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# The Dynamic Relationship Between the Ovaries and Endometrium and Its Connection to Ovarian Cancer

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## ABSTRACT

The menstrual cycle is a complex process involving a dynamic interaction between the ovaries and the endometrium, essential for egg maturation and the preparation of the uterine lining for implantation. Disruptions in this interaction, as seen in Polycystic Ovary Syndrome (PCOS), can increase the risk of ovarian cancer, where hormonal imbalances and insulin resistance lead to endometrial dysfunction. Furthermore, factors such as psychological stress and infections can also disrupt the menstrual cycle and trigger systemic inflammation associated with an increased risk of ovarian cancer. Understanding these dynamics is crucial for reproductive health and the prevention of ovarian cancer.

***Keywords:*** Menstrual Cycle, Ovary, Endometrium, Ovarian Cancer, PCOS.

## INTRODUCTION

The menstrual cycle is a complex physiological process involving coordinated interactions between the hypothalamus, pituitary gland, ovaries, and uterus. This process is divided into two main components, namely the ovarian cycle and the endometrial cycle. The ovarian cycle consists of the follicular and luteal phases, which regulate oocyte maturation and reproductive hormone production. Meanwhile, the endometrial cycle consists of the proliferative, secretory, and menstrual phases, which prepare the endometrial lining for implantation (Martínez-Sánchez et al., 2025).

Disruptions in menstrual cycle regulation, such as those found in polycystic ovary syndrome (PCOS), can have a significant impact on women's reproductive function and long-term health. PCOS, also known as Stein-Leventhal syndrome or hyperandrogenic anovulation, is the most common endocrine disorder in women of reproductive age. This condition is characterized by chronic anovulation, hyperandrogenism, and polycystic ovarian morphology. In addition to being a major cause of ovulatory infertility, PCOS is also closely associated with menstrual dysfunction and hyperandrogenic manifestations such as hirsutism (Nazir & Sadhu, 2024).

Furthermore, women with PCOS and chronic menstrual cycle disorders are known to have a higher risk of endometrial hyperplasia and endometrial cancer, due to exposure to estrogen that is not balanced by progesterone. In addition, 50 years of prospective evidence shows that irregular menstrual cycles are also associated with an increased risk of ovarian cancer incidence and mortality. This risk is known to increase with age (Cirillo et al., 2016).

Given the complexity of the relationship between the menstrual cycle, endocrine disorders such as PCOS, and the risk of ovarian and endometrial cancer, a comprehensive understanding based on a synthesis of the latest scientific evidence is required. Therefore, this systematic review was conducted to evaluate the dynamic relationship between the menstrual cycle, ovulation disorders, and the risk of ovarian cancer, as well as to identify the underlying pathophysiological mechanisms.

## MATERIALS & METHODS

Literature searches were conducted in the PubMed, Embase, Scopus, Google Scholar, and Science Direct databases, using the keywords: prostate cancer, deep learning, radiology, pathology. Studies included were original research or systematic reviews from 2019 to 2024, and from internationally indexed journals.

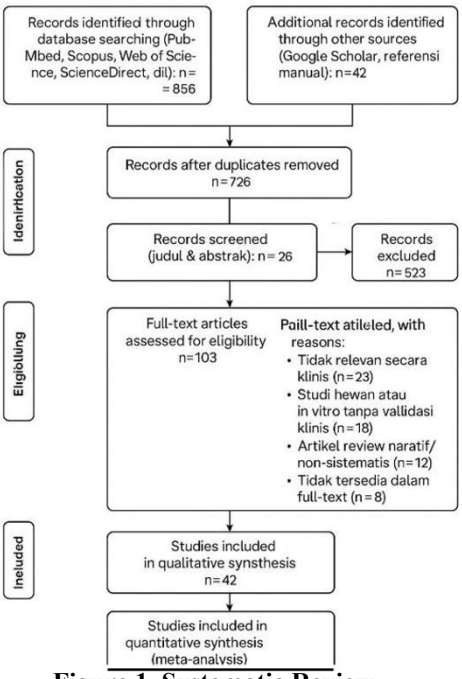


**Figure 1. Systematic Review**

## RESULT AND DISCUSSION

### 1. Follicular Phase (Proliferative)

- Ovaries: An important stage in the menstrual cycle involving the growth and maturation of ovarian follicles. This process begins with the recruitment of primordial follicles, which then undergo a series of growth and differentiation to become primary, secondary, and finally antral follicles, characterized by the presence of a fluid-filled cavity. The final stage of the follicular phase is the selection of the dominant follicle, which will continue to grow and eventually undergo ovulation. Throughout this process, various factors such as hormones, growth factors, and signaling pathways work together to coordinate follicular enlargement and maturation. Granulosa cells, which surround the oocyte, play a crucial role in supporting its maturation by providing nutrients and growth factors. MicroRNAs (miRNAs) also play a crucial role in regulating all stages of follicular development, from growth to regression (atresia) and ovulation (Kusumaningtyas et al., 2024).
- Endometrium: The period during which the ovaries prepare themselves by developing follicles, which then produce estrogen. Estrogen plays an important role in stimulating endometrial proliferation, which is the thickening of the uterine lining in preparation for possible embryo implantation (Kusumaningtyas et al., 2024).

### 2. Ovulation

- Ovaries: Ovulation is an integral part of the menstrual cycle, during which an egg is released from the ovary. In the ovulatory cycle, there are two distinct hormonal phases: the follicular phase, with increased estradiol levels, and the luteal phase, characterized by high progesterone and moderate estradiol levels. The release of the egg and high progesterone production are key markers of ovulation, distinguishing it from anovulatory cycles that do not release eggs or produce high progesterone (Naderi et al., 2025).
- Endometrium: Ovulation is a crucial part of the menstrual cycle that occurs after the follicular phase, during which ovarian hormones, particularly estradiol, increase rapidly and peak before

ovulation. The surge in ovarian hormones, especially progesterone, which dominates after ovulation, plays an important role in preparing the endometrium for possible implantation. Progesterone transforms the endometrium from the proliferative phase to the secretory phase, making it receptive to the embryo. Thus, ovulation indirectly regulates important changes in the endometrium that are essential for reproductive function (Naderi et al., 2025).

**3. Luteal Phase (Secretory)**

- Ovaries: The luteal phase is an important part of the menstrual cycle in which the corpus luteum in the ovaries begins to secrete progesterone and estrogen. After a brief decline in estrogen following ovulation, both estrogen and progesterone levels increase and peak around the middle of the luteal phase. Subsequently, levels of both hormones decline sharply at the end of the luteal phase (LL), which then triggers menstruation (Yen et al., 2019).
- Endometrium: The luteal phase of the endometrium in the menstrual cycle is the period during which the corpus luteum primarily secretes progesterone. After a slight decrease in estrogen, both estrogen and progesterone increase and peak around the mid-luteal phase, then decline rapidly in the late luteal phase (LL) to trigger menstruation (Yen et al., 2019).
- Ovarian Cancer: Overview and Relationship to Ovarian Function Ovarian cancer, the fifth leading cause of cancer death in women, has few modifiable risk factors. Psychological stress, including depression, anxiety, PTSD, social isolation, and widowhood, individually or in combination, has been associated with an increased risk of ovarian cancer, affecting tumor growth, invasion, apoptosis, and biological processes such as DNA damage and inflammation (Roberts et al., 2023). The relationship between the ovaries and endometrium is crucial in the menstrual cycle, particularly in conditions such as Polycystic Ovary Syndrome (PCOS). In individuals with PCOS, abnormal expression of ESR1 leads to increased expression of Ki-67 in the endometrial epithelium and stroma, which in turn reduces endometrial receptivity. The LIF STAT3 pathway, which is important for endometrial receptivity, is inactivated in PCOS, resulting in Ltf and Muc1 production that indicates an unreceptive endometrium. Disregulation of the Wnt/ß-catenin/Msx1 pathway also disrupts endometrial receptivity, with increased Msx1. Insulin resistance, which often accompanies PCOS, exacerbates progesterone resistance and disrupts endometrial function. Additionally, elevated androgen levels affect the integrity of tight junctions in the endometrial epithelium by reducing Cldn4 and Cldn1. All these changes collectively contribute to endometrial dysfunction (Parker & Hofstee, 2025). In the context of the menstrual cycle, infection can also disrupt the hypothalamic-pituitary-ovarian-endometrial axis, causing changes in the menstrual cycle due to systemic inflammation that affects the endometrium and vascularization. The menstrual cycle itself involves complex interactions between various tissues, hormones, and organ systems, and can be altered by various physiological and pathological variables, including viral infections. Physiological processes in the female reproductive system involve inflammatory elements such as cytokines and chemokines, which regulate the uterine environment. This inflammatory response interferes with tissue repair, angiogenesis, degradation, remodeling, and proliferation of the endometrium. Changes in the menstrual cycle may be related to the acute phase immune response, inflammation, endogenous hormone levels, and/or

immune cells in the endometrium (Anastácio et al., 2025).

## CONCLUSION

The menstrual cycle is a complex process involving dynamic interactions between the hypothalamus, pituitary gland, ovaries, and uterus. The ovaries regulate egg maturation through the follicular and luteal phases, which directly affect the endometrium, the lining of the uterus, to prepare for implantation through estrogen-stimulated proliferation and progesterone-induced secretory changes. Disruption of this ovary-endometrium interaction, as occurs in polycystic ovary syndrome (PCOS), may increase the risk of ovarian cancer. In PCOS, hormonal imbalance and insulin resistance cause endometrial dysfunction and reduced receptivity, potentially increasing the risk of endometrial cancer. Additionally, external factors such as psychological stress and infection can also disrupt the hypothalamic-pituitary-ovarian-endometrial axis, triggering systemic inflammation that affects the endometrium and alters the menstrual cycle, and is correlated with an increased risk of ovarian cancer. Therefore, a deep understanding of the ovarian-endometrial dynamics and the factors that influence them is crucial in ovarian reproduction.

## Recommendations

1. Improved Translational Research:
   Further studies are needed to understand the molecular and hormonal mechanisms that regulate ovarian-endometrial interactions.
   Focus on inflammatory pathways, angiogenesis, and cyclic hormonal signaling that may contribute to ovarian carcinogenesis.
2. Improved Early Detection:
   The development of combined biomarkers that reflect physiological changes in both the endometrium and ovary could improve early detection of ovarian cancer.
3. Integrated Approach:
   A multidisciplinary approach integrating gynecology, oncology, molecular biology, and imaging technology is needed to study this dynamic relationship.
4. Expansion of Study Population:
   Studies should include various age groups and reproductive statuses (pre-menopausal, post-menopausal, infertile, etc.) to strengthen the generalization of results.
5. Longitudinal and Prospective Studies:
   Long-term cohort data can help explain the temporality of dynamic changes and the emergence of ovarian cancer.

### *Declaration by Authors*

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## REFERENCES

1. Anastácio, Z. C., Fernandes, S. C., Alves, R. F., Antão, C. M., Carvalho, P. O., Benevides Ferreira, S. M., & Condessa, M. I. C. (2025). The Relationship between COVID-19 Infection, Vaccination, and Changes in the Menstrual Cycle among Portuguese Adolescents in Higher Education. Healthcare (Swiss), 13(1), 1–16. https://doi.org/10.3390/healthcare13010002
2. Cirillo, P. M., Wang, E. T., Cedars, M. I.,Chen, L.-M., & Cohn, B. A. (2016). Irregular menstruation predicts ovarian cancer: Prospective evidence from the Child Health and Development Study. International Journal of Cancer, 139(5), 1009–1017. https://doi.org/10.1002/ijc.30144
3. Kusumaningtyas, I., Dasuki, D., Harjana, S. M., Sadewa, A. H., Sweety, M. C., & Septiani, L. (2024). Uncovering the role of microRNA as a key factor in folliculogenesis and ovarian disease. Middle East Fertility Society Journal, 29(1). https://doi.org/10.1186/s43043-024-00173-x
4. Nazir, S., & Sadhu, S. (2024). The Effect of Pilates on Menstrual Cycle Regulation in Women with Polycystic Ovary Syndrome. European Journal of Obstetrics and Gynecology and Reproductive Biology: X,

21(August 2023), 100271. https://doi.org/10.1016/j.eurox.2023.100271
5. Parker, J., & Hofstee, P. (2025). Special Issue "New Challenges and Perspectives in Polycystic Ovary Syndrome." International Journal of Molecular Sciences, 26(6). https://doi.org/10.3390/ijms26062665
6. Roberts, A. L., Ratanatharathorn, A., Chibnik, L., Kubzansky, L. D., & Tworoger, S. S. (2023). Multiple types of distress are prospectively associated with increased risk of ovarian cancer. Cancer Medicine, 12(14), 15404 15413 https://doi.org/10.1002/cam4.6125
7. Yen, J. Y., Lin, H. C., Lin, P. C., Liu, T. L., Long, C. Y., & Ko, C. H. (2019). Early-and late-luteal-phase estrogen and progesterone levels of women with premenstrual dysphoric disorder. International Journal of Environmental Research and Public Health, 16(22), 1–12. https://doi.org/10.3390/ijerph16224352

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