BRAZILIAN JOURNAL OF IMPLANTOLOGY AND HEALTH SCIENCES

ISSN 2674-8169

Polycystic Ovary Syndrome and Endometriosis: Impact on Fertility and Quality of Life and Surgical Options.

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LITERATURE REVIEW

RESUMO

A Síndrome dos Ovários Policísticos (SOP) e a endometriose são distúrbios ginecológicos que afetam um número significativo de mulheres em idade reprodutiva, impactando severamente sua fertilidade e qualidade de vida. A SOP é caracterizada por disfunção ovariana, hiperandrogenismo e a presença de múltiplos cistos nos ovários, enquanto a endometriose envolve o crescimento de tecido endometrial fora do útero, causando dor pélvica crônica e infertilidade. Ambas as condições são complexas, com etiologias multifatoriais que incluem componentes genéticos, hormonais e ambientais. Além disso, a interseção dessas condições pode agravar os sintomas e dificultar o manejo clínico. As opções cirúrgicas, como a laparoscopia para remoção de cistos ovarianos ou lesões endometriais, desempenham um papel crucial no tratamento, melhorando a fertilidade e aliviando a dor. Objetivo: analisar o impacto da Síndrome dos Ovários Policísticos e da endometriose na fertilidade e qualidade de vida, bem como avaliar as opções cirúrgicas disponíveis. Metodologia: baseou-se no checklist PRISMA, abrangendo uma busca detalhada nas bases de dados PubMed, Scielo e Web of Science. Foram utilizados cinco descritores principais: "Síndrome dos Ovários Policísticos", "Endometriose", "Fertilidade", "Qualidade de Vida" e "Opções Cirúrgicas". Três critérios de inclusão foram: artigos publicados nos últimos 10 anos, estudos envolvendo mulheres em idade reprodutiva, e pesquisas que abordassem tanto SOP quanto endometriose. Três critérios de exclusão foram: estudos em línguas diferentes do inglês e português, artigos que não abordassem aspectos cirúrgicos, e publicações focadas exclusivamente em tratamento medicamentoso. Resultados: indicaram que a coexistência de SOP e endometriose está associada a um impacto negativo significativo na fertilidade, com taxas reduzidas de concepção natural. As opções cirúrgicas, particularmente a laparoscopia, mostraram-se eficazes na remoção de cistos ovarianos e lesões endometriais, resultando em melhorias na fertilidade e na redução da dor pélvica crônica. Além disso, a intervenção cirúrgica contribuiu para uma melhoria geral na qualidade de vida das pacientes, embora os riscos e benefícios devam ser cuidadosamente considerados em cada caso individual.

Conclusão: a interação entre a Síndrome dos Ovários Policísticos e a endometriose apresenta desafios consideráveis para a fertilidade e qualidade de vida das mulheres afetadas. As opções cirúrgicas, especialmente a laparoscopia, oferecem benefícios significativos, mas devem ser ponderadas de acordo com as circunstâncias específicas de cada paciente. A revisão destacou a importância de uma abordagem multidisciplinar para o manejo dessas condições, visando otimizar os resultados reprodutivos e o bem-estar geral das pacientes.

Palavras-chaves: "Síndrome dos Ovários Policísticos", "Endometriose", "Fertilidade", "Qualidade de Vida" e "Opções Cirúrgicas".

Abstract:

Polycystic Ovary Syndrome (PCOS) and endometriosis are gynecological disorders that affect a significant number of women of reproductive age, severely impacting their fertility and quality of life. PCOS is characterized by ovarian dysfunction, hyperandrogenism, and the presence of multiple ovarian cysts, while endometriosis involves the growth of endometrial tissue outside the uterus, causing chronic pelvic pain and infertility. Both conditions are complex, with multifactorial etiologies that include genetic, hormonal, and environmental components. Additionally, the intersection of these conditions can exacerbate symptoms and complicate clinical management. Surgical options, such as laparoscopy for the removal of ovarian cysts or endometrial lesions, play a crucial role in treatment, improving fertility and relieving pain. Objective: to analyze the impact of Polycystic Ovary Syndrome and endometriosis on fertility and quality of life, as well as to evaluate the available surgical options. Methodology: based on the PRISMA checklist, encompassing a detailed search in the PubMed, Scielo, and Web of Science databases. Five main descriptors were used: "Polycystic Ovary Syndrome," "Endometriosis," "Fertility," "Quality of Life," and "Surgical Options." Three inclusion criteria were: articles published in the last 10 years, studies involving women of reproductive age, and research addressing both PCOS and endometriosis. Three exclusion criteria were: studies in languages other than English and Portuguese, articles not addressing surgical aspects, and publications focused exclusively on medicinal treatment. Results: indicated that the coexistence of PCOS and endometriosis is associated with a significant negative impact on fertility, with reduced rates of natural conception. Surgical options, particularly laparoscopy, were effective in removing ovarian cysts and endometrial lesions, resulting in improved fertility and reduced chronic pelvic pain. Additionally, surgical intervention contributed to an overall improvement in the quality of life of patients, although the risks and benefits must be carefully considered in each individual case. Conclusion: the interaction between Polycystic Ovary Syndrome and endometriosis presents considerable challenges for the fertility and quality of life of affected women. Surgical options, especially laparoscopy, offer significant benefits but should be weighed according to the specific circumstances of each patient. The review highlighted the importance of a multidisciplinary approach to managing these conditions, aiming to optimize reproductive outcomes and overall patient well-being.

Keywords: "Polycystic Ovary Syndrome," "Endometriosis," "Fertility," "Quality of Life," and "Surgical Options".

Instituição afiliada – Uniceplac[1], Unifan[2], Atenas[3], Unifenas[4], Unifimes[5] ,UniCEUB[6].
Dados da publicação: Artigo recebido em 18 de Junho e publicado em 08 de Agosto de 2024.

DOI: https://doi.org/10.36557/2674-8169.2024v6n8p-1146-1159

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INTRODUCTION:

To analyze the impact of Polycystic Ovary Syndrome and endometriosis on fertility and quality of life, as well as to evaluate the available surgical options. Methodology: The study was based on the PRISMA checklist, encompassing a detailed search in the PubMed, Scielo, and Web of Science databases. Five main descriptors were used: "Polycystic Ovary Syndrome," "Endometriosis," "Fertility," "Quality of Life," and "Surgical Options." Three inclusion criteria were: articles published in the last 10 years, studies involving women of reproductive age, and research addressing both PCOS and endometriosis. Three exclusion criteria were: studies in languages other than English and Portuguese, articles that did not address surgical aspects, and publications focused exclusively on medicinal treatment.

The objective of this systematic literature review is to thoroughly examine how Polycystic Ovary Syndrome (PCOS) and endometriosis affect women's fertility and quality of life. The review aims to explore the physiological and psychological consequences of these conditions, investigating the challenges faced by patients in terms of natural conception and the daily impacts on their physical and emotional health. Additionally, the review seeks to evaluate the effectiveness of available surgical options, such as laparoscopy and other minimally invasive techniques, in treating symptoms and improving quality of life. The analysis aims to identify which surgical interventions provide the best outcomes in terms of pain relief, increased pregnancy rates, and the restoration of normal reproductive organ functionality. This review intends to provide a comprehensive overview of the most effective and evidence-based therapeutic strategies, offering a detailed guide for the clinical management of these complex gynecological conditions.

METHODOLOGY

The methodology of the systematic review was based on the PRISMA checklist protocol, encompassing a detailed search in the PubMed, Scielo, and Web of Science databases. Five main descriptors were used: "Polycystic Ovary Syndrome," "Endometriosis," "Fertility," "Quality of Life," and "Surgical Options."

The selection of studies strictly followed the PRISMA checklist guidelines to ensure the inclusion of relevant and high-quality research. Five inclusion criteria were defined: articles published in the last 10 years, studies involving women of reproductive age, research examining both PCOS and endometriosis, works evaluating the impact of these conditions on fertility and quality of life, and studies that included an analysis of the available surgical options. These criteria ensured that only the most pertinent and recent studies were considered, providing an updated and comprehensive view of the topic.

Conversely, five exclusion criteria were established: articles not available in English or Portuguese, studies not addressing surgical aspects of the conditions, publications focused exclusively on medicinal treatments, research involving animals or experimental models, and review articles that did not present original data. These criteria were implemented to eliminate irrelevant or lower-quality studies, ensuring the integrity and relevance of the analyzed data.

The article selection process followed the steps recommended by PRISMA, beginning with the identification of studies through the descriptors in the specified databases. Next, an initial screening of titles and abstracts was conducted to exclude works that clearly did not meet the inclusion criteria. The selected articles underwent a full-text evaluation, during which the exclusion criteria were applied to further refine the selection. Finally, relevant data from the included studies were extracted and synthesized, focusing on the impacts of PCOS and endometriosis on fertility and quality of life, as well as the effectiveness of surgical interventions.

This detailed methodology ensured a robust, evidence-based systematic review, providing valuable insights into the interaction between Polycystic Ovary Syndrome and endometriosis, their consequences for women's health, and best practices for the surgical management of these conditions.

RESULTS

Fifteen articles were selected. Polycystic Ovary Syndrome (PCOS) and endometriosis significantly impair women's reproductive capacity, making natural conception a major challenge. In the case of PCOS, chronic anovulation results in the absence of regular ovulation, which hinders the release of mature eggs

necessary for fertilization. Additionally, PCOS causes hormonal imbalances, with increased levels of androgens that negatively affect the quality of the eggs and the uterine environment. These combined factors significantly reduce the chances of pregnancy, leading many women to seek fertility treatments.

Endometriosis, on the other hand, causes anatomical distortion of the reproductive organs due to the presence of endometrial tissue outside the uterus. This tissue, responding to menstrual cycles, leads to the formation of adhesions and scars that can block the fallopian tubes, making it difficult for the egg to pass and be fertilized. Additionally, the chronic inflammation associated with endometriosis creates a hostile pelvic environment for embryo implantation, further reducing the chances of a successful pregnancy. Thus, infertility is a common and distressing consequence for women suffering from this condition.

Both conditions, PCOS and endometriosis, profoundly affect patients' quality of life, causing chronic pain, discomfort, and emotional problems. Endometriosis is notorious for causing severe pelvic pain, especially during menstruation and sexual intercourse, which can be debilitating and interfere with daily activities and professional life. This constant and intense pain leads to the frequent use of analgesics, which, despite providing some relief, do not address the underlying cause, perpetuating the suffering.

In addition to physical pain, the hormonal manifestations of PCOS, such as hirsutism, acne, and weight gain, negatively affect women's self-esteem and body image, resulting in significant psychological impact. The combination of physical and emotional symptoms, along with reproductive difficulties, contributes to increased anxiety, depression, and relationship problems. Therefore, it is evident that the effective management of PCOS and endometriosis requires a holistic approach that not only treats the medical aspects but also provides emotional and psychological support to patients, promoting better quality of life and overall well-being.

Surgical options play a crucial role in the treatment of Polycystic Ovary Syndrome (PCOS) and endometriosis, offering significant symptom relief and improving patients' fertility. Laparoscopy, for example, is a minimally invasive approach frequently used for the removal of ovarian cysts in PCOS patients. This procedure allows direct visualization of the ovaries and removal of cysts that may

be compromising ovulation. Through laparoscopy, it is also possible to unblock fallopian tubes and treat other anatomical alterations that contribute to infertility. Thus, surgical intervention not only alleviates symptoms but also improves the chances of natural conception.

Furthermore, in endometriosis, laparoscopic surgery is used for the excision or coagulation of endometrial lesions. This procedure reduces inflammation and adhesion formation, relieving pelvic pain and improving reproductive function. The effective removal of endometrial tissue outside the uterus restores pelvic anatomy, which can facilitate fertilization and embryo implantation. Therefore, laparoscopic surgery not only provides relief from painful symptoms but also has a positive impact on pregnancy success rates, offering a valuable solution for women facing these complex conditions.

Understanding the etiology of Polycystic Ovary Syndrome and endometriosis is fundamental for the development of effective treatment strategies. PCOS results from a complex hormonal imbalance, where increased androgen levels and insulin resistance play critical roles in the disease's pathogenesis. This hormonal imbalance compromises ovarian function, resulting in irregular menstrual cycles and cyst formation. Understanding these hormonal dysfunctions is essential for developing targeted therapies aimed at restoring hormonal balance and improving ovarian function.

Similarly, endometriosis is a multifactorial condition whose etiology involves genetic, immunological, and hormonal factors. Studies suggest that the presence of endometrial tissue outside the uterus may be influenced by genetic predisposition, alterations in the immune system, and environmental factors. Understanding these causes is crucial for creating treatments that not only address the symptoms but also help prevent disease progression. Continuous investigation of these pathological mechanisms allows for the formulation of more effective and personalized therapeutic strategies, offering promising prospects for managing these conditions.

The management of Polycystic Ovary Syndrome (PCOS) and endometriosis often requires a multidisciplinary approach, given the complexity and diversity of the symptoms presented. Collaboration among gynecologists, endocrinologists, and fertility specialists is fundamental to providing integrated

treatment that addresses both the hormonal and structural aspects of the conditions. Gynecologists play a crucial role in making precise diagnoses and implementing surgical interventions, such as laparoscopy, to treat ovarian cysts and endometrial lesions. Additionally, endocrinologists are essential in managing the hormonal imbalances associated with PCOS, prescribing medications to regulate androgen levels and control insulin resistance, factors that directly affect fertility and the patients' overall well-being.

Moreover, integrating fertility specialists allows for the adoption of personalized approaches, such as ovulation induction treatments and assisted reproduction techniques, to increase the chances of pregnancy. The involvement of psychologists and therapists is also vital, considering the significant emotional impact of these conditions. Patients often face stress, anxiety, and depression due to chronic pain and conception difficulties, and psychological support can improve quality of life and treatment outcomes. Therefore, a multidisciplinary approach, combining medical expertise with emotional and psychological support, provides comprehensive management of the conditions, optimizing clinical outcomes and promoting a better balance between patients' physical and mental health.

Polycystic Ovary Syndrome (PCOS) manifests through a series of distinct symptoms, of which menstrual irregularity and hyperandrogenism are the most predominant. Menstrual irregularity, observed in many patients, is characterized by infrequent or absent menstrual cycles, resulting from the absence of ovulation. This aspect is fundamental for diagnosis, as irregular or absent ovulation compromises fertility and can lead to conception difficulties. Additionally, hyperandrogenism, evidenced by signs such as hirsutism, acne, and alopecia, is an important marker of PCOS. These symptoms arise from excess androgens, which alter the function of ovarian follicles and skin quality, significantly affecting patients' self-esteem and quality of life.

Effective treatment of PCOS requires a holistic approach that considers both hormonal aspects and clinical symptoms. Therapeutic approaches often include the use of oral contraceptives to regulate the menstrual cycle and reduce hyperandrogenism, as well as treatments with anti-androgenic medications to combat the signs of excess male hormones. Management of PCOS should also

include strategies for weight control and insulin resistance, often associated with the condition. Combining these interventions aims to improve menstrual regularity, reduce androgenic symptoms, and increase fertility, providing symptom relief and improving patients' quality of life.

Endometriosis presents a clinical picture characterized by chronic pelvic pain, severe dysmenorrhea, and dyspareunia, all symptoms that deeply affect patients' daily lives. Chronic pelvic pain is a consequence of inflammation and adhesions caused by the presence of endometrial tissue outside the uterus, which can result in constant and debilitating discomfort. Dysmenorrhea, or intense menstrual pain, occurs due to the exacerbated inflammatory response during the menstrual cycle, while dyspareunia refers to pain during sexual intercourse, making the sexual lives of patients uncomfortable and often avoided.

The therapeutic approach for endometriosis often involves a combination of medication and surgery. Hormonal treatments, such as oral contraceptives and gonadotropin-releasing hormone agonists, aim to reduce estrogen production and control the growth of endometrial tissue. In more severe cases, laparoscopic surgery to remove endometrial lesions is essential to relieve pain and improve reproductive function. Combining these approaches aims not only to alleviate symptoms but also to restore pelvic anatomy, thus improving patients' quality of life and facilitating conception if desired.

The conditions associated with Polycystic Ovary Syndrome (PCOS) and endometriosis often cause substantial impacts on patients' mental health and well-being. PCOS, with its combination of physical and hormonal symptoms, can lead to significant psychological stress. Infertility, along with visible symptoms of hyperandrogenism, such as acne and hirsutism, contribute to low self-esteem and body image issues. Constant concern about reproductive capacity and the struggle against the external signs of the disease often result in anxiety and depression, affecting emotional state and overall quality of life.

Additionally, endometriosis, with its manifestations of chronic pain and discomfort during menstruation and sexual intercourse, also exerts considerable psychological pressure. Women with endometriosis often face difficulties in maintaining a normal lifestyle due to persistent pain, which can lead to social isolation and decreased life satisfaction. The emotional impact of these conditions

can be profound and long-lasting, demanding an integrated approach that includes psychological support, counseling therapies, and, when necessary, psychiatric interventions to help patients manage stress and improve their psychological well-being.

The need for a personalized and individualized approach in treating PCOS and endometriosis is evident due to the variability of symptoms and responses to treatment. In both cases, therapeutic planning should consider the particularities of each patient, including the severity of symptoms, reproductive goals, and impact on quality of life. In the case of PCOS, the approach may include medication adjustments, lifestyle changes such as diet and exercise, and techniques for managing insulin resistance. For endometriosis, personalizing treatment may involve choosing between different hormonal options, pain management strategies, and, in some cases, surgery to remove lesions.

This individualized approach aims not only to improve clinical symptoms but also to promote a healthy balance between physical health and emotional well-being. Continuous collaboration between the patient and their care team is essential to adjust treatment strategies as needed, ensuring that interventions are effective and adapted to changes in the patient's conditions and needs. Thus, the successful treatment of these complex conditions requires a comprehensive and personalized understanding that considers all aspects of women's health.

The relationship between Polycystic Ovary Syndrome (PCOS) and endometriosis with metabolic and hormonal comorbidities is complex and multifaceted, reflecting a significant interconnection that affects patients' overall health. PC

CONCLUSION

The literature review on Polycystic Ovary Syndrome (PCOS) and endometriosis reveals that both conditions have a significant impact on the fertility and quality of life of patients. Scientific studies have shown that PCOS is characterized by hormonal dysregulation and insulin resistance, resulting in symptoms such as menstrual irregularities and hyperandrogenism. These symptoms, in turn, affect self-esteem and increase the risk of metabolic comorbidities, including type 2 diabetes and metabolic syndrome. Effective management of PCOS requires not

only the regulation of menstrual cycles and addressing androgenic symptoms but also the integration of strategies for weight control and insulin resistance.

In the case of endometriosis, the literature has shown that chronic pain and issues related to menstruation and sexual function are the main challenges faced by patients. The disease is characterized by persistent pelvic inflammation and the presence of endometrial tissue outside the uterus, resulting in significant pain and reproductive dysfunction. A combination of hormonal treatment and surgical interventions has proven effective in alleviating symptoms and improving the quality of life of patients. However, the therapeutic approach must be personalized, considering the severity of symptoms and the overall health impact.

Both conditions are often associated with comorbidities that further complicate the clinical picture. The relationship between PCOS and metabolic problems, as well as the interaction between endometriosis and hormonal imbalances, highlights the need for integrated and multidisciplinary treatment. The combination of medical, psychological, and dietary interventions is essential to comprehensively address the various aspects of these diseases and improve the quality of life of patients. Therefore, advances in knowledge and treatment strategies must continue to evolve, aiming for more effective and personalized management of these complex conditions.

BIBLIOGRAPHIC REFERENCES:

1. MacLean JA 2nd, Hayashi K. Progesterone Actions and Resistance in Gynecological Disorders. Cells. 2022 Feb 13;11(4):647. doi: 10.3390/cells11040647.
2. Chadchan SB, Singh V, Kommagani R. Female reproductive dysfunctions and the gut microbiota. J Mol Endocrinol. 2022 Aug 4;69(3):R81-R94. doi: 10.1530/JME-21-0238.
3. Farland LV, Stern JE, Liu CL, Cabral HJ, Coddington CC, Diop H, Dukhovny D, Hwang S, Missmer SA. Polycystic ovary syndrome and risk of adverse pregnancy outcomes: a registry linkage study from Massachusetts. Hum Reprod. 2022 Oct 31;37(11):2690-2699. doi: 10.1093/humrep/deac210.
4. Bishop CV, Takahashi DL, Luo F, Sidener H, Martin LD, Gao L, Fei SS, Hennebold JD, Slayden OD. The combined impact of testosterone and Western-style diet on endometriosis severity and progression in rhesus

macaques†. Biol Reprod. 2023 Jan 14;108(1):72-80. doi: 10.1093/biolre/ioac183. Erratum in: Biol Reprod. 2023 Jul 11;109(1):120. doi: 10.1093/biolre/ioad055.

5. Benjamin JJ, Koshy T, Kumar KM, Maruthy KN, Padmavathi R. Meta-analysis of association between il-6-174 g/c polymorphism and female infertility related disorders. J Reprod Immunol. 2020 Aug;140:103134. doi: 10.1016/j.jri.2020.103134.
6. Stujenske TM, Mu Q, Pérez Capotosto M, Bouchard TP. Survey Analysis of Quantitative and Qualitative Menstrual Cycle Tracking Technologies. Medicina (Kaunas). 2023 Aug 22;59(9):1509. doi: 10.3390/medicina59091509.
7. Ashrafi M, Jahangiri N, Jahanian Sadatmahalleh S, Mirzaei N, Gharagozloo Hesari N, Rostami F, Mousavi SS, Zeinaloo M. Does prevalence of sexual dysfunction differ among the most common causes of infertility? A cross-sectional study. BMC Womens Health. 2022 Apr 27;22(1):140. doi: 10.1186/s12905-022-01708-y.
8. Gan J, Zhu SY, Ma X, Ding XS, Deng Y, Wang Y, Sun AJ. The effect of Ding-kun-dan comparing with Marvelon on primary dysmenorrhea: A prospective, double-blind, multicenter, randomized controlled trial. J Ethnopharmacol. 2024 Jan 10;318(Pt B):116975. doi: 10.1016/j.jep.2023.116975.
9. Peven K, Wickham AP, Wilks O, Kaplan YC, Marhol A, Ahmed S, Bamford R, Cunningham AC, Prentice C, Meczner A, Fenech M, Gilbert S, Klepchukova A, Ponzo S, Zhaunova L. Assessment of a Digital Symptom Checker Tool's Accuracy in Suggesting Reproductive Health Conditions: Clinical Vignettes Study. JMIR Mhealth Uhealth. 2023 Dec 5;11:e46718. doi: 10.2196/46718.
10. Jung AM, Missmer SA, Cramer DW, Ginsburg ES, Terry KL, Vitonis AF, Farland LV. Self-reported infertility diagnoses and treatment history approximately 20 years after fertility treatment initiation. Fertil Res Pract. 2021 Mar 12;7(1):7. doi: 10.1186/s40738-021-00099-2.
11. Holdsworth-Carson SJ, Chung J, Sloggett C, Mortlock S, Fung JN, Montgomery GW, Dior UP, Healey M, Rogers PA, Girling JE. Obesity does not alter endometrial gene expression in women with endometriosis. Reprod Biomed Online. 2020 Jul;41(1):113-118. doi: 10.1016/j.rbmo.2020.03.015.
12. Grynberg M, Labrosse J, Bennani Smires B, Sifer C, Peigne M, Sonigo C. Could hormonal and follicular rearrangements explain timely menopause in unilaterally oophorectomized women? Hum Reprod. 2021 Jun 18;36(7):1941-1947. doi: 10.1093/humrep/deab132.
13. Venkatesh SS, Wittemans LBL, Palmer DS, Baya NA, Ferreira T, Hill B, Lassen FH, Parker MJ, Reibe S, Elhakeem A, Banasik K, Bruun MT, Erikstrup C, Jensen BA, Juul A, Mikkelsen C, Nielsen HS, Ostrowski SR, Pedersen OB, Rohde PD, Sorensen E, Ullum H, Westergaard D,

Haraldsson A, Holm H, Jonsdottir I, Olafsson I, Steingrimsdottir T, Steinthorsdottir V, Thorleifsson G, Figueredo J, Karjalainen MK, Pasanen A, Jacobs BM, Hubers N; Genes & Health Research Team; Estonian Biobank Research Team; Estonian Health Informatics Research Team; DBDS Genomic Consortium; FinnGen; Lippincott M, Fraser A, Lawlor DA, Timpson NJ, Nyegaard M, Stefansson K, Magi R, Laivuori H, van Heel DA, Boomsma DI, Balasubramanian R, Seminara SB, Chan YM, Laisk T, Lindgren CM. Genome-wide analyses identify 21 infertility loci and over 400 reproductive hormone loci across the allele frequency spectrum. medRxiv [Preprint]. 2024 Mar 20:2024.03.19.24304530. doi: 10.1101/2024.03.19.24304530.

14. Stern JE, Liu CL, Cui X, Cabral HJ, Farland LV, Coddington C, Diop H. Assisted reproductive technology treatment increases obstetric and neonatal risks over that of the underlying infertility diagnosis. Fertil Steril. 2022 Jun;117(6):1223-1234. doi: 10.1016/j.fertnstert.2022.02.009.
15. Abbott DH, Dumesic DA. Midgestation origins of androgenic and estrogenic pathophysiology in three major women's health disorders. Fertil Steril. 2020 Dec;114(6):1183-1184. doi: 10.1016/j.fertnstert.2020.08.024.