

SYSTEMATIC REVIEW

Efficacy and role of vitamin D (25-OH-D serum) in the treatment of endometriosis:
A systematic review

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Article Info	ABSTRACT
Received Mar 15, 2025 Revised Apr 30, 2025 Accepted May 16, 2025 Published Aug 1, 2025 *Corresponding author: Yuli Ayu Diani yuliayu.obgynfkub@gmail.com Keywords: 25-OH-D serum Chronic inflammation Endometriosis Immunologic response Maternal health Plasma level Vitamin D	Objective: Vitamin D, an essential element in women’s reproductive health, has shown potential benefits in endometriosis management by improving plasma concentrations and modulating immune responses in chronic inflammatory conditions, including endometriosis. This study aimed to elucidate the pivotal role of vitamin D in alleviating chronic pain and infertility associated with endometriosis and to provide new insights into its therapeutic application in reproductive medicine. Materials and Methods: This systematic review examined literature retrieved from PubMed, ScienceDirect, ResearchGate, and Google Scholar, screening 1,156 records and including 20 studies for qualitative assessment. The review focused on the therapeutic contribution of vitamin D in endometriosis management. Eligible studies were those published in the last decade, in English, involving non-pregnant, healthy women, particularly patients with chronic pelvic pain or infertility. Accepted study designs comprised experimental, cohort, longitudinal, case reports, pilot, and observational studies. Excluded were non-English articles, animal or pregnant populations, reviews, inaccessible full texts, and studies lacking relevance to vitamin D or endometriosis. Results: Twenty selected studies were analyzed, encompassing 5,346 women and 60 girls aged 12–50 years, with or without endometriosis, from Iran, the USA, South Korea, Russia, Turkey, Brazil, Poland, Italy, Germany, and Japan. These studies indicated that multiple therapeutic approaches were attempted, suggesting that endometriosis may be partially ameliorated by vitamin D administration. Conclusion: This systematic review highlights that women with endometriosis presented with lower vitamin D levels; however, the evidence regarding supplementation efficacy remains uncertain. Further large-scale, rigorously designed trials are necessary to establish vitamin D’s therapeutic role in the management of endometriosis.

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Highlights:

1. Endometriosis frequently causes pelvic damage and infertility, and vitamin D has been proposed as a therapeutic option owing to its involvement in immune regulation and reproductive health.
2. Vitamin D may contribute to the modulation of inflammatory pathways and decrease the risk of hyperplasia and malignancy, with several studies indicating that it might also impact infertility related to endometriosis.



INTRODUCTION

Endometriosis is a gynecological disorder defined by the ectopic presence of endometrial glands and stroma outside the uterine cavity, and it is widely recognized as an estrogen-dependent pathology.^{1,2} Globally, this condition represents the most prevalent gynecological disease, affecting 10 to 15% of reproductive-aged women and occurring at higher rates among infertile women (30 to 50%).² Despite multiple hypotheses proposed to explain the pathophysiology of endometriosis, its underlying cause and associated risk factors remain uncertain. Endometriosis is regarded as a multifactorial illness, with genetic, hormonal, immunological, and environmental factors all implicated in its development.³

Although the etiology of endometriosis has not been fully established, inflammatory mechanisms are considered to play a pivotal role in disease onset and progression.³ Moreover, the high prevalence of autoimmune disorders in women with endometriosis has been suggested as an additional contributing factor.⁴ The ectopic growth of endometrial tissue beyond the uterus may result in pelvic damage and impair fertility by disrupting uterine blood vessels, thereby compromising uterine oxygenation and nutrient supply. Clinical manifestations of endometriosis commonly include chronic pelvic pain and infertility.⁵ These complications significantly affect quality of life. Several investigations have reported that this pro-inflammatory state is associated with elevated cytokine and growth factor levels, diminished apoptosis, and increased angiogenesis, collectively contributing to symptom severity and pain.^{1,5}

Multiple therapeutic strategies have been proposed for endometriosis. Vitamin D acts through specific receptors and enzymes expressed in cervical and uterine tissues, vagina, endometrium, cervical epithelium, fallopian tubes, ovaries, and pituitary gland.⁶ It is recognized to exert immunomodulatory effects in chronic inflammatory states. This observation suggests that it may serve as a potential treatment for endometriosis, which shares features with autoimmune and neoplastic disorders.⁷ Several studies have indicated that polymorphisms of Vitamin D receptors (VDR) binding to Retinoid X Receptors (RXR) may constitute genetic risk factors associated with endometriosis-related infertility.⁸ Conversely, other research demonstrated that its capacity to increase plasma levels underscores a distinctive therapeutic role in endometriosis.⁸ Additional studies have also reported that vitamin D may reduce hyperplasia and malignancy risk by attenuating cellular proliferation and inducing apoptosis in tumor cells.⁹

This review explored the potential therapeutic role and efficacy of vitamin D (25-OH-D serum) in the management of endometriosis, with emphasis on alleviating chronic pain and infertility. We hypothesized that vitamin D supplementation may enhance clinical outcomes through modulation of inflammatory pathways and reduction of disease-related symptoms. Nonetheless, while numerous studies support beneficial effects of vitamin D in regulating immune responses and improving endometriosis manifestations, other findings have shown no significant improvement, highlighting inconsistency in available data and the necessity for further rigorous investigations.

MATERIALS AND METHODS

Literature searching

The present study comprised a comprehensive review of published literature. For this analysis, relevant articles were retrieved from electronic databases including PubMed, ScienceDirect, ResearchGate, and Google Scholar. The search strategy combined Medical Subject Headings (MeSH) with keyword phrases for Vitamin D, alongside MeSH and keyword terms for Endometriosis, Measurement Methods and Analysis, or Endometriosis in Gynecology. To optimize retrieval, search phrases were adapted according to the requirements of each database. For this review, all publications from 2014 to 2024 were identified and carefully evaluated for relevance and scientific rigor. The process was meticulously conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure transparency and reproducibility.

Eligibility criteria

The dataset for this review was classified into two categories: inclusion and exclusion criteria. Eligible designs included experimental studies, cohort studies, longitudinal investigations, case reports, social or pilot studies, and observational research, published within the last decade and written in English. Subjects were restricted to non-pregnant, healthy women, with or without endometriosis, regardless of ethnicity, with a particular focus on individuals experiencing chronic pain and infertility. An additional inclusion criterion required studies to report outcomes using a comparable unit of measurement, and when discrepancies occurred, standardized calculations were applied to ensure consistency and comparability across findings.

Study selection and screening

The reviewers independently conducted the screening of retrieved records. All titles, abstracts, and keywords were systematically assessed. Study quality was evaluated using both the PRISMA framework and the Mixed Methods Appraisal Tool (MMAT). The MMAT comprises five criteria for each study category, with assessments scored as Y (YES = 1), N (NO = 0), or C (Cannot tell = 0). Accordingly, the cumulative favorable responses determined the final methodological score and provided a structured framework for assessing overall study validity.

Data extraction

The methodology for this review adhered to defined core elements. The systematic review concentrated on endometriosis, a chronic, estrogen-dependent disorder associated with pain and infertility due to ectopic proliferation of endometrial tissue,^{7,10} and on vitamin D, particularly 25-hydroxyvitamin D (25-OH-D), which is central in maintaining calcium homeostasis and influencing immune regulation.¹¹ Included studies comprised experimental, cohort, review, and observational designs involving women of reproductive age (12–50 years). Various biochemical approaches were utilized across the studies, while extracted data encompassed study period, geographical setting, characteristics of intervention and control groups, outcome measures, and principal findings—including treatment effects on psychological symptoms as well as any documented adverse events or reported safety considerations.

RESULTS AND DISCUSSION

A total of 1,156 studies were initially identified, and following the removal of 710 duplicates, 446 articles remained eligible for title and abstract screening. Based on the predefined selection criteria, 313 studies were excluded. Subsequently, 133 full-text articles were assessed for eligibility, with 123 records excluded due to irrelevant outcomes, active control group designs, or non-English publication. Ultimately, 20 studies were included in the qualitative synthesis. [Figure 1](#) illustrates the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart outlining the research selection process.

In this systematic review, the overall population encompassed 5,346 women and 60 female rats with and without endometriosis, aged 12–50 years. The majority of studies were conducted in Iran,⁷ USA,³ South Korea,² Russia,² Turkey,¹ Brazil,¹ Poland,¹ Italy,¹ Germany,¹ and Japan.¹ [Table 1](#) provides descriptions of the 20 primary articles that were analyzed in this review.

Endometriosis is a chronic, painful, and persistent gynecological disorder characterized by the ectopic growth of endometrial glands, stroma, and endometrial-like tissue beyond the uterine cavity.^{14,15} It affects approximately 6–10% of women of reproductive age, increasing to 25–38% among those with chronic pelvic pain and 30–50% among infertile women.^{1,2,15} The clinical presentation commonly includes dysmenorrhea, dyspareunia, chronic pelvic pain, abnormal uterine bleeding, and infertility.¹⁵ Several theories, including retrograde menstruation and metaplasia, have been proposed, although these alone cannot explain the disease. Genetic, hormonal, and immunological factors are also considered significant contributors.⁴ Evidence from Iranian research indicates that endometriosis mimics autoimmune and malignant disorders by promoting angiogenesis and invasion of endometrial tissue into surrounding organs.^{5,7} Multiple treatment modalities have been recommended to improve patients' quality of life, including hormonal and metabolic therapy, surgical interventions, and lifestyle modifications such as exercise and dietary adjustments.⁵

Vitamin D, often referred to as the “secosteroid” vitamin because of its steroid-like structure with a cleaved carbon ring, is critical for numerous metabolic processes, particularly within female reproductive physiology.⁶ Several investigations suggest that vitamin D plays a role in regulating appropriate cellular proliferation and differentiation.⁷ It also modulates immune responses by enhancing anti-inflammatory cytokines while reducing pro-inflammatory cytokines.^{6,7} Vitamin D supplementation is considered essential in endometriosis, given the presence of receptors and enzymes required for its activation.⁶ All studies included in this review reported that women with endometriosis exhibited reduced serum concentrations of vitamin D compared with the general population. One study specifically identified hypovitaminosis D3 as a risk factor for endometriosis.⁵ Nevertheless, vitamin D levels were not significantly associated with disease severity, although one study demonstrated that serum 25-OH-D levels correlated with gravidity.^{3,4}

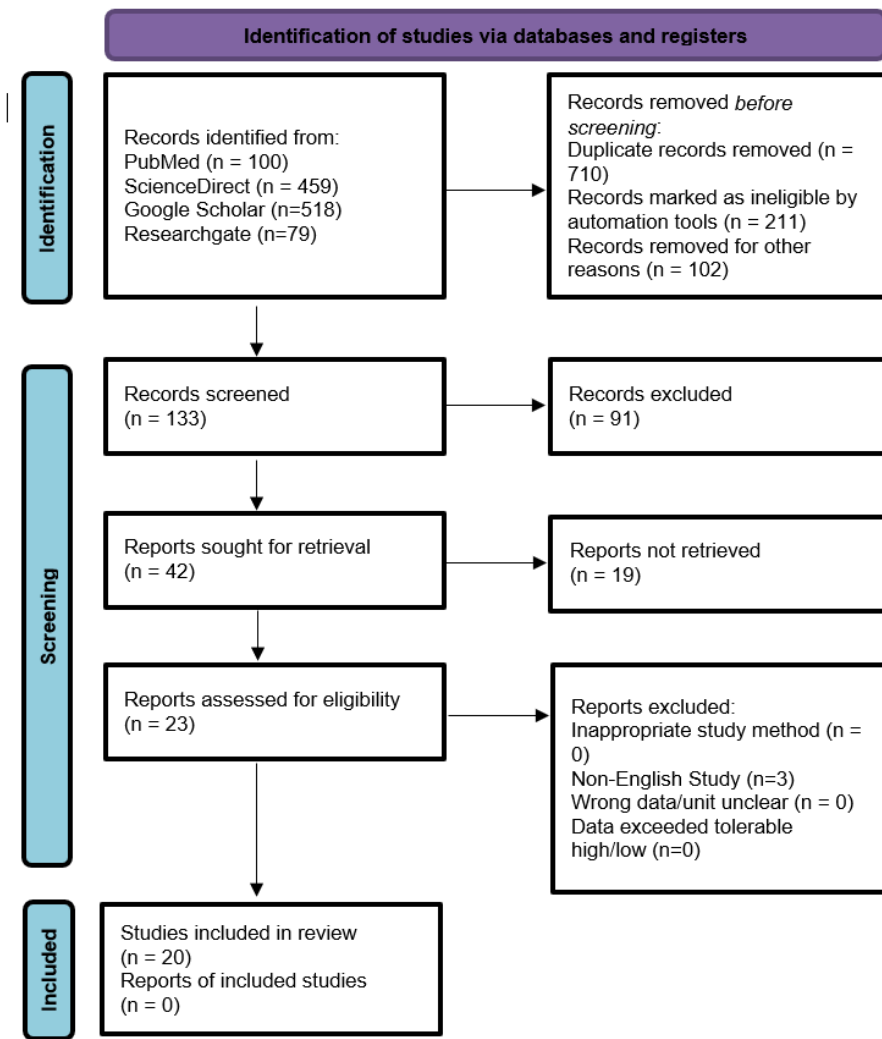


Figure 1. PRISMA flowchart of the literature selection

Table 1. Selected review studies

	Author(s) and article titles	Methods	Determinant variables	Conclusions
1	Nodler, James L et al (2020) With the title "Supplementation with vitamin D or ω-3 fatty acids in adolescent girls and young women with endometriosis (SAGE)"	1. Study Design: A double-blind, randomized, placebo-controlled experiment. 2. Research location: Pediatric Gynecology Clinic at Boston Children's Hospital (BCH). 3. Population: aged 12-25 females having a surgical diagnosis of endometriosis. 4. Sample: 69 participants	1. Age 2. Race 3. BMI 4. VAS pain score 5. Severity or staging of diagnosis (endometriosis)	Supplementing teenage women with Vitamin D after surgically diagnosed endometriosis resulted in a statistically significant improve in pelvic pain status.
2	Akyol, Alpaslan et al (2015) With the title "Efficacies of vitamin D and omega-3 polyunsaturated fatty acids on experimental endometriosis"	1. Study Design: Prospective, single-blind, randomized, controlled experimental investigation. 2. Research location: Firat University Experimental Research Center. 3. Population: mature female Wistar albino rats weighing 200-220 g. 4. Sample: 30 female rats	1. Weight 2. Endometriosis induction 3. Laparoscopic surgery	The study found that Vitamin D supplementation reduced the size and histopathologic changes in endometriosis. However, the regression of omega-3 fatty acids is more substantial than Vitamin D.

3	Baek, Jong Chul et al (2019) With the title "Differences in 25-hydroxy vitamin D and vitamin D-binding protein concentrations according to the severity of endometriosis"	1. Study Design: Observational Study 2. Research Location: Gyeongsang National University Hospital, Jinju, Korea 3. Population: All patients underwent laparoscopy to stage the severity of their endometriosis Sample: 32 participants	1. Age 2. Race 3. BMI 4. Gravidity 5. Parity 6. Diagnosis 7. Laparoscopy diagnostic 8. Vitamin D serum level	According to research, the blood level of 25(OH)D is not substantially connected with the severity of endometriosis, however it is correlated with pregnancy. It is determined that the 25(OH)D serum level correlates with the frequency of births.
4	Cho, Min-Chul et al (2019) With the title "Analysis of vitamin D-binding protein (VDBP) gene polymorphisms in Korean women with and without endometriosis"	1. Study Design: Prospective, observational study 2. Research Location: Gyeongsang National University Hospital, Jinju, Korea 3. Population: All patients with endometriosis had a definitive diagnosis on a pathological review of their surgical specimens 4. Sample: 32 participants	1. Age 2. Race 3. BMI 4. Diagnosis 5. Laparoscopy diagnostic 6. Vitamin D serum level	This study showed that Korean women with endometriosis disease have lower level of Vitamin D serum
5	Nameni, Farah and Mahssadat Ebrahimmosavi (2023) With the title "The Effects of Vitamin D3 Supplementation and Simultaneous Exercise on Aldehyde Dehydrogenase Gene Expression in Endometriosis Female Rats"	1. Study Design: The experimental method with a post-test design 2. Research Location: Islamic Azad University, Varamin, Iran 3. Population: three-month-old female Wistar rats (mean weight = 200 - 250 g) 4. Sample: 30 female rats divided into 6 categories: (1) healthy group, (2) endometriosis group, (3) endometriosis and placebo group, (4) endometriosis and Vitamin D group, (5) endometriosis and simultaneous exercise, (6) endometriosis and simultaneous exercise and Vitamin D	1. Age 2. Weight 3. Endometriosis Induction 4. Exercise 5. Vitamin D supplementation	Hypovitaminosis D3 is a risk factor for endometriosis, and vitamin D supplementation increases the ALDH genes for detoxification of endometriosis-produced aldehydes. Exercise is shown to reduce endometriosis symptoms.
6	Lopes, Vinicius Medina et al (2017) With the title "Highly prevalence of vitamin D deficiency among Brazilian women of reproductive age"	1. Study Design: retrospective cross-sectional design 2. Research Location: record of patients who visited a Brazilian assisted reproduction center between January 1, 2012 and May 15, 2012 3. Population: all infertile patients who were treated between January 1 and May 15, 2012. The control group included 30–45-year-old women who were treated at the clinic 4. Sample: 369 eligible women	1. Age 2. Race 3. Infertility condition 4. Chronical pain 5. Endometriosis	The study found that 32.9% of Brazilian women met the criterion for vitamin D supplementation; however, there was no significant variation in 25(OH)D blood levels based on reproductive status.
7	Almassinokiani, Fariba et al (2016) With the title "Effects of Vitamin D on Endometriosis-Related Pain"	1. Study Design: randomized, double-blind clinical trial 2. Research Location: single tertiary university hospital in Iran 3. Population: Women with age of 15–40 years, proven endometriosis by laparoscopy and a VAS test score of 3 or more for dysmenorrhea and/or pelvic pain 4. Sample: 39 participants	1. Age 2. Race 3. BMI 4. Laparoscopic diagnostic 5. VAS test 3 for dysmenorrhea and/or pelvic pain	Although there may be a link between vitamin D with endometriosis pathogenesis, our study found that vitamin D was ineffective in treating endometriosis-related pain. Larger clinical trials had to establish the potential benefits of vitamin D supplementation in endometriosis therapy.
8	Szczepanska, Malgorzata et al (2015) With the title "Polymorphic variants in vitamin D signaling pathway genes and the risk of endometriosis-associated infertility"	1. Study Design: Prospective, Observational Study 2. Research Location: The Gynecologic and Obstetrical University Hospital, Division of Reproduction at Poland 3. Population: A total of 154 subjects were infertile women with endometriosis, and 347 women	1. Age 2. Race 3. BMI 4. Laparoscopic Diagnostic for endometriosis or infertility 5. Duration of infertility	The study demonstrated that the genetic factor can be one of the risk factors of endometriosis. VDR haplotype had a risk factor for endometriosis-associated infertility and supplementation of Vitamin D can help improvement of the endometriosis symptoms.

		were used as fertile controls 4. Sample: 501 participants	6. Parity	
9	Tabassi, Zohreh et al (2017) With the title “Clinical and Metabolic Response to Vitamin D Supplementation in Endometrial Hyperplasia”	1. Study Design: randomized double-blind placebo-controlled clinical trial 2. Research Location: Naghavi Clinic in Kashan, Iran 3. Population: premenopausal women diagnose with endometrial disorder (such as endometrial hyperplasia, endometriosis etc), aged 35–55 years old 4. Sample: 60 participants	1. Weight 2. Height 3. Race 4. Age	Vitamin D supplementation for 12 weeks effect in glucose metabolism, serum hs-CRP, and plasma TAC concentration. Vitamin D may play indirect role to decrease the complication of endometrial disorder.
10	Yarmolinskaya, Maria et al (2021) With the title “Vitamin D significance in pathogenesis of endometriosis”	1. Study Design: Observational Study 2. Research Location: The Research Institute of Obstetrics, Gynecology and Reproductology, Russia 3. Population: women of reproductive age with GE diagnosis and confirmed morphologically 4. Sample: 211 participants	1. Age 2. Race 3. BMI 4. Gynecological Endometriosis confirmed after laparoscopic diagnostic	This study found that the cholecalciferol level and pain syndrome in endometriosis are conflicting. There is no significant difference in dysmenorrhea and persistent pelvic pain reduction following colecalciferol treatment compared to placebo.
11	Delbandi, Ali-Akbar et al (2015) 1,25-Dihydroxy Vitamin D3 Modulates Endometriosis-Related Features of Human Endometriotic Stromal Cells	1. Study Design: Pilot Study 2. Research Location: Iran University of Medical Sciences, Tehran, Iran 3. Population: women with ovarian endometriosis aged 29 and nonendometriosis with mean age 32 4. Sample: 45 participants	1. Age 2. Laparoscopy diagnostic 3. Three months not taken any hormonal medication	Overall, the study demonstrated for the very first time that 1,25(OH)2D3 has several favorable impacts on endometriosis-related aspects of ESCs from endometriotic patients, indicating the potential utility of this hormone in endometriosis treatment.
12	Mehdizadehkashi, Abolfazl et al (2021) The effect of vitamin D supplementation on clinical symptoms and metabolic profiles in patients with endometriosis	1. Study Design: randomized double-blind placebo-controlled clinical trial 2. Research Location: Rasoul Akram Hospital, Tehran, Iran 3. Population: women with endometriosis aged 18–40 year without diabetes mellitus, thyroid disease, hypertension, hyperprolactemia, and Cushing syndrome 4. Sample: 40 participants	1. Age 2. BMI 3. Malondialdehyde (MDA) status 4. Other metabolic status correlate to endometriosis	The current study found that Vitamin D administration in endometriosis patients resulted in a substantial reduction in chronic pain, total cholesterol/HDL ratio, hs-CRP, and TAC levels. Another clinical and metabolic symptom has no effect.
13	Xie, Baoli et al (2023) With the title “Association between vitamin D and endometriosis among American women: National Health and Nutrition Examination Survey ¹² ”	1. Study Design: population-based cross-sectional survey 2. Research Location: The National Center for Health Statistics 3. Population: American women around aged 20–54 years from 2001 to 2006 4. Sample: 3,232 women, of whom 257 had endometriosis and 2,975 did not	1. Age 2. Pregnancy 3. Race 4. Marital Status 5. Education Level 6. Vigorous/Moderate activity 7. Smoking status	In representative sample of American women, higher serum of 25(OH)-D concentration will decrease the risk of endometriosis.
14	Yaghoubi, Hadi Mohagheghian et al (2020) Immunomodulatory effects of vitamin D3 on gene expression of MDGF, EGF and PDGFB in endometriosis	1. Study Design: In-vitro Experimental study 2. Research Location: Iran University of Medical Sciences, Iran 3. Population: Thirty-eight patients with a clinical diagnosis of endometriosis and 26 non-endometriotic women with benign gynaecological problems 4. Sample: PFMC from 10 women with endometriosis and 10 control participants	1. Age 2. BMI 3. Cycle phase 4. Marital status 5. Infertility	This study discovered that in-vitro results suggested that Vitamin D3 might significantly reduce PDGFB and EGF gene expression, which was reported to be enhanced in the peritoneal fluids of endometriosis patients.
15	Chamgordani, Samira Najafi et al (2024) Evaluation of the natural killer cell subsets and their relationship with	1. Study Design: Case-control study 2. Research Location: The Immunology Department of Isfahan University of Medical Sciences, Iran	1. Age 2. Race 3. BMI 4. Marital status	In conclusion of this study, the level of serum in vitamin D and IFN-γ has increased in women with endometriosis compared to control group

	serum interferon gamma and vitamin D levels in women with stages III and IV endometriosis ¹³	3. Population: women of reproductive age (18–45 yr) 4. Sample: 59 participants		
16	Ciavattini, Andrea et al (2016) With the title “Ovarian endometriosis and vitamin D serum levels”	1. Study Design: Cohort, Observational study 2. Research Location: Polytechnic University of Marche, Ancona, Italy 3. Population: childbearing-age women diagnosed with singleton ovarian endometrioma 4. Sample: 49 participants	1. Age 2. BMI 3. Tobacco use 4. Menarche 5. Infertility 6. Number of pregnancies	This study examined that the hypotaminosis D could have role in development of endometriosis disease and correlate with the severity of this disease. This study also suggested that supplementation of Vitamin D is novel, safe, and low-cost treatment of endometriosis.
17	Agic, Admir (2014) Relative Expression of 1,25-Dihydroxyvitamin D3 Receptor, Vitamin D 1α-Hydroxylase, Vitamin D 24-Hydroxylase, and Vitamin D 25-Hydroxylase in Endometriosis and Gynecologic Cancers	1. Study Design: Experimental Study 2. Research Location: University of Schleswig-Holstein, Department of Gynecology and Obstetrics, Ratzeburgerallee, Germany 3. Population: women undergoing laparoscopy and women with endometrial and ovarian cancer 4. Sample: 79 participants	1. Age 2. BMI 3. Marital status 4. Menarche 5. Infertility	Given the emerging evidence of vitamin D's anti-proliferative and anti-inflammatory actions, ⁴⁰ we hypothesize that the vitamin may influence the activity of local immune cells and also their cytokine production, which have previously been identified as important factors in the development and also maintenance of endometriosis.
18	Miyashita, Mariko et al (2016) With the title “Effects of 1,25-Dihydroxy Vitamin D3 on Endometriosis”	1. Study Design: Experimental, in-vitro Study 2. Research Location: University of Tokyo 3. Population: Endometriosis tissues in patients with ovarian endometriosis 4. Sample: 35 participants	1. Age 2. BMI 3. Endometriosis status	This study indicated that Vitamin D supplementation may reduce disease development, and lower Vitamin D levels were connected with endometriosis.
19	Denisova, Alexander S. et al (2021) With the title “Assessment of 25(OH)D status in patients with genital endometriosis and clinical efficacy of cholecalciferol in the treatment of the disease”	1. Study Design: Observational Study 2. Research Location: D.O. Ott Scientific Research Institute of Obstetrics, Gynecology, and Reproduction 3. Population: patients with genital endometriosis with age around 33.7 ± 5.8 years and had various degrees of disease prevalence 4. Sample: 440 participants	1. Age 2. BMI 3. Endometriosis-associated pain 4. EGE grades I-IV	This study found that a dosage of 2 mg combined with cholecalciferol was the most beneficial for endometriosis.
20	Pazhohan, Azar et al (2020) With the title “The modulating effects of vitamin D on the activity of b-catenin in the endometrium of women with endometriosis”	Study Design: randomized exploratory trial Research Location: Alzahra hospital, Iran Population: women with endometriosis stage III and VI diagnosed using laparoscopic with age 22–37 year Sample: 34 participants	1. Age 2. BMI 3. Endometriosis diagnosed after laparoscopic 4. Menstrual cycle	This study demonstrated that vitamin D can change the defective pathway of wnt/b-catenin and signaling in the endometrium of endometriosis patients by inactivating b-catenin.

Several in vitro experiments and population-based investigations among American women have demonstrated that adequate serum levels of vitamin D may inhibit the progression of endometriosis, indicating that lower vitamin D concentrations are associated with increased prevalence of this disease.¹⁶⁻¹⁹ Multiple reports have emphasized the significant role of vitamin D as both an anti-proliferative and anti-neoplastic factor, exerting effects through genomic and non-genomic pathways. The genomic pathway, mediated through the vitamin D receptor (VDR), appears particularly critical since VDR expression is markedly elevated in endometriotic tissue. When vitamin D supplementation binds to VDR, it may reduce disease

progression.¹⁹ A Russian study highlighted the genetic contribution of vitamin D in endometriosis-associated infertility, demonstrating that reduced serum 25-OH-D levels correlate with specific gene variations, thereby playing an important role in limiting the progression of endometriosis.¹⁰ Supporting this hypothesis, another study identified a particular VDR haplotype within endometrial tissue of affected women as a risk factor for endometriosis.⁸ In contrast, research from Brazil found no significant relationship between vitamin D serum levels and infertility status in women with endometriosis, thereby underscoring persistent controversy regarding the association of vitamin D with the disease.⁶

Oral vitamin D3 supplementation has been suggested as a potentially safe, accessible, and low-cost therapeutic approach for managing endometriosis.¹⁹⁻²⁰ Mechanistic evidence indicates that vitamin D may inactivate β -catenin signaling in endometriosis patients, thereby limiting disease progression.²¹ Moreover, supplementation has been shown to decrease peritoneal fluid concentrations of sCD44 in affected individuals.²² Several studies reported improved outcomes in chronic pain management following vitamin D supplementation when combined with surgical intervention. Additional findings support that vitamin D intake enhances not only chronic pelvic pain relief but also improves metabolic parameters such as total/HDL cholesterol ratio, hs-CRP levels, and TAC activity.²³ Nevertheless, a study from Iran revealed no significant efficacy of vitamin D supplementation in alleviating endometriosis-associated pain.⁷ Further evidence suggests that vitamin D may contribute primarily to delaying or regressing disease progression rather than exerting substantial effects on pain or infertility management.⁹

This review provides a comprehensive synthesis of the association between vitamin D levels and endometriosis, offering an important preliminary foundation for evaluating vitamin D as both a potential risk factor and therapeutic adjunct in disease management. However, inconsistent findings across studies regarding supplementation outcomes complicate the ability to establish definitive conclusions. Furthermore, the lack of adequately powered, large-scale randomized clinical trials remains a major limitation in confirming the clinical significance and therapeutic benefit of vitamin D supplementation for endometriosis.

CONCLUSION

This review indicates that women with endometriosis exhibit lower vitamin D levels, and deficiency of vitamin D has been described as one of the potential risk factors for endometriosis. However, the association between vitamin D supplementation and endometriosis treatment remains controversial. While certain studies demonstrate clinical improvement, others report no significant correlation or therapeutic benefit of vitamin D supplementation in the management of endometriosis. Therefore, larger well-designed trials are required to further investigate and clarify the possible therapeutic effects of vitamin D supplementation in endometriosis treatment.

DISCLOSURES

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Conflict of interest

No conflicting interests are present in this review.

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Author contribution

All authors have contributed to all process in this research, including preparation, data gathering and analysis, drafting and approval for publication of this manuscript.

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