the gold standard for detecting the disease. However, transvaginal ultrasound and magnetic resonance imaging have been increasingly used to identify deep lesions, al-though their predictive values vary according to the location and size of the lesions (AMRO et al., 2022; KONINCKX et al., 2021;).

Given the etiopathogenic complexity of endometriosis and the associated diagnostic difficulties, it is essential to improve strategies for early detection of the disease. Recent advances suggest that assessing the peritoneal microbiota and analyzing epigenetic biomarkers could become promising tools for a less invasive and more accurate diagnosis. In addition, understanding the role of oxidative stress in the genesis of endometriosis may open up new therapeutic perspectives in both the prevention and treatment of the disease (AMRO et al., 2022; KONINCKX et al., 2021; PAŠALIĆ; TAMBUWALA; HROMIĆ-JAHJEFENDIĆ, 2023).

METHODOLOGY

This study consists of a literature review with the aim of summarizing the latest information on diagnostic strategies for endometriosis. To this end, a systematic search was carried out in the PubMed database, including articles published in the last five years. The descriptors used were "Endometriosis" and "Diagnosis", following the terminology standardized by the Medical Subject Headings (MeSH). The selection of studies was conducted in a rigorous manner, with the aim of guaranteeing the relevance and timeliness of the scientific evidence used in the composition of the article.

The inclusion criteria adopted were: articles published between 2019 and 2024, available in full and written in English or Portuguese, which directly addressed advances in diagnostic methods for endometriosis, including imaging techniques, biological markers and clinical approaches. Priority was given to original studies, narrative reviews and meta-analyses that contributed to understanding emerging diagnostic strategies and their application in clinical practice.

Articles that did not meet the previously established inclusion criteria were excluded from the analysis, including studies not available on PubMed, publications in languages other than English or Portuguese, as well as articles that predominantly addressed the treatment of endometriosis without detailed exploration of diagnostic methods. Case studies and expert opinions without robust empirical evidence were also excluded.

The articles were selected in three stages. Initially, titles and abstracts were analyzed for preliminary screening. Next, the full texts were assessed to check that they met the established criteria. Finally, the selected articles were critically analyzed to ensure the quality and relevance of the information included in the review. This method made it possible to build a comprehensive and up-to-date overview of diagnostic strategies for endometriosis, ensuring transparency and reproducibility of the study.

RESULTS AND DISCUSSION

Endometriosis is a complex condition whose diagnosis presents significant challenges, mainly due to the variability of its clinical manifestations and the heterogeneity of the lesions. Superficial pelvic endometriosis requires laparoscopic confirmation, while cystic-ovarian endometriosis can be detected using ultrasound or magnetic resonance imaging. Transvaginal ultrasound - although historically it has proven to be an effective method for detecting deep invasive endometriosis, with high sensitivity (up to 98%) and specificity (close to 100%), indicating that it is a reliable diagnostic tool for assessing patients with suspected endometriosis, aiding in early diagnosis and treatment planning for patients - also has its limitations relating to technique and technology (XIANG; WANG; ZHOU; WANG; YANG, 2022).

When it comes to deep lesions, for example, the accuracy of imaging tests becomes controversial, especially for smaller lesions. Studies indicate that although diagnostic tests have a sensitivity and specificity of over 95%, their positive and negative predictive values can drop dramatically in low-prevalence populations, making careful interpretation of the results essential (AMRO et al., 2022).

Imaging technologies have made significant progress in recent years. Advanced ultrasound, with 3D mapping capabilities and blood flow analysis, has enabled more detailed visualization of endometriotic lesions. Magnetic resonance imaging (MRI) has also evolved, incorporating specific sequences that improve the detection of deep foci of the disease (GRIFFITHS et al., 2024).

Recent literature highlights that specialized transvaginal ultrasound (eTVUS) remains highly specific for deep endometriosis and endometriomas, although its sensitivity for superficial lesions is still limited. The introduction of features such as elastography, Doppler and contrast with rectal water has increased its accuracy. In addition, the use of artificial intelligence integrated into imaging shows promising potential in improving diagnostic detection (AVERY et al., 2024a).

In the field of magnetic resonance imaging, significant progress has been made with the adoption of specific sequences such as SWI, T2 and DWI, which improve the identification of deep foci of the disease. eMRI is especially useful in patients who cannot tolerate transvaginal examination, with a sensitivity of between 91% and 93.5% and specificity of between 86% and 87.5%, the ability to visualize the pelvis in a panoramic view and greater standardization between operators (AVERY et al., 2024b).

However, the accuracy of imaging tests is greater in referral centers, where the prevalence of deep endometriosis is higher, and the effectiveness of these tests in detecting nodules

smaller than 1 cm remains uncertain, which limits their applicability as the sole criterion for indicating laparoscopy. Imaging, although useful for surgical planning and preoperative counseling, does not significantly alter the surgical approach, and laparoscopy is still the gold standard for definitive diagnosis. Bayesian statistical evaluation reinforces that the added value of imaging in indicating surgical intervention is marginal, reinforcing the need for careful clinical judgment in decision-making. (AMRO et al., 2022)

The classification of endometriosis remains a challenge in clinical practice, since the current systems do not adequately take into account the diversity and complexity of the disease. The widely used rASRM classification has significant limitations, as it was developed before subtle lesions and deep endometriosis were recognized. In addition, the proposed categories do not adequately reflect the severity and clinical impact of the disease. Studies show that, in most cases, stages I and II of the AFS classification correspond predominantly to superficial lesions, while stages III and IV refer to ovarian cystic endometriosis. The proposal for a separate score for deep endometriosis, as in the #ENZIAN score, suggests progress, but still lacks validation to demonstrate a clinically useful predictive value (KONINCKX et al., 2021).

Given the variability of the clinical presentation and the limitations of existing classifications, there is a growing consensus that the severity of deep endometriosis should be assessed considering the volume and extent of the lesions. Reports in the literature indicate that volumetric measurement of the lesions at the end of excision may provide a more reliable criterion for assessing severity, since tissue retraction tends to make the lesions more spherical. This approach can contribute to a more precise stratification of cases and the definition of individualized therapeutic strategies (KONINCKX et al., 2021).

The search for non-invasive diagnostic methods for endometriosis has intensified in recent decades, especially given the limitations of the surgical approach as the gold standard. Recent studies indicate that serum and urinary biomarkers may represent promising tools for both early diagnosis and therapeutic monitoring of the disease. Among the most investigated biomarkers are inflammatory cytokines, angiogenic factors, acute phase proteins and microRNAs, which are associated with the inflammatory and immunoendocrine pathophysiology of endometriosis. In addition, emerging technologies such as proteomics, genomics and miRNA microarrays offer new perspectives for identifying disease-specific molecular signatures, although the clinical translation of these findings still depends on greater methodological standardization and large-scale validation (ANASTASIU et al., 2020).

Recently, the use of circulating microRNAs (miRNAs) as non-invasive biomarkers has been highlighted. A systematic review identified 141 differentially expressed miRNAs, particularly miR-17-5p, miR-451a and let-7b-5p. Despite the variability between studies, miRNAs show potential as a complementary diagnostic tool to imaging and laparoscopy (VANHIE et al., 2024).

In summary, the diagnosis of endometriosis continues to evolve, but still faces substantial challenges. The need for laparoscopic confirmation for most cases, the limitations of imaging for smaller lesions and the lack of effective biomarkers reinforce the importance of a multidisciplinary approach. In addition, the reformulation of classification criteria may be essential to improve the clinical management of the disease, enabling a more accurate diagnosis and a more effective therapeutic approach.

CONCLUSION

The diagnosis of endometriosis remains one of the biggest challenges in modern gynecology. Although laparoscopy is still considered the gold standard, new approaches are emerging, offering less invasive alternatives with great potential to improve early detection of the disease. Advanced imaging techniques, combined with epigenetic testing and analysis of the peritoneal microbiota, have shown promising results. In addition, innovations such as DNA methylation profiles and exosome transcriptomics offer high sensitivity for identifying the disease at early stages, which could revolutionize the way endometriosis is diagnosed.

Another significant advance is the use of nanotechnology and artificial intelligence in the analysis of imaging exams, technologies that can not only improve diagnostic accuracy, but also anticipate the diagnosis of endometriosis by up to five years compared to traditional methods. The growing understanding of the role of mesenchymal stem cells and immune modulation as early indicators and potential therapeutic targets is also contributing to developments in the management of the disease.

Analysis of the reproductive tract microbiota, meanwhile, has shown promise, with patterns of dysbiosis associated with endometriosis opening up possibilities for non--invasive and more accessible screening tests. However, while these advances are exciting, they need to undergo wider clinical validation before being incorporated into everyday practice.

In addition, traditional classification systems, such as rASRM, have proved insufficient to capture the complexity and diversity of endometriosis. More recent proposals, such as the #ENZIAN score, have emerged as promising alternatives, but require further clinical validation to ensure their practical applicability.

It is therefore essential to adopt a multimodal, interdisciplinary and personalized approach to the diagnosis and management of endometriosis. Integrating these technological innovations with careful clinical assessment can speed up diagnosis and, at the same time, provide more effective management and a better quality of life for affected women. With the gradual implementation of these new tools, the future of endometriosis treatment looks more optimistic, with significant advances in early detection and personalization of care.

REFERENCES

AMRO, B. et al. New Understanding of Diagnosis, Treatment and Prevention of Endometriosis. *International Journal of Environmental Research and Public Health*, v. 19, n. 11, p. 6725, 31 maio 2022.

ANASTASIU, C. V. et al. Biomarkers for the noninvasive diagnosis of endometriosis: state of the art and future perspectives. *International Journal of Molecular Sciences*, v. 21, n. 5, p. 1750, 2020. DOI: 10.3390/ijms21051750.

AVERY, J. C. et al. Noninvasive diagnostic imaging for endometriosis part 1: a systematic review of recent developments in ultrasound, combination imaging, and artificial intelligence. *Fertility and Sterility*, v. 121, n. 2, p. 164–188, 2024a. DOI: 10.1016/j. fertnstert.2023.12.008.

AVERY, J. C. et al. Noninvasive diagnostic imaging for endometriosis part 2: a systematic review of recent developments in magnetic resonance imaging, nuclear medicine and computed tomography. *Fertility and Sterility*, v. 121, n. 2, p. 189–211, 2024b. DOI: 10.1016/j.fertnstert.2023.12.017.

FU, Q.; FU, L. Engineering nanosystems for regulating reproductive health in women. *Theranostics*, 2025. https://pmc.ncbi.nlm.nih.gov/articles/PMC11671389/.

GRIFFITHS, M. J. et al. Endometriosis: recent advances that could accelerate diagnosis and improve care. *Trends in Molecular Medicine*, v. 30, n. 9, p. 875-889, 2024.

KONINCKX, P. R. et al. Pathogenesis Based Diagnosis and Treatment of Endometriosis. *Frontiers in Endocrinology*, v. 12, p. 745548, 2021. DOI: https://doi.org/10.3389/fendo.2021.745548.

LI, M. et al. Unveiling DNA methylation: early diagnosis, risk assessment, and therapy for endometrial cancer. *Frontiers in Oncology*, 2025. Disponível em: https://pmc.ncbi.nlm.nih.gov/articles/PMC11788147/.

PAŠALIĆ, E.; TAMBUWALA, M. M.; HROMIĆ-JAHJEFENDIĆ, A. Endometriosis: Classification, pathophysiology, and treatment options. *Pathology - Research and Practice*, v. 251, p. 154847, nov. 2023. DOI: https://doi.org/10.1016/j.prp.2023.154847.

VANHIE, Arne et al. Circulating microRNAs as Non-Invasive Biomarkers in Endometriosis Diagnosis—A Systematic Review. *Biomedicines*, v. 12, n. 4, p. 888, 2024. DOI: https://doi.org/10.3390/biomedicines12040888.

XIANG, Yuanhua; WANG, Gang; ZHOU, Lingjuan; WANG, Qin; YANG, Qinjie. A systematic review and meta-analysis on transvaginal ultrasonography in the diagnosis of deep invasive endometriosis. *Annals of Palliative Medicine*, v. 11, n. 1, p. 281-290, jan. 2022. DOI: http://dx.doi.org/10.21037/apm-21-3761.

YOU, W. et al. Stem cell theory: A new horizon for the treatment of endometriosis by targeting mesenchymal stem cell. *International Journal of Gynecology & Obstetrics*, 2025. https://obgyn.onlinelibrary.wiley.com/doi/abs/10.1002/ijgo.70046.

ZHENG, Q. et al. Reproductive tract microbiome dysbiosis associated with gynecological diseases. *Frontiers in Cellular and Infection Microbiology*, 2025.