Medicinska istraživanja 2025; 58(2):125-131 | DOI: 10.5937/medi58-53292

OPEN ACCESS

Medical Research | Published by Faculty of Medicine University of Belgrade

ORIGINAL ARTICLE

Reproductive challenges of endometrial polyps: the influence of women's age and associated risk factors

Sladjana Mihajlovic[1,2], Svetlana Vujovic[2,3], Mina Hagen[4], Milan Lackovic[1], Sanja Milic[1], Antoan Stefan Sojat[3], Kristina Saravinovska[2,3], Natalija Antic[3], Djurdjica Kalicanin[1], Ljiljana V. Marina[2,3]

[1] Clinical Hospital Centre "Dr Dragisa Misovic - Dedinje", Hospital for Gynecology and Obstetrics, Belgrade, Serbia

[2] University of Belgrade, Faculty of Medicine, Belgrade, Serbia

[3] Clinic of Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Belgrade, Serbia

[4] Department of Psychology, Faculty of Media and Communications, Singidunum University

Submitted: 25 October 2024

Revised: 04 June 2025

Accepted: 06 June 2025

Published: 30 June 2025

Check for updates

Correspondence to:
Sladjana Mihajlovic

Clinical Hospital Centre "Dr Dragisa Misović - Dedinje", Hospital for Gynecology and Obstetrics, 11000 Belgrade

E-mail: drsladjanamihajlovic@gmail.com

Summary

Introduction / Aim: Endometrial polyps (EPs) are abnormal benign growths that originate from the endometrium. Risk factors associated with EPs are hormonal changes related to ageing, Tamoxifen use, hormone replacement therapy, overweight or obesity. The exact causal relationship between EPs and infertility remains unclear, but multiple mechanisms including mechanical obstruction and biochemical changes are proposed. The "gold standard" for diagnosing and treating EPs is hysteroscopy. This study aims to provide comprehensive understanding of the interplay between EP, age and infertility**.**

Material and methods: Our study included 301 women undergoing hysteroscopic polypectomy due to infertility treatment, which were divided into two groups based on their age (age ≤ 35 and age > 35). Data were collected from patients' medical histories and pathology reports. Study variables included infertility type, type 2 diabetes mellitus, insulin resistance, polycystic ovary syndrome, endometriosis, hypothyreosis, previous unsuccessful intrauterine insemination and *in vitro fertilization (IVF)*, menstrual cycle irregularities and abnormal uterine bleeding, polyp size and histopathology type.

Results: At least one out of five participants had insulin resistance, polycystic ovary syndrome and abnormal uterine bleeding. Endometriosis, insulin resistance and primary infertility were more common in the younger group then in the older group. Previous history of unsuccessful IVF cycles, hypothyreosis and secondary infertility were associated with older age.

Conclusion: The prevalence of EPs tends to increase with advanced women's age, period marked by natural decline in ovarian reserve, hormonal changes and changes in endometrial health. Addressing EPs through appropriate diagnostic and therapeutic measure and understanding the hormonal influence on EPs and EM is crucial for improving fertility outcomes.

Keywords: endometrial polyps, infertility, hysteroscopy

Cite this article as: Mihajlovic S, Vujovic S, Hagen M, Lackovic M, Milic S, Sojat A. S, Saravinovska K, Antic N, Kalicanin Dj, Marina Lj. V. Reproductive challenges of endometrial polyps: the influence of women's age and associated risk factors; Medicinska istraživanja 2025; 58(2):125-131 DOI: 10.5937/medi58-53292

INTRODUCTION

Endometrial polyps (EPs), also known as uterine polyps, are abnormal growths that originate from the endometrium. They consist of glands, stroma, and blood vessels. The size of EPs can range significantly, they can be as small as 5 mm, but they can also fulfill the entire uterine cavity. Based on their attachment to the uterine surface, there are two main types of EPs. If an EP is attached by a narrow-elongated pedicle, then it is known as pedunculated. However, if they have a large flat base, they are known as sessile. The gross morphological appearance of these polyps can vary, but they often present as smooth structures with a tan to yellow coloration. EPs are quite common among women, with estimates suggesting they affect about 25% of women. While EPs can occur at any age, they are statistically more prevalent in women aged 40 to 49 years, primarily due to hormonal changes and fluctuations that this age group tends to experience (1,2). Estrogen's role in stimulating endometrial growth and thickening each month makes it a significant factor in the development of EPs. Understanding and managing conditions that result in elevated estrogen levels are essential in minimizing the risk of polyp formation and ensuring reproductive health (3). Aside from hormonal changes related to aging, other risk factors associated with EPs have also been identified, such as Tamoxifen use and hormone replacement therapy (HRT). There is an increased risk of EPs in women who are overweight or obese as well. Higher levels of adipose tissue can lead to increased estrogen production, which may contribute to the development of polyps (3,4).

EPs are typically asymptomatic but they can manifest as abnormal uterine bleeding (AUB). The AUB include irregular menstrual periods (unpredictable timing and flow), unusually heavy flow during menstrual period, bleeding or spotting between periods, vaginal spotting or bleeding after menopause. AUB may be the primary symptom of EPs, occurring in more than a half of all women with the condition, and its incidence appears to increase with age (5,6).

Correlation between EPs and infertility is a special concern. While the exact causal relationship between EPs and infertility remains unclear, multiple mechanisms including mechanical obstruction and biochemical changes are proposed. EPs may induce an inflammatory response in the endometrium, which could disturb embryo implantation, similar to the effects seen with an intrauterine device. Also, EPs have been found to exhibit altered levels of matrix metalloproteinases (MMPs), cytokines like interferon gamma, and proteins such as glycodelin and placenta protein 14. These biochemical changes can interfere with sperm function, inhibit embryonic development, and affect the endometrial environment needed for successful implantation (1,7).

Hysteroscopy with guided biopsy not only serves as the definitive method for diagnosing EPs but also facilitates precise localization and allows for immediate therapeutic intervention through simultaneous resection. These advantages underscore its status as the "gold standard" in clinical practice for managing EPs. While there is still disagreement in the literature regarding the routine removal of EPs before attempting pregnancy (both natural and assisted), there is a tendency towards removing polyps before initiating assisted reproductive technologies (ART) such as intrauterine insemination (IUI) and in vitro fertilization (IVF). Therefore, the decision-making process should involve a thorough assessment of each patient's unique circumstances and preferences, guided by current evidence-based practices and clinical judgment (8).

This study aims to provide comprehensive understanding of the interplay between EP, age and infertility, ultimately guiding more effective diagnostic and therapeutic strategies to enhance reproductive success for women experiencing such challenges.

MATERIAL AND METHODS

Study design and participants

The study was performed in the Clinical Hospital Centre (CHC) "Dr Dragisa Misovic - Dedinje" in Belgrade, Serbia. It included 301 women undergoing hysteroscopic polypectomy due to infertility treatment. The age ranged from 24 to 44 (mean 35.91 ± 4.63). Patients were treated at the Hospital of Gynecology and Obstetrics and recruited from 2019 to 2024. The study was approved by the CHC's Institutional Review Board (No 18328/4-2024, Date: 29.08.2024).

Study participants were divided into two groups based on their age.

The first, younger group (age ≤ 35) consisted of 131 participants where age ranged from 24 to 35 (mean 31.50 ± 3.00). Second, older group (age > 35) included 170 participants, with age ranging from 36 to 44 (mean 39.31 ± 2.12).

Study inclusion and exclusion criteria

Study included women aged between 18 and 45 who were treated during a five year long time frame at the CHC "Dr Dragisa Misovic - Dedinje". Women older than 45 or younger than 18 were excluded from the study. All women included in the study were normal weight and had body mass index (BMI) of between 18.5 and 24.9 kg/m2. Obese women were excluded.

Study variables

Data on infertility type (primary or secondary), type 2 diabetes mellitus, insulin resistance, polycystic ovarian

syndrome, endometriosis, hypothyreosis, previous unsuccessful intrauterine insemination and in vitro fertilization, previous hysteroscopic polypectomy, menstrual cycle irregularities and abnormal uterine bleeding, were collected from patients' medical histories. Data on polyp size and histopathology type were collected from pathology reports.

Statistical analysis

Descriptive statistics are presented as frequencies and percentages for categorical data, and as mean, median, SD and range for continuous data. The descriptives were presented for the total sample, and for the younger and older group of participants. To test the relationship between age groups and other relevant variables in our study, we used Fisher's Exact Test for categorical data and Mann-Whitney U test for continuous data. A significance level of $p < 0.05$ was set. Statistical analysis was conducted using IBM SPSS version 23.0.

RESULTS

The characteristics and prevalence of comorbidities, previous ART and hysteroscopy procedures and menstrual cycle disorders in the sample

In order to describe the characteristics of the age groups regarding significant variables related to infertility, we calculated the number of conditions within two groups and in the total sample. In order to examine the relationship between age groups and significant variables, we performed Fisher's Exact test. The results including frequencies, percentages and p values (two-tailed) are displayed in **Table 1**.

Looking at the results for the whole sample presented in **Table 1**, we can observe that at least one out of five participants have insulin resistance, PCOS and abnormal uterine bleeding – and those were the most common conditions. The majority of the sample (85.4%) had a regular menstrual cycle.

Inspecting the differences between the age group, we can see that in the younger group (age ≤ 35), the more common conditions are endometriosis ($p = 0.011$), insulin resistance ($p = 0.021$) and primary infertility ($p = 0.017$). The prevalence for endometriosis in the younger group was 8.4% compared to the 1.4% in the older group. Insulin resistance was present in 30.5% of cases in the younger group, compared to the 18% in the older group. Regarding primary infertility, there were 90.1% diagnosed participants in the younger group, compared to the 79.4% in the older group.

In the older group there was a significantly higher number of cases with hypothyroidism ($p = 0.014$), previous unsuccessful IVF ($p < 0.001$) and secondary infertility ($p = 0.017$). Every fourth patient had hypothyroidism (25.3%) in the older group compared to every sixth patient (13.7%) in the younger group. The prevalence of previous unsuccessful IVF was 18.8% in the older group compared to the 4.6% in the younger group. Regarding secondary infertility there were 20.6 % diagnosed women in the older group compared to the 9.9% in the younger group.

The characteristic polyp size and histopathology type in the sample

The size of EPs can vary significantly; they can be as small as 5mm, but they can also fulfill the entire uterine cavity. EPs are usually benign, but in some cases, they can be associated with a risk of malignancy, especially in postmenopausal women or in those with abnormal bleeding

Table 1. Frequencies, percentages of participants with endometriosis, insulin resistance, PCOS, hypothyroidism, unsuccessful IUI and IVF, previous hysteroscopic polypectomy, regular menstrual cycle, abnormal uterine bleeding withing total sample and subsamples and statistical significance (p value, two tailed) of Fisher's Exact test.

	total sample (n = 301)	**age ≤ 35 (n = 131)**	**age > 35 (n = 170)**	**p**
	N. yes (%)	N. yes (%)	N. yes (%)	
endometriosis	14 (4.7)	11 (8.4)	3 (1.8)	0.011
insulin resistance	72 (23.9)	40 (30.5)	32 (18.8)	0.021
PCOS	73 (24.3)	38 (29.0)	35 (20.6)	0.104
hypothyroidism	61 (20.3)	18 (13.7)	43 (25.3)	0.014
IUI	3 (1.0)	3 (2.3)	0 (0)	0.081
IVF	38 (12.6)	6 (4.6)	32 (18.8)	<0.001
previous hysteroscopic polypectomy	48 (15.9)	16 (12.2)	32 (18.8)	0.153
regular menstrual cycle	257 (85.4)	115 (87.8)	142 (83.5)	0.327
abnormal uterine bleeding	79 (26.2)	33 (25.2)	46 (27.1)	0.792
primary infertility	252 (84.1)	118 (90.1)	135 (79.4)	0.017
secondary infertility	48 (15.9)	13 (9.9)	35 (20.6)	0.017

Note: PCOS – polycystic ovarian syndrome; IUI – unsuccessful intrauterine insemination; IVF – unsuccessful in vitro fertilization

patterns. In the total sample the size of the polyp ranged from 2 mm to 50 mm (M = 12.88; SD = 6.57; Median = 10). We used Mann-Whitney U test to discover whether there was a significant difference in average size between the age groups. There were no significant differences (p = .813) between the Mean Rank in the younger group (149.67) compared to the older group (152.03).

We also checked the histopathology type and compared the groups. In the total sample in 96.7% of cases it was confirmed polyp, and in 3.3% cases other diagnosis. In the younger group the prevalence of other diagnosis was 3.1% whereas in the older group was 3.5%. The results of Fisher's Exact test showed that these differences were not statistically significant (p = 1.000).

Association Between Endometriosis and Type of Infertility

To investigate the potential association between endometriosis prevalence and the type of infertility (primary vs. secondary), we performed Fisher's Exact Test. The prevalence of endometriosis was 5.1% among patients with primary infertility and 2.1% among those with secondary infertility. However, this difference was not statistically significant (p = 0.706).

DISCUSSION

Our study included 301 women dealing with infertility, who were diagnosed with EPs. Subjects were divided in two subgroups, based on age, which was defined for the purpose of this study as older or younger than 35. A total of 12 variables related to EP and infertility treatment were assessed, but statistical relevance was found for only two parameters, concomitant presence of endometriosis and the history of previous IVF failure.

The age for the diagnosis of type 2 diabetes mellitus (T2DM) has decreased over the last few decades (9). Guidelines specifically created for this group of patients are still lacking, and recommendations are primarily extrapolated from the evidence in older people (10). However, only three cases of T2DM were observed in the group of women who were older than 35, and there were no participants with T2DM among participants in the first group (35 or younger) so therefore statistical comparison between the two groups was not performed.

Women's fertility starts to decline after the age of 30, and after the age of 35 the fertility decline rate accelerates. The underlying etiology is associated with the oocyte number and quality depletion, and this is the primary reason why women over 35 are more commonly seeking fertility counselling and are more commonly exposed to the methods of assisted reproduction (11). The highest number of ART procedures in the United States (US) are actually carried out among women aged between 35 and 40. Centers for Disease Control and Prevention (CDC) reported the average age of women undergoing ART procedures to be 36.2 years. Women aged between 35 and 40 represent 43.3% of all women undergoing ART procedures in the US (12).

Advanced women's age is a well-known risk factor for prolonged time to conception. Without involvement of ART techniques before the age of 30 women have approximately 85% chance to conceive within one year, while after the age of 35 these chances drop to 66%, and go further down reaching a probability of 44% by the age of 40. Unfortunately, reproductive challenges at this age are not limited only to the conception difficulties. At this age women deal with other burdens of unfavorable pregnancy outcomes as well, such as a miscarriage. More than a quarter of all clinical pregnancies terminate as a miscarriage at the age of 40, compared to 16% at the age of 30 (11,13).

Our results are in unison with the fact that advanced women's age is associated with higher number of unsuccessful IVF cycles (14), and this is the most probable explanation why women over 35 in our study did undergo IVF procedures more often compared to the group of women who were 35 years or younger.

Our study showed higher prevalence of endometriosis in younger patients with EP. Both EP and endometriosis are conditions related to the uterine lining, but they are distinct in their nature and presentation. While EP are growths that occur in the endometrium, endometriosis is a condition where endometrial tissue grows outside the uterus, causing pain, irregular bleeding and fertility issues. Even though EP and endometriosis are two different conditions, there's often an overlap in clinical presentation and possibly in the pathophysiological mechanism leading to it. Although the exact pathophysiological mechanism is not completely understood yet, several research groups have reported increased prevalence of EP in women with endometriosis dealing with infertility simultaneously (15,16).

It is known that adhesions associated with anatomical disturbances are the leading mechanism resulting in infertility in endometriosis patients, but the importance of endocrine and immunological disturbances should not be neglected either, especially since the exact pathophysiological mechanism explaining endometriosis is so far not fully understood (17).

Endometriosis and EP are influenced by hormonal changes, particularly those related to estrogen, but they do so in different manners. Estrogen stimulates the growth of the endometrial lining resulting in the development of EP, and estrogen fluctuations affect the growth of EP in a more complex manner. Estrogen receptor pattern and aromatase activity expression are altered in both EP and endometriosis patients, and estrogen fluctuation levels are the probable intrinsic factor linking EP, endometriosis and infertility (18-20). Furthermore, vascular changes associated with Endometriosis could be

in relationship with the evolution of the EP vessel's axis as well. Machado et al. have found that levels of inflammatory markers in endometrium, such as vascular endothelial growth factor (VEGF), matrix metalloproteinases (MMP) and angiogenesis factors 1 and 2, are higher in patients with EP who suffer from endometriosis at the same time (21). Additionally, Wang et al. have reported significant association between endometriosis and EP in their research and emphasized that all patients dealing with endometriosis should be carefully evaluated for the concomitant presence of EP, regardless of the ultrasonography findings (22).

Unlike EP which have a peak incidence between the age of 40 and 49 (23), endometriosis typically affects women during their 30s. Even though between 10 and 15% of all women of reproductive age are affected by endometriosis, and despite all the improvements and progress in technology and diagnostics, there is still a shocking average delay of nearly seven years in establishing endometriosis diagnosis (24).

Estrogen levels reach their peak during women's late 20s. By the age of 50 there is a 50% decline in estrogen levels compared to their peak levels, with further dramatical decrease during and after perimenopause (25). Endometriosis is known to be highly dependent on estrogen, but it is known that even if estrogen level would decline, endometriosis symptoms would not necessarily decrease (26). In this context, younger age, 35 or less, is beyond doubt related with higher estrogen levels and consequently with higher endometriosis incidence, and our result supports this interdependence.

Endometriosis affects women's quality of life in a similar manner as Crohn's disease, T2DM and rheumatoid arthritis, and despite a significant percentage of women of reproductive age living with it, therapeutic approaches for endometriosis are still limited exclusively to the management of symptoms caused by endometriosis. In fact, treatment options are oriented only to infertility or pelvic pain treatment, without any targeted therapy designated for the treatment of endometriosis (27). Endometriosis is defined as an inherited, autoimmune, long-life diseases, which has to be treated from the time of diagnosis, continuously with the individually tailored treatment according to patients' overall status, age and complaints, in order to control the pain and further dissemination (28). Therefore, associations between endometriosis and EP, as well as the role of estrogen and its receptors, must be demystified, and more comprehensive and causal treatment offered to patients affected by it.

CONCLUSION

The prevalence of EPs tends to increase with advanced women's age, a period marked by natural decline in ovarian reserve, hormonal changes and changes in endometrial health. Addressing EPs through appropriate diagnostic and therapeutic measures and understanding the hormonal influence on EPs and EM is crucial for improving fertility outcomes. Ongoing research and clinical practice must continue to focus on optimizing treatment strategies to address EP pathology, ultimately supporting better reproductive outcomes for women across various age groups. The interplay between EPs, age and infertility underscores the importance of comprehensive reproductive evaluation and tailored interventions to enhance fertility perspectives and support women towards their journey to better reproductive outcomes.

Acknowledgement: The authors express sincere gratitude to the Clinical Hospital Centre "Dr Dragisa Misovic - Dedinje" for providing the necessary resources and facilities, as well as to all employees working at the Hospital for Gynecology and Obstetrics "Dr Dragisa Misovic - Dedinje".

Funding information: The authors reported no funding associated with the work featured in this article.

Conflict of Interest Statement: No conflict of interest to report.

Author contributions: S. M, Lj. M, S. V, and M. H, conceptualization, supervision, methodology, investigation, formal analysis, and writing—original draft; M. L, S. M, and Dj. K, methodology, formal analysis, visualization, and writing—original draft; A. S. S, K. S, and N. A, conceptualization, visualization, writing- original draft. All authors have read and agreed to the published version of the manuscript.

Ethical approval: The study was approved by the Institutional Review Board (IRB) of the University Hospital "Dragisa Misovic" in Belgrade, Serbia, (No. 18328/4, Date: 29.08.2024).

References

1. Nijkang NP, Anderson L, Markham R, Manconi F. Endometrial polyps: Pathogenesis, sequelae and treatment. SAGE Open Med. 2019 May 2;7:2050312119848247. doi: 10.1177/2050312119848247. PMID: 31105939; PMCID: PMC6501471.
2. Vitale SG, Haimovich S, Laganà AS, Alonso L, Di Spiezio Sardo A, Carugno J; From the Global Community of Hysteroscopy Guidelines Committee. Endometrial polyps. An evidence-based diagnosis and management guide. Eur J ObstetGynecolReprod Biol. 2021 May;260:70-77. doi: 10.1016/j.ejogrb.2021.03.017. Epub 2021 Mar 13. PMID: 33756339.
3. Yu K, Huang ZY, Xu XL, Li J, Fu XW, Deng SL. Estrogen Receptor Function: Impact on the Human Endometrium. Front Endocrinol (Lausanne). 2022 Feb 28;13:827724. doi: 10.3389/fendo.2022.827724. PMID: 35295981; PMCID: PMC8920307.
4. Nappi L, Indraccolo U, Di Spiezio Sardo A, Gentile G, Palombino K, Castaldi MA, Spinelli M, Greco P. Are diabetes, hypertension, and obesity independent risk factors for endometrial polyps? J Minim Invasive Gynecol. 2009 Mar-Apr;16(2):157-62. doi: 10.1016/j.jmig.2008.11.004. Epub 2009 Jan 21. PMID: 19162559.

5. Achanna KS, Nanda J. Evaluation and management of abnormal uterine bleeding. Med J Malaysia. 2022 May;77(3):374-383. PMID: 35638495.
6. Wouk N, Helton M. Abnormal Uterine Bleeding in Premenopausal Women. Am Fam Physician. 2019 Apr 1;99(7):435-443. PMID: 30932448.
7. Jee BC, Jeong HG. Management of endometrial polyps in infertile women: A mini-review. Clin Exp Reprod Med. 2021 Sep;48(3):198-202. doi: 10.5653/cerm.2020.04119. Epub 2021 Jul 30. PMID: 34352167; PMCID: PMC8421660.
8. Moore JF, Carugno J. Hysteroscopy. 2023 Jul 18. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 33232015.
9. Kyrou I, Tsigos C, Mavrogianni C, Cardon G, Van Stappen V, Latomme J, Kivelä J, Wikström K, Tsochev K, Nanasi A, Semanova C, Mateo-Gallego R, Lamiquiz-Moneo I, Dafoulas G, Timpel P, Schwarz PEH, Iotova V, Tankova T, Makrilakis K, Manios Y; Feel-4Diabetes-study Group. Sociodemographic and lifestyle-related risk factors for identifying vulnerable groups for type 2 diabetes: a narrative review with emphasis on data from Europe. BMC EndocrDisord. 2020 Mar 12;20(Suppl 1):134. doi: 10.1186/s12902-019-0463-3. PMID: 32164656; PMCID: PMC7066728.
10. Sargeant JA, Brady EM, Zaccardi F, Tippins F, Webb DR, Aroda VR, Gregg EW, Khunti K, Davies MJ. Adults with early-onset type 2 diabetes (aged 18-39 years) are severely underrepresented in diabetes clinical research trials. Diabetologia. 2020 Aug;63(8):1516-1520. doi: 10.1007/s00125-020-05174-9. Epub 2020 Jun 2. PMID: 32483683; PMCID: PMC7351852.
11. Delbaere I, Verbiest S, Tydén T. Knowledge about the impact of age on fertility: a brief review. Ups J Med Sci. 2020 May;125(2):167-174. doi: 10.1080/03009734.2019.1707913. Epub 2020 Jan 22. PMID: 31964217; PMCID: PMC7721003.
12. https://www.cdc.gov/art/reports/2020/summary.html (assessed on August 17th 2024)
13. Delbaere I, Verbiest S, Tydén T. Knowledge about the impact of age on fertility: a brief review. Ups J Med Sci. 2020 May;125(2):167-174. doi: 10.1080/03009734.2019.1707913. Epub 2020 Jan 22. PMID: 31964217; PMCID: PMC7721003.
14. Yan J, Wu K, Tang R, Ding L, Chen ZJ. Effect of maternal age on the outcomes of in vitro fertilization and embryo transfer (IVF-ET). Sci China Life Sci. 2012 Aug;55(8):694-8. doi: 10.1007/s11427-012-4357-0. Epub 2012 Aug 30. PMID: 22932885.
15. Shen L, Wang Q, Huang W, Wang Q, Yuan Q, Huang Y, Lei H. High prevalence of endometrial polyps in endometriosis-associated infertility. Fertil Steril. 2011 Jun 30;95(8):2722-4.e1. doi: 10.1016/j.fertnstert.2011.04.067. Epub 2011 May 14. PMID: 21575952.
16. Kim MR, Kim YA, Jo MY, Hwang KJ, Ryu HS. High frequency of endometrial polyps in endometriosis. J Am Assoc GynecolLaparosc. 2003 Feb;10(1):46-8. doi: 10.1016/s1074-3804(05)60233-2. PMID: 12554993.
17. Chua SJ, Danhof NA, Mochtar MH, van Wely M, McLernon DJ, Custers I, Lee E, Dreyer K, Cahill DJ, Gillett WR, Righarts A, Strandell A, Rantsi T, Schmidt L, Eijkemans MJC, Mol BWJ, van Eekelen R. Age-related natural fertility outcomes in women over 35 years: a systematic review and individual participant data meta-analysis. Hum Reprod. 2020 Aug 1;35(8):1808-1820. doi: 10.1093/humrep/deaa129. PMID: 32696041.
18. Lopes RG, Baracat EC, de Albuquerque Neto LC, Ramos JF, Yatabe S, Depesr DB, Lippi UG. Analysis of estrogen- and progesterone-receptor expression in endometrial polyps. J Minim Invasive Gynecol. 2007 May-Jun;14(3):300-3. doi: 10.1016/j.jmig.2006.10.022. PMID: 17478359.
19. Noble LS, Simpson ER, Johns A, Bulun SE. Aromatase expression in endometriosis. J Clin Endocrinol Metab. 1996 Jan;81(1):174-9. doi: 10.1210/jcem.81.1.8550748. PMID: 8550748.
20. Maia H Jr, Pimentel K, Silva TM, Freitas LA, Zausner B, Athayde C, Coutinho EM. Aromatase and cyclooxygenase-2 expression in endometrial polyps during the menstrual cycle. Gynecol Endocrinol. 2006 Apr;22(4):219-24. doi: 10.1080/09513590600585955. PMID: 16723309.
21. Machado DE, Berardo PT, Palmero CY, Nasciutti LE. Higher expression of vascular endothelial growth factor (VEGF) and its receptor VEGFR-2 (Flk-1) and metalloproteinase-9 (MMP-9) in a rat model of peritoneal endometriosis is similar to cancer diseases. J Exp Clin Cancer Res. 2010 Jan 19;29(1):4. doi: 10.1186/1756-9966-29-4. PMID: 20085636; PMCID: PMC2826344.
22. Wang N, Zhang Y, Liu B. Demographic and Clinical Features of Endometrial Polyps in Patients with Endometriosis. Biomed Res Int. 2016;2016:1460793. doi: 10.1155/2016/1460793. Epub 2016 May 3. PMID: 27243030; PMCID: PMC4868887.
23. Kolhe S. Management of abnormal uterine bleeding - focus on ambulatory hysteroscopy. Int J Womens Health. 2018 Mar 22;10:127-136. doi: 10.2147/IJWH.S98579. PMID: 29606892; PMCID: PMC5868607.
24. Chua SJ, Danhof NA, Mochtar MH, van Wely M, McLernon DJ, Custers I, Lee E, Dreyer K, Cahill DJ, Gillett WR, Righarts A, Strandell A, Rantsi T, Schmidt L, Eijkemans MJC, Mol BWJ, van Eekelen R. Age-related natural fertility outcomes in women over 35 years: a systematic review and individual participant data meta-analysis. Hum Reprod. 2020 Aug 1;35(8):1808-1820. doi: 10.1093/humrep/deaa129. PMID: 32696041.
25. Lephart ED. A review of the role of estrogen in dermal aging and facial attractiveness in women. J Cosmet Dermatol. 2018 Jun;17(3):282-288. doi: 10.1111/jocd.12508. Epub 2018 Feb 13. PMID: 29436770.
26. Chantalat E, Valera MC, Vaysse C, Noirrit E, Rusidze M, Weyl A, Vergriete K, Buscail E, Lluel P, Fontaine C, Arnal JF, Lenfant F. Estrogen Receptors and Endometriosis. Int J Mol Sci. 2020 Apr 17;21(8):2815. doi: 10.3390/ijms21082815. PMID: 32316608; PMCID: PMC7215544.
27. Zondervan KT, Becker CM, Koga K, Missmer SA, Taylor RN, Viganò P. Endometriosis. Nat Rev Dis Primers. 2018 Jul 19;4(1):9. doi: 10.1038/s41572-018-0008-5. PMID: 30026507.
28. Vujović S, Ivovic M, Tančić-Gajić M, Marina L, Ljubic A, Dragojević-Dikić S, Genazzani AR. Endometrium receptivity in premature ovarian insufficiency - how to improve fertility rate and predict diseases? Gynecol Endocrinol. 2018 Dec;34(12):1011-1015. doi: 10.1080/09513590.2018.1490715. Epub 2018 Jul 25. PMID: 30044147.

REPRODUKTIVNI IZAZOVI KOD ŽENA SA ENDOMETRIJALNIM POLIPIMA: UTICAJ STAROSTI I POVEZANIH FAKTORA RIZIKA

Slađana Mihajlović[1,2], Svetlana Vujović[2,3], Mina Hagen[4], Milan Lacković[1], Sanja Milić[1], Antoan Stefan Šojat[3], Kristina Saravinovska[2,3], Natalija Antić[3], Đurđica Kaličanin[1], Ljiljana V. Marina[2,3]

Sažetak

Uvod / Cilj: Endometrijalni polipi (EP) predstavljaju benigne tumore poreklom iz endometrijuma. Najčešći faktori rizika koji dovode do pojave EP su hormonske promene povezane sa starenjem, upotreba tamoksifena, supstituciona hormonska terapija, prekomerna težina i gojaznost. Tačna uzročna veza između EP-a i infertiliteta ostaje nejasna, ali najčešće predlagani patofiziološki mehanizmi jesu mehaničke prepreke i biohemijske promene na nivou endometrijalnog tkiva. „Zlatni standard" dijagnostike i lečenja EP je histeroskopija. Cilj ove studije je da se ispita povezanost godina starosti, endometrijalnih polipa i infertiliteta. **Materijal i metode:** Istraživanje je obuhvatilo 301 pacijentkinju podvrgnutu histeroskopskoj polipektomiji radi lečenja infertiliteta, koje su podeljene u dve grupe na osnovu starosti (starost ≤ 35 i starost > 35 godina). Podaci su prikupljeni iz istorija bolesti i histopatoloških izveštaja, i analizirane su sledeće varijable: tip infertiliteta, prisustvo insulinske rezistencije, sindroma policističnih jajnika, endometrioze, hipotireoze, prethodni neuspešni pokušaji intrauterine inseminacije i vantelesne oplodnje (*IVF*), nepravilnosti menstrualnog ciklusa i abnormalno krvarenje iz materice, veličina polipa i histopatološki tip. **Rezultati**: Najmanje jedna od pet ispitanica imala je insulinsku rezistenciju, sindrom policističnih jajnika i abnormalno krvarenje iz materice. Endometrioza, insulinska rezistencija i primarni infertilitet bili su češći u mlađoj grupi nego u starijoj. Prethodna istorija neuspešnih *IVF* ciklusa, hipotireoza i sekundarni infertilitet bili su povezani sa uznapredovalim godinama.

Zaključak: Prevalencija EP ima tendenciju rasta sa godinama starosti žene, periodom koji je obeležen prirodnim padom rezerve jajnika, hormonskim promenama, kao i promenama u strukturi endometrijuma. Primena odgovarajućih dijagnostičkih i terapijskih mera, kao i razumevanje uticaja godina, hormonskog statusa i povezanosti EP i endometrioze, ključni su u lečenju EP, kao i u sveukupnom poboljšanju ishoda lečenja infertiliteta.

Ključne reči: endometrijalni polip, infertilitet, histeroskopija

Primljen: 25.10.2024. I **Revidiran:** 04.06.2025. I **Prihvaćen:** 06.06.2025. I **Objavljen:** 30.06.2025.

Medicinska istraživanja 2025; 58(2):125-131