MERAL Publications and Solutions Pvt. Ltd.

Review Article

Personalized approach to infertility treatment in endometriosis: results of a prospective cohort study

Seda Uvaysovna Imieva[1], Maria Andreevna Manuilova[2], Akhmed Gasainaevich Vagidov[2], Gadzhimurad Magomedovich Magomedov[3], Rayana Skandarbekowna Yunusova[4], Svetlana Sergeevna Poleeva[5], Magomed Bashirovich Zugunov[6], Mikail Akhmedovich Makhmudov[7]*

[1] Faculty of Pediatrics, North Ossetian State Medical Academy, Vladikavkaz, Republic of North Ossetia-Alania, Russia. [2]Faculty of Medicine, Kuban State Medical University, Krasnodar, Russia. [3]Faculty of Medicine, Dagestan State Medical University, Makhachkala, Republic of Dagestan, Russia. [4]Faculty of Medicine and Prevention, Rostov State Medical University, Rostov-on-Don, Russia. [5]Faculty of Pediatrics, Rostov State Medical University, Rostov-on-Don, Russia. [6]Faculty of Medicine, Saratov State Medical University named after V.I. Razumovsky, Saratov, Russia. [7]Faculty of Medicine, Russian University of Medicine, Moscow, Russia.

Correspondence: Mikail Akhmedovich Makhmudov, Faculty of Medicine, Russian University of Medicine, Moscow, Russia. publab@bk.ru

ABSTRACT

The present study evaluated the effectiveness of various endometriosis treatment methods in restoring fertility in 120 women of reproductive age with a confirmed diagnosis. The patients were divided into three groups: surgical treatment (n=40), conservative therapy (n=40), and a combined approach (n=40). The results showed the advantage of combination therapy with a pregnancy rate of 57.5% versus 35.0% for surgical and 22.5% for conservative treatment. The surgical method demonstrated efficacy in stages I-II (41.7%), but was accompanied by a decrease in the level of anti-Muller hormone from 3.2±1.5 to 2.1±1.0 ng/ml. In all groups, there was an improvement in endometrial parameters (thickness increased from 6.1±1.2 to 7.8±1.4 mm) and a decrease in systemic inflammation (C-reactive protein decreased from 8.2±3.1 to 3.5±1.8 mg/l). The greatest improvement in the quality of life was recorded in the combined group (a decrease in the scores of the Endometriosis Health Profile questionnaire-30 from 68.2±12.4 to 28.7±8.3). The information gathered demonstrates that the best course of action is combined therapy with assisted reproductive technologies, particularly during phases III–IV, while surgical treatment may be the method of choice in the early stages in patients with preserved ovarian reserve, which justifies the need for a personalized approach taking into account the stage of the disease and the reproductive status of the patient.

Keywords: Endometriosis, Infertility, Fertility, Surgical treatment, Combination therapy, Assisted reproductive technologies

Introduction

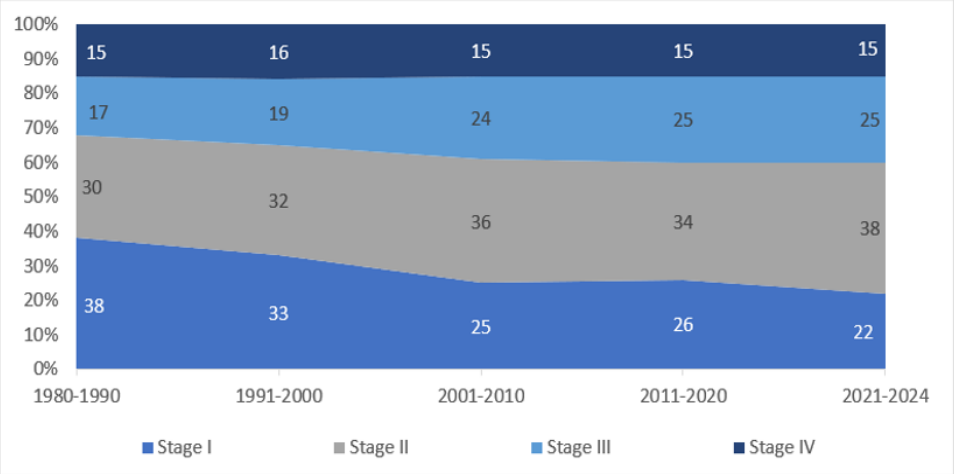
Endometriosis is one of the most common and complex gynecological diseases that has a significant impact on women's quality of life and their reproductive function [1, 2]. It is a chronic, often progressive condition in which tissue morphologically and functionally similar to the endometrium grows outside the uterine cavity – in the ovaries, fallopian tubes, peritoneum, bladder, and even distant organs [3, 4]. The main clinical manifestations of endometriosis are chronic pelvic pain, dysmenorrhea (painful menstruation), dyspareunia (painful sexual intercourse), and, most importantly, impaired fertility [5-7].

Although cases of its detection have been reported in adolescents, the condition primarily affects women of reproductive age, most frequently between the ages of 25 and 45 [8–10]. After the tubo-peritoneal factor, endometriosis is the second most common cause of infertility in women [11]. According to world statistics, endometriosis is diagnosed in 6-10% of women of childbearing age, and among patients with infertility, its frequency reaches 25-50% [12, 13]. In Russia, according to recent studies, the

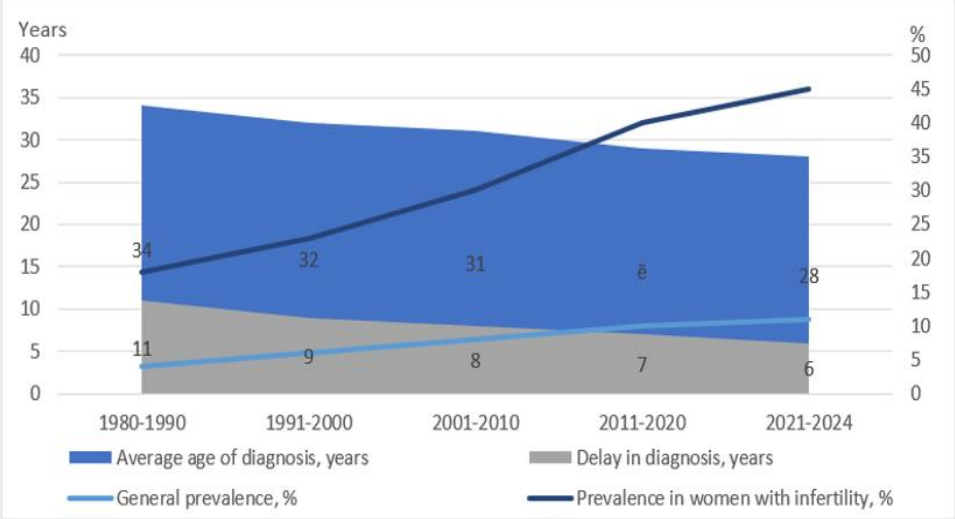
Access this article online	
Website: www.japer.in	**E-ISSN:** 2249-3379

How to cite this article: Imieva SU, Manuilova MA, Vagidov AG, Magomedov GM, Yunusova RS, Poleeva SS, et al. Personalized approach to infertility treatment in endometriosis: results of a prospective cohort study. J Adv Pharm Educ Res. 2025;15(1):124-32. https://doi.org/10.51847/FUILJKAFCfs

prevalence of endometriosis is about 7-15% among women of reproductive age, while 30-40% of them have difficulties with pregnancy [14]. **Figure 1** shows information on the prevalence statistics of the disease from 1980 to 2024 [15-17].



a)



b)

Figure 1. Statistics of endometriosis: a) distribution by stage; b) dynamics of prevalence by year.

Although the pathophysiology of endometriosis has not been well investigated, John Sampson's 1927 proposal of retrograde menstruation is still the most widely accepted theory [18]. According to this hypothesis, endometrial cells enter the abdominal cavity through the fallopian tubes during menstruation, where they implant and begin to grow [19]. However, many women have retrograde menstruation without developing endometriosis, which indicates the role of additional factors such as genetic predisposition, immune disorders, hormonal imbalance, and inflammatory processes [20, 21].

The effect of endometriosis on fertility is multifactorial and can be associated with both anatomical changes and functional disorders of the reproductive system [22]. The most obvious mechanism of decreased fertility is a mechanical obstacle to the transport of eggs and spermatozoa, resulting from adhesions in the pelvis, deformation of the fallopian tubes, or the formation of endometrioid cysts (endometriomas) in the ovaries [23, 24]. However, even with minimal forms of endometriosis, when anatomical changes are poorly expressed, women often experience a decrease in ovarian reserve, ovulation disorders, and deterioration in oocyte quality [25, 26].

Chronic inflammation and local hormonal imbalance play an important role in the pathogenesis of infertility in endometriosis. Foci of endometriosis produce pro-inflammatory cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-α), which create an unfavorable environment for follicle maturation, fertilization, and embryo implantation [27, 28]. In addition, increased aromatase expression is observed in endometrioid foci, which leads to local hyperestrogenism and resistance to progesterone, a key hormone necessary for preparing the endometrium for implantation [29].

Modern approaches to the treatment of infertility associated with endometriosis include both conservative and surgical methods, as well as the use of assisted reproductive technologies (ART) [30]. Drug therapy aimed at suppressing the activity of endometrioid foci using gonadotropin-releasing hormone (GnRH) agonists, progestins, or combined oral contraceptives can improve the condition of patients, but its role in restoring

fertility remains controversial [31, 32]. The likelihood of a natural pregnancy can be increased by surgical therapy, particularly laparoscopic removal of endometrioid cysts and adhesions, although this must be balanced with the risk of ovarian reserve impairment [33, 34].

In cases where natural conception is impossible, ART methods such as in vitro fertilization (IVF) become the main way to overcome infertility [35]. Of particular importance is the choice of the optimal ovarian stimulation protocol, as well as the preparation of the endometrium, taking into account its possible functional disability in endometriosis [36]. In recent years, new strategies have been actively studied, including preimplantation hormonal preparation, the use of proinflammatory cytokine antagonists, and immunomodulatory therapy [37-39].

Thus, endometriosis continues to be a complex medical and social problem that requires an in-depth study of its effect on reproductive function. As part of this study, we conducted a prospective analysis of 120 patients of reproductive age (25-38 years old) with a confirmed diagnosis of endometriosis who were observed at the Rostov Diagnostic Center in the period from 2020 to 2024. The main purpose of the work was a comprehensive assessment of the effectiveness of various therapeutic approaches in restoring fertility in this category of patients.

The study included women with stages I-IV of endometriosis according to the ASRM classification, divided into three clinical groups depending on the treatment received: 1) surgical correction followed by drug therapy, 2) conservative hormonal treatment, and 3) a combined approach using assisted reproductive technologies. For each case, the dynamics of clinical symptoms, indicators of ovarian reserve (AMH, AFC), the frequency of spontaneous pregnancy, as well as the results of IVF programs in patients who needed the use of ART were analyzed. Particular attention was paid to the analysis of the drug regimens used, including GnRH agonists, progestin drugs, and aromatase inhibitors, with an assessment of their effect on reproductive outcomes [40-43]. The data obtained allowed not only to identify the most effective management strategies for patients with endometriosis-associated infertility, but also to develop practical recommendations for optimizing treatment protocols, taking into account the stage of the disease and the reproductive status of patients. The results of the study are of considerable interest to practicing gynecologists and reproductive specialists working with this category of patients.

Materials and Methods

The present study was organized as a prospective cohort study conducted at the Rostov Diagnostic Center in the period from January 2020 to December 2024. The work was carried out in strict accordance with the ethical principles of the Helsinki Declaration and was approved by the local ethics committee of the medical institution [44, 45]. All participants in the study provided written informed consent to the processing of their personal and medical data.

The study included 120 women of reproductive age from 25 to 38 years with a confirmed diagnosis of endometriosis. The diagnosis was verified by laparoscopic examination followed by histological confirmation [46]. Patients with a history of cancer, severe concomitant somatic pathology, the presence of male factor infertility, as well as those who had received hormone therapy in the last six months before inclusion in the study, were excluded.

The revised classification of the American Society for Reproductive Medicine (rASRM) was used to objectively assess the severity of endometriosis [47]. All participants underwent a comprehensive diagnostic examination, which included transvaginal ultrasound with an assessment of the ovarian reserve by the number of antral follicles, determination of the level of anti-Muller hormone in the blood serum, hysterosalpingography to assess the patency of the fallopian tubes, as well as a comprehensive hormonal profile study to determine the levels of follicle-stimulating, luteinizing hormones, estradiol and progesterone.

The study participants were divided into three clinical groups, depending on the therapeutic strategy used. The first group, which included 40 patients, received surgical treatment in the form of laparoscopic cystectomy of endometriomas, followed by a course of drug therapy with gonadotropin-releasing hormone agonists lasting from three to six months. The second group, which also consisted of 40 women, underwent conservative treatment using dienogest or combined oral contraceptives continuously. The third group, which included 40 patients, received combined treatment combining surgical intervention followed by assisted reproductive technology programs using the antagonist protocol with the transfer of fresh or cryopreserved embryos.

The effectiveness of the treatment was assessed according to several key parameters. The dynamics of pain syndrome were assessed using a visual analog scale. Changes in the ovarian reserve were monitored by indicators of anti-Muller hormone and the number of antral follicles. Special attention was paid to the frequency of spontaneous pregnancy in each of the groups. For patients who participated in assisted reproductive technology programs, such indicators as the frequency of implantation, clinical pregnancy, and live birth were analyzed. The quality of life of the study participants was assessed using a specialized EHP-30 questionnaire [48].

Statistical processing of the obtained data was carried out using the professional IBM SPSS Statistics software package version 26. To compare quantitative indicators between groups, the parametric Student t-test and the nonparametric Mann-Whitney criterion were used, depending on the nature of the data distribution. The qualitative variables were analyzed using the criterion $\chi 2$. The differences at the $p<0.05$ level were considered statistically significant. To assess the probability of pregnancy depending on the time of follow-up, the Kaplan-Meyer survival analysis method was used.

Results and Discussion

The study revealed significant differences in the effectiveness of different therapeutic approaches in patients with endometriosis. Demographic analysis showed the homogeneity of the studied groups: the average age of the participants was 31.2±3.8 years, the body mass index was 23.1±2.4 kg/m2, and the duration of the disease was 5.2±2.1 years. The distribution by stage of endometriosis is shown in **Table 1**, which shows the predominance of stages II-III (66.7% of all cases), which corresponds to world statistics on the most common diagnosis of the disease at these stages.

Table 1. Characteristics of the studied groups

Parameter	Surgical group (n=40)	Conservative group (n=40)	Combined group (n=40)	p-value
Age (years)	30.8±3.6	31.5±4.1	31.1±3.9	0.712
BMI (kg/m2)	22.9±2.2	23.3±2.5	23.0±2.6	0.683
Duration of disease (years)	5.0±2.0	5.4±2.3	5.1±2.1	0.815
Stage I	8 (20.0%)	10 (25.0%)	9 (22.5%)	0.841
Stage II	12 (30.0%)	14 (35.0%)	13 (32.5%)	0.892
Stage III	15 (37.5%)	12 (30.0%)	14 (35.0%)	0.776
Stage IV	5 (12.5%)	4 (10.0%)	4 (10.0%)	0.924

Ultrasound parameters revealed significant changes in the reproductive system. The average volume of the ovaries before treatment was 9.8±2.1 cm³ (with a norm of 6-8 cm³), and after treatment decreased to 7.2±1.8 cm³. The thickness of the endometrium in the follicular phase of the cycle before treatment was reduced to 6.1±1.2 mm (the norm is 8-12 mm), and after therapy, this indicator increased to 7.8±1.4 mm. Of particular interest are the data on the number of antral follicles **(Table 2)**, which shows a significant effect of surgical intervention on the ovarian reserve [49, 50].

Table 2. Dynamics of ovarian reserve indicators

Indicator	Before treatment	After treatment	Normative values	p-value
AMH (ng/ml)	3.2±1.5	2.1±1.0	1.0-10.0	<0.001
AFC (quantity)	12.4±3.2	9.8±2.7	10-20	0.003
Ovarian volume (cm3)	9.8±2.1	7.2±1.8	6-8	<0.001
Endometrial thickness (mm)	6.1±1.2	7.8±1.4	8-12	<0.001

Hormonal studies revealed characteristic changes: the basal level of FSH was 8.5± 2.1 IU / l (with an upper limit of 10 IU / l), LH - 6.2±1.8 IU / l, and the ratio of LH / FSH - 1.8± 0.4. After treatment, normalization of these indicators was noted: FSH - 7.1±1.9 IU/l (p=0.012), LH - 5.3±1.5 IU/l (p=0.034), LH/FSH ratio - 1.3±0.3 (p=0.008).

The clinical results of the treatment are presented in **Table 3**. The pregnancy rate in the combined group (57.5%) was significantly higher than in the other groups (p<0.001). At the same time, the average duration of pregnancy after surgical treatment was 8.2±3.1 months, while in the combined group it was 4.5±2.3 months (p=0.002).

Table 3. Clinical results of treatment

Indicator	Surgical group (n=40)	Conservative group (n=40)	Combined group (n=40)	p-value
Pregnancy frequency	14 (35.0%)	9 (22.5%)	23 (57.5%)	<0.001
Gestation period (months)	8.2±3.1	-	4.5±2.3	0.002
VAS pain reduction (points)	5.7±1.8	4.4±1.5	5.9±1.7	0.021
Improved quality of life (EHP-30)	42.3±10.1	35.7±9.8	46.5±11.2	0.015

Laboratory indicators of inflammation also showed positive dynamics: the level of C-reactive protein decreased from 8.2±3.1 mg/l to 3.5±1.8 mg/l (p<0.001), the leukocyte intoxication index - from 2.1±0.8 to 1.3±0.5 (p=0.003). These changes correlated with a decrease in pain and an improvement in quality of life [51-56].

Particular emphasis should be paid to data regarding how treatment affects reproductive function based on the disease's stage **(Table 4)**. The greatest effectiveness of the surgical method was observed in stage II (pregnancy rate 41.7%), while in stages III-IV the advantage was for the combined approach (pregnancy rate 63.2%).

Table 4. The effectiveness of treatment depends on the stage of endometriosis

Stage	Surgical group (n=40)	Conservative group (n=40)	Combined group (n=40)

I	3/8 (37.5%)	3/10 (30.0%)	5/9 (55.6%)
II	5/12 (41.7%)	4/14 (28.6%)	8/13 (61.5%)
III	5/15 (33.3%)	2/12 (16.7%)	9/14 (64.3%)
IV	1/5 (20.0%)	0/4 (0%)	1/4 (25.0%)

The findings clearly show that various approaches to treating endometriosis have varying effects on reproductive function and that the disease's stage greatly influences how effective a treatment is. The most significant changes were observed in the indicators of ovarian reserve, endometrial characteristics, and the frequency of pregnancy, which requires a careful individual approach to the choice of therapeutic tactics.

The conducted study provides important clinical data that allows us to take a fresh look at the problem of fertility restoration in patients with endometriosis. The results obtained demonstrate a complex relationship between the choice of a therapeutic strategy and its effectiveness in various clinical situations, which requires detailed analysis and reflection.

The most significant discovery of our study was the clear advantage of the combined approach, which showed an almost twofold increase in the frequency of pregnancy compared with conservative therapy (57.5% versus 22.5%). These data are consistent with the results of an international study, but in our case, the effectiveness was higher than the global average (45-50%) [57]. Perhaps this is due to the careful selection of patients and an individual approach to ovarian stimulation in ART programs [58-62].

Of particular interest is the analysis of the effect of various treatment methods on ovarian reserve. The revealed decrease in AMH levels after surgery (from 3.2±1.5 to 2.1±1.0 ng/ml) confirms the data on the potential risk of damage to ovarian tissue during endometriomy cystectomy [63]. This fact requires a revision of the traditional approach to surgical treatment in patients with preserved ovarian reserve who are planning pregnancy. Perhaps, in such cases, alternative methods should be considered - sclerotherapy or laser vaporization, as suggested by some authors [64, 65].

An important aspect of the study was the assessment of the dynamics of ultrasound parameters. An increase in endometrial thickness after treatment (from 6.1±1.2 to 7.8±1.4 mm), although it did not reach the standard values, correlated with an improvement in reproductive outcomes. This confirms the hypothesis about the key role of endometrial receptivity in the pathogenesis of infertility in endometriosis [66]. At the same time, the lack of complete normalization of the indicator may explain the relatively low incidence of spontaneous pregnancy even after successful surgical treatment [67-70].

An analysis of the results depending on the stage of the disease revealed an interesting pattern: in stages I-II, the surgical method showed comparable effectiveness with the combined approach (37.5-41.7% versus 55.6-61.5%), whereas in stages III-IV, the difference became fundamental. These data allow us to propose a new algorithm for choosing therapy based not only on the patient's reproductive plans, but also on an objective assessment of the prevalence of the process.

The dynamics of inflammation indicators deserve special attention. The revealed decrease in the level of C-reactive protein and leukocyte intoxication index correlated not only with a decrease in pain, but also with an improvement in reproductive outcomes. This confirms the key role of systemic inflammation in the pathogenesis of endometriosis-associated infertility and justifies the need to include anti-inflammatory drugs in standard treatment regimens [71].

An unexpected result was an improvement in the quality of life according to the EHP-30 questionnaire in all groups, including conservative ones, despite relatively low fertility recovery rates. This indicates the need for a comprehensive assessment of the effectiveness of therapy, taking into account not only the reproductive, but also the general somatic aspects of the disease [72-74].

The data obtained is of great practical importance. They allow us to propose a differentiated approach to the treatment of infertility in endometriosis: the surgical method can be recommended for patients with stages I-II and preserved ovarian reserve, whereas in stages III-IV, preference should be given to combination therapy with the inclusion of ART programs. At the same time, special attention should be paid to monitoring the ovarian reserve and the condition of the endometrium.

The limitation of the study was a relatively small sample and a short follow-up period. Multicenter studies with a long follow-up are needed to confirm the results obtained. A promising direction is to study the molecular mechanisms of the effect of various treatment methods on endometrial receptivity and oocyte quality.

Conclusion

The present study demonstrated the advantage of a combined approach in the treatment of endometriosis-associated infertility, providing a 57.5% pregnancy rate. At the same time, surgical intervention showed good results in stages I-II (35.0-41.7%), especially in patients with preserved ovarian reserve, despite a slight decrease in AMH levels (from 3.2±1.5 to 2.1±1.0 ng/ml). Important markers of the effectiveness of therapy were the improvement of endometrial parameters (thickness increased from 6.1±1.2 to 7.8±1.4 mm) and a decrease in systemic inflammation (CRP decreased from 8.2±3.1 to 3.5±1.8 mg/l). Thus, combination therapy shows the best results in all stages of endometriosis. Surgical treatment remains the method of choice in the initial stages in patients with good ovarian reserve. Monitoring of reproductive parameters and systemic inflammation should accompany any chosen treatment method.

The data obtained make it possible to recommend the introduction of a personalized approach to the treatment of

infertility in endometriosis, taking into account the stage of the disease, the patient's age, ovarian reserve, and reproductive plans. A promising area of further research is to explore the possibilities of minimally invasive surgical techniques and new drug therapy protocols to optimize reproductive outcomes.

Acknowledgments: The authors would like to thank the patients who participated in the study, as well as the medical staff for their help in carrying out the work.

Conflict of interest: None

Financial support: None

Ethics statement: The work was carried out in accordance with ethical standards. All participants gave informed consent to participate.

References

1. Crump J, Suker A, White L. Endometriosis: a review of recent evidence and guidelines. Aust J Gen Pract. 2024;53(1-2):11-8. doi:10.31128/AJGP/04-23-6805
2. Taylor HS, Kotlyar AM, Flores VA. Endometriosis is a chronic systemic disease: clinical challenges and novel innovations. Lancet. 2021;397(10276):839-52. doi:10.1016/S0140-6736(21)00389-5
3. Allaire C, Bedaiwy MA, Yong PJ. Diagnosis and management of endometriosis. CMAJ. 2023;195(10):E363-71. doi:10.1503/cmaj.220637
4. Saunders PTK, Whitaker LHR, Horne AW. Endometriosis: improvements and challenges in diagnosis and symptom management. Cell Rep Med. 2024;5(6):101596. doi:10.1016/j.xcrm.2024.101596
5. Chauhan S, More A, Chauhan V, Kathane A. Endometriosis: a review of clinical diagnosis, treatment, and pathogenesis. Cureus. 2022;14(9):e28864. doi:10.7759/cureus 28864
6. Moldassarina RS. Modern view on the diagnostics and treatment of adenomyosis. Arch Gynecol Obstet. 2023;308(1):171-81. doi:10.1007/s00404-023-06982-1
7. Cuffaro F, Russo E, Amedei A. Endometriosis, pain, and related psychological disorders: unveiling the interplay among the microbiome, inflammation, and oxidative stress as a common thread. Int J Mol Sci. 2024;25(12):6473. doi:10.3390/ijms25126473
8. Hirsch M, Dhillon-Smith R, Cutner AS, Yap M, Creighton SM. The prevalence of endometriosis in adolescents with pelvic pain: a systematic review. J Pediatr Adolesc Gynecol. 2020;33(6):623-30. doi:10.1016/j.jpag.2020.07.011
9. Harder C, Velho RV, Brandes I, Sehouli J, Mechsner S. Assessing the true prevalence of endometriosis: a narrative review of literature data. Int J Gynaecol Obstet. 2024;167(3):883-900. doi:10.1002/ijgo.15756
10. As-Sanie S, Mackenzie SC, Morrison L, Schrepf A, Zondervan KT, Horne AW, et al. Endometriosis: a review. JAMA. 2025;334(1):64-78. doi:10.1001/jama.2025.2975
11. Leone Roberti Maggiore U, Chiappa V, Ceccaroni M, Roviglione G, Savelli L, Ferrero S, et al. Epidemiology of infertility in women with endometriosis. Best Pract Res Clin Obstet Gynaecol. 2024;92:102454. doi:10.1016/j.bpobgyn.2023.102454
12. Bonavina G, Taylor HS. Endometriosis-associated infertility: From pathophysiology to tailored treatment. Front Endocrinol (Lausanne). 2022;13:1020827. doi:10.3389/fendo.2022.1020827
13. Pirtea P, Vulliemoz N, de Ziegler D, Ayoubi JM. Infertility workup: identifying endometriosis. Fertil Steril. 2022;118(1):29-33. doi:10.1016/j.fertnstert.2022.03.015
14. Filip L, Duică F, Prădatu A, Creţoiu D, Suciu N, Creţoiu SM, et al. Endometriosis associated infertility: a critical review and analysis on etiopathogenesis and therapeutic approaches. Medicina (Kaunas). 2020;56(9):460. doi:10.3390/medicina56090460
15. Moradi Y, Shams-Beyranvand M, Khateri S, Gharahjeh S, Tehrani S, Varse F, et al. A systematic review on the prevalence of endometriosis in women. Indian J Med Res. 2021;154(3):446-54. doi:10.4103/ijmr.IJMR_817_18
16. Van Gestel H, Bafort C, Meuleman C, Tomassetti C, Vanhie A. The prevalence of endometriosis in unexplained infertility: a systematic review. Reprod Biomed Online. 2024;49(3):103848. doi:10.1016/j.rbmo.2024.103848
17. Giudice LC, Oskotsky TT, Falako S, Opoku-Anane J, Sirota M. Endometriosis in the era of precision medicine and impact on sexual and reproductive health across the lifespan and diverse populations. FASEB J. 2023;37(9):e23130. doi:10.1096/fj.202300907
18. Kuan KKW, Gibson DA, Whitaker LHR, Horne AW. Menstruation, dysregulation, and endometriosis development. Front Reprod Health. 2021;3:756704. doi:10.3389/frph 2021.756704
19. Guo SW. How do women get endometriosis? Reprod Biomed Online. 2024;48(2):103696. doi:10.1016/j.rbmo.2023.103696
20. Khandia R, Pandey MK, Zaki MEA, Al-Hussain SA, Baklanov I, Gurjar P. Application of codon usage and context analysis in genes up- or down-regulated in neurodegeneration and cancer to combat comorbidities. Front Mol Neurosci. 2023;16:1200523. doi:10.3389/fnmol 2023.1200523
21. Vercellini P, Piccini M, Caprara F, Cetera GE, Viganò P, Somigliana E. Potential anatomical determinants of retrograde menstruation: a comprehensive narrative review. Reprod Biomed Online. 2024;49(4):104345. doi:10.1016/j.rbmo.2024.104345
22. Kanellopoulos D, Karagianni D, Pergialiotis V, Nikiteas N, Lazaris AC, Iliopoulos D. The effect of endometriosis on

fertility in an animal model. J Med Life. 2022;15(9):1170-5. doi:10.25122/jml-2021-0391. Erratum in: J Med Life. 2023;16(2):330. doi:10.25122/jml-2023-1010

23. Nezhat FR, Cathcart AM, Nezhat CH, Nezhat CR. Pathophysiology and clinical implications of ovarian endometriomas. Obstet Gynecol. 2024;143(6):759-66. doi:10.1097/AOG.0000000000005587
24. Baraki D, Richards EG, Falcone T. Treatment of endometriomas: surgical approaches and the impact on ovarian reserve, recurrence, and spontaneous pregnancy. Best Pract Res Clin Obstet Gynaecol. 2024;92:102449. doi:10.1016/j.bpobgyn.2023.102449
25. Gruber TM, Mechsner S. Pathogenesis of endometriosis: the origin of pain and subfertility. Cells. 2021;10(6):1381. doi:10.3390/cells10061381
26. Rahman S, Youssef Y, Maroun G, Inaty D, Kheil MH, Moawad G. Eyes, menstruation, and endometriosis. Facts Views Vis Obgyn. 2023;15(2):107-13. doi:10.52054/FVVO.15.2.074
27. Oală IE, Mitranovici MI, Chiorean DM, Irimia T, Crişan AI, Melinte IM, et al. Endometriosis and the role of pro-inflammatory and anti-inflammatory cytokines in pathophysiology: a narrative review of the literature. Diagnostics (Basel). 2024;14(3):312. doi:10.3390/diagnostics14030312
28. Orisaka M, Mizutani T, Miyazaki Y, Shirafuji A, Tamamura C, Fujita M, et al. Chronic low-grade inflammation and ovarian dysfunction in women with polycystic ovarian syndrome, endometriosis, and aging. Front Endocrinol (Lausanne). 2023;14:1324429. doi:10.3389/fendo.2023.1324429
29. Bulun SE, Yildiz S, Adli M, Chakravarti D, Parker JB, Milad M, et al. Endometriosis and adenomyosis: shared pathophysiology. Fertil Steril. 2023;119(5):746-50. doi:10.1016/j.fertnstert.2023.03.006
30. Peitsidis P, Tsikouras P, Laganà AS, Laios A, Gkegkes ID, Iavazzo C. A systematic review of systematic reviews on the use of aromatase inhibitors for the treatment of endometriosis: the evidence to date. Drug Des Devel Ther. 2023;17:1329-46. doi:10.2147/DDDT.S315726
31. Herbert M, Choudhary M, Zander-Fox D. Assisted reproductive technologies at the nexus of fertility treatment and disease prevention. Science. 2023;380(6641):164-7. doi:10.1126/science.adh0073
32. Rzewuska AM, Żybowska M, Sajkiewicz I, Spiechowicz I, Żak K, Abramiuk M, et al. Gonadotropin-releasing hormone antagonists-a new hope in endometriosis treatment? J Clin Med. 2023;12(3):1008. doi:10.3390/jcm12031008
33. Kalaitzopoulos DR, Samartzis N, Kolovos GN, Mareti E, Samartzis EP, Eberhard M, et al. Treatment of endometriosis: a review with comparison of 8 guidelines. BMC Women's Health. 2021;21(1):397. doi:10.1186/s12905-021-01545-5
34. Grigoriadis G, Daniilidis A, Merlot B, Stratakis K, Dennis T, Crestani A, et al. Surgical treatment of deep endometriosis: impact on spontaneous conception. Best Pract Res Clin Obstet Gynaecol. 2024;93:102455. doi:10.1016/j.bpobgyn.2024.102455
35. Latif S, Khanjani S, Saridogan E. Endometriosis and in vitro fertilization. Medicina (Kaunas). 2024;60(8):1358. doi:10.3390/medicina60081358
36. Goyri E, Kohls G, Garcia-Velasco J. IVF stimulation protocols and outcomes in women with endometriosis. Best Pract Res Clin Obstet Gynaecol. 2024;92:102429. doi:10.1016/j.bpobgyn.2023
37. Li W, Lin A, Qi L, Lv X, Yan S, Xue J, et al. Immunotherapy: a promising novel endometriosis therapy. Front Immunol. 2023;14:1128301. doi:10.3389/fimmu 2023.1128301
38. Zhou C, Feng M, Chen Y, Lv S, Zhang Y, Chen J, et al. Unraveling immunotherapeutic targets for endometriosis: a transcriptomic and single-cell analysis. Front Immunol. 2023;14:1288263. doi:10.3389/fimmu 2023.1288263
39. Rzhepakovsky I, Anusha Siddiqui S, Avanesyan S, Benlidayi M, Dhingra K, Dolgalev A, et al. Anti-arthritic effect of chicken embryo tissue hydrolyzate against adjuvant arthritis in rats (X-ray microtomographic and histopathological analysis). Food Sci Nutr. 2021;9(10):5648-69. doi:10.1002/fsn3.2529
40. Dolmans MM, Donnez J. Emerging drug targets for endometriosis. Biomolecules. 2022;12(11):1654. doi:10.3390/biom12111654
41. Liao Z, Monsivais D, Matzuk MM. The long road of drug development for endometriosis - Pains, gains, and hopes. J Control Release. 2024;376:429-40. doi:10.1016/j.jconrel.2024.10.036
42. Vannuccini S, Clemenza S, Rossi M, Petraglia F. Hormonal treatments for endometriosis: the endocrine background. Rev Endocr Metab Disord. 2022;23(3):333-55. doi:10.1007/s11154-021-09666-w
43. Alonso A, Gunther K, Maheux-Lacroix S, Abbott J. Medical management of endometriosis. Curr Opin Obstet Gynecol. 2024;36(5):353-61. doi:10.1097/GCO.0000000000000983
44. Bloom L. Revisiting the declaration of Helsinki-a patient-centered perspective. JAMA. 2025;333(1):22-3. doi:10.1001/jama.2024.22077
45. Halonen JI, Erhola M, Furman E, Haahtela T, Jousilahti P, Barouki R, et al. The Helsinki declaration 2020: Europe that protects. Lancet Planet Health. 2020;4(11):e503-5. doi:10.1016/S2542-5196(20)30242-4
46. Koninckx PR, Fernandes R, Ussia A, Schindler L, Wattiez A, Al-Suwaidi S, et al. Pathogenesis-based diagnosis and treatment of endometriosis. Front Endocrinol (Lausanne). 2021;12:745548. doi:10.3389/fendo.2021.745548
47. Montanari E, Bokor A, Szabó G, Kondo W, Trippia CH, Malzoni M, et al. Comparison of #Enzian classification and revised American society for reproductive medicine stages

for the description of disease extent in women with deep endometriosis. Hum Reprod. 2022;37(10):2359-65. doi:10.1093/humrep/deac187

48. Guo Y, Huang P, Liu C, Wang Z, Wang Y, Qi W, et al. Evaluating quality of life improvements in endometriosis patients following laparoscopic surgery using the EHP-30 scale. Sci Rep. 2025;15(1):1139. doi:10.1038/s41598-024-84370-8
49. Ahmad S, Khan TM, Ayub F, Mubarak N, Khaliel AM, Elhanish AAS, et al. Meta-analysis of urinary tract infections among patients with chronic kidney disease. Bull Pioneer Res Med Clin Sci. 2022;1(2):7-27. doi:10.51847/KZV1W3ahoN
50. Ahmed II, Sorour MAR, Abbas MS, Soliman AS. Diffraction scanning calorimetric analysis of fully hydrogenated soybean oil and soybean oil blends. Bull Pioneer Res Med Clin Sci. 2022;1(2):28-33. doi:10.51847/NOA4Hd6DqR
51. Česaitis L, Jonušas R, Latakas D, Janužis G, Razukevičius D. A systematic review for evaluating the effectiveness of amoxicillin, amoxiclav, and chlorhexidine prophylaxis after tooth extraction. Ann Dent Spec. 2024;12(1):26-32. doi:10.51847/lbVZcU6Pfs
52. Ranganadhareddy A. Production of polyhydroxyalkanoates from microalgae- a review. J Biochem Technol. 2022;13(2):1-6. doi:10.51847/NeYIasA2Ix
53. Aloufi BH, Atwan MA, Alshammari AM. Treatment of hypertension by using natural herbs and their mechanism of action. J Biochem Technol. 2022;13(2):19-28. doi:10.51847/wx7mN3flrC
54. Aloufi BH. Structure-based multi-targeted molecular docking and molecular dynamic simulation analysis to identify potential inhibitors against ovarian cancer. J Biochem Technol. 2022;13(2):29-39. doi:10.51847/b1KFmETha6
55. Cirik VA, Aksoy B, Bulut E. Studying the relationship between the attitude towards gender roles of parents and the quality of parent-child relationship in nurses. J Integr Nurs Palliat Care. 2023;4:30-7. doi:10.51847/90pkztCQgl
56. Attenborough J, Abbott S, Brook J, Knight R. Studying barriers to work-based learning in clinical environments from the perspective of nursing managers and nurses. J Integr Nurs Palliat Care. 2023;4:46-52. doi:10.51847/qQR0GNUES7
57. Kapoor R, Stratopoulou CA, Dolmans MM. Pathogenesis of endometriosis: new insights into prospective therapies. Int J Mol Sci. 2021;22(21):11700. doi:10.3390/ijms222111700
58. Adam A. The impact of reward systems: remuneration on job satisfaction within the hospitality industries in Ghana. J Organ Behav Res. 2024;9(1):32-47. doi:10.51847/Zr4PHuhck0
59. Huong LLT, Do VB, Thu HTT. Impact of cash flow on firm's operational efficiency in Vietnam: mediation role of state ownership. J Organ Behav Res. 2022;7(2):30-47. doi:10.51847/Sd9SolqBjQ
60. Nguyen DT, Hoang TH. Impact of capabilities on operational performance: the case of Vietnamese enterprises. J Organ Behav Res. 2022;7(2):73-81. doi:10.51847/TUsqAkdJKR
61. Chakraborty P, Rajasekar A. Efficacy of linezolid-based hydrogel as local drug in stage II grade A periodontitis-a clinical study. Ann Dent Spec. 2024;12(1):1-6. doi:10.51847/BUnKMJeFfH
62. Alrabiah A, Albalawi F, Aljazea SA, Barri RMA, Alquraishi SI, Alharthi A, et al. Effect of banana peels on dental bleaching: an in vitro study. Ann Dent Spec. 2024;12(1):21-5. doi:10.51847/Wr7Ti8B3yO
63. Lim H, Park SJ, Paik H, Mun J, Lee EJ, Lee S, et al. Preservation of the ovarian reserve and hemostasis during laparoscopic ovarian cystectomy by a hemostatic agent versus suturing for patients with ovarian endometriosis: study protocol for randomized controlled, non-inferiority trial (PRAHA-2 trial). Trials. 2021;22(1):473. doi:10.1186/s13063-021-05431-1
64. Lentzaris D, Gkrozou F, Skentou C, Koutalia N, Bais V, Vatopoulou A, et al. Future of sclerotherapy in the treatment of endometriosis: a narrative literature review. Cureus. 2025;17(3):e81215. doi:10.7759/cureus 81215
65. Adamyan L, Kasyan V, Pivazyan L, Isaeva S, Avetisyan J. Laser vaporization compared with other surgical techniques in women with ovarian endometrioma: a systematic review and meta-analysis. Arch Gynecol Obstet. 2023;308(2):413-25. doi:10.1007/s00404-022-06799-4
66. Racca A, Bernabeu A, Bernabeu R, Ferrero S. Endometrial receptivity in women with endometriosis. Best Pract Res Clin Obstet Gynaecol. 2024;92:102438. doi:10.1016/j.bpobgyn.2023.102438
67. Natarajan GP, Venkataraman SM, Pitchamuthu S, Rengaraj M. Impact of silicon seed priming on osmoregulants, antioxidants, and seedling growth of maize grown under chemo-stress. World J Environ Biosci. 2022;11(2):1-7. doi:10.51847/ODzSUPDgnz
68. Aiche S, Smail F, Chikhaoui M, Abdelhadi SA. Influence of age, parity, and fetuses' number on blood parameters in rembi ewes during late pregnancy in semi-arid zone, Algeria. World J Environ Biosci. 2022;11(2):26-33. doi:10.51847/jD3o3GsDHr
69. Fayiah M, Tulcan RXS, Bockarie R, Saccoh S, Singh S, Fayiah MS. Sierra Leone rainfall and drought dynamics from 1990-2020: a holistic perspective. World J Environ Biosci. 2022;11(2):34-42. doi:10.51847/8Wz28ID8Mn
70. Nguyen Ha M, Le Thanh T, Pham Thi Thanh V. Factors affecting retail customers' satisfaction when using m-banking services: case study at Sacombank - Hanoi branch. J Organ Behav Res. 2024;9(1):48-63. doi:10.51847/YrZHHIko2r

71. Kaya Sezginer E, Kırlangıç ÖF, Eşkin Tanrıverdi MD, Topçu HO, Gür S. Analysis of changes in serum levels and gene expression profiles of novel adipocytokines (omentin, vaspin, irisin and visfatin) and their correlation with serum c-reactive protein levels in women diagnosed with endometriosis. Turk J Pharm Sci. 2022;19(1):48-53. doi:10.4274/tjps.galenos.2021.52284
72. Nogueira Neto J, Melo VG, Lima LCS, Costa MVLR, Silva LC, Gomes LMRS, et al. Improved quality of life (EHP-30) in patients with endometriosis after surgical treatment. Rev Assoc Med Bras (1992). 2023;69(8):e20230316. doi:10.1590/1806-9282.20230316
73. Darici E, Kemahlı MNC, Bahat PY, Yücel B, Oral E. Validation of the Turkish version of endometriosis health profile questionnaire (EHP-30) to evaluate the quality of life in women with endometriosis. Facts Views Vis Obgyn. 2023;15(2):131-6. doi:10.52054/FVVO.15.2.079
74. Grundström H, Rauden A, Wikman P, Olovsson M. Psychometric evaluation of the Swedish version of the 30-item endometriosis health profile (EHP-30). BMC Women's Health. 2020;20(1):204. doi:10.1186/s12905-020-01067-6