

## SYSTEMATIC REVIEW

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

Yuli Ayu Diani<sup>ID\*</sup>, I Wayan Arsana Wiyasa<sup>ID</sup>

Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia

Article Info	ABSTRACT
<p>Received Mar 15, 2025 Revised Apr 30, 2025 Accepted May 16, 2025 Published Aug 1, 2025</p> <p><b>*Corresponding author:</b> Yuli Ayu Diani yuliyau.obgynfkub@gmail.com</p> <p><b>Keywords:</b> 25-OH-D serum Chronic inflammation Endometriosis Immunologic response Maternal health Plasma level Vitamin D</p>	<p><b>Objective:</b> A vital component of women's reproductive health, vitamin D has also demonstrated promise in the treatment of endometriosis by enhancing plasma levels and controlling immunological responses in chronic inflammation, including endometriosis. This study sought to shed light on the critical role that vitamin D plays in treating chronic pain and infertility related to endometriosis, as well as to offer fresh perspectives on the therapeutic application of vitamin D in reproductive medicine.</p> <p><b>Materials and Methods:</b> This systematic review analyzed literature from PubMed, ScienceDirect, ResearchGate, and Google Scholar, screening 1,156 articles and selecting 20 studies for qualitative synthesis. The focus was on the therapeutic role of vitamin D in treating endometriosis. Inclusion criteria included studies published in the last ten years, in English, involving non-pregnant, healthy women, particularly those with chronic pelvic pain or infertility. Accepted study designs included experimental, cohort, longitudinal, case reports, pilot, and observational studies. Exclusion criteria included non-English publications, animal or pregnant subjects, reviews, inaccessible full texts, and studies lacking relevant on vitamin D or endometriosis.</p> <p><b>Results:</b> Twenty eligible studies were selected, involving 5346 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 found that many treatments were tried or done to be able to say that endometriosis can be cured in part by vitamin D.</p> <p><b>Conclusion:</b> This systematic review demonstrates that women with endometriosis had reduced vitamin D levels, but evidence on supplementation benefits remains inconclusive. Larger, well-designed trials are needed to confirm vitamin D's role in endometriosis treatment.</p>

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#### Highlights:

1. A frequent gynecological condition that affects 10–15% of women who are fertile is endometriosis, often leading to pelvic damage and infertility, and has been suggested to be treated with vitamin D due to its role in the immune system and reproductive health.
2. Vitamin D may help regulate inflammatory responses and reduce the risk of hyperplasia and cancer, with some studies suggesting it could also influence infertility associated with endometriosis.



## INTRODUCTION

Endometriosis is a gynecological condition characterized by the development of endometrial glands and stroma outside the uterus, and it is well known as an estrogen-dependent pathology.<sup>1,2</sup> According to worldwide data, this condition is the most common gynecological disease, involving 10 to 15% of reproductive women and being more prevalent in infertile women (30 to 50%).<sup>2</sup> Despite various ideas attempting to explain the pathophysiology of endometriosis, the cause and associated risk factors remain unknown. Endometriosis is a complex illness, since genetic, hormonal, immunological, and environmental variables have all been linked to it.<sup>3</sup>

Although the etiology of endometriosis is unknown, the inflammatory process is thought to have a crucial role in its development and progression.<sup>3</sup> Another aspect revealed that autoimmune illness is widespread in women with endometriosis, which is believed to be one of the contributing factors.<sup>4</sup> Endometrial tissue growth outside the uterine cavity can cause pelvic injury and impede fertility by disrupting the uterine blood arteries, causing harm to the uterus's oxygenation and feeding. Endometriosis symptoms can include persistent pelvic discomfort and infertility.<sup>5</sup> This will also have an impact on their life. According to several research, this pro-inflammatory condition is characterized by raised cytokine and growth factor levels, reduced cell apoptosis, and enhanced angiogenesis, all of which contribute to increased pain.<sup>1,5</sup>

Several treatments have been suggested to treat this disease. Vitamin D is a vitamin that affects certain receptors and enzymes in cervical, uterine tissues, vaginal, endometrial, cervical epithelia, and epithelial cells in fallopian tubes, ovaries, also pituitary glands.<sup>6</sup> It is reported to have immune regulatory effects in chronic inflammatory responses. This suggested that its can be used to treat endometriosis, which mimics some autoimmune and malignant diseases.<sup>7</sup> Some studies have found that Vitamin D receptors (VDR) that bind to Retinoid X Receptors (RXR) variations may be genetic risk factors related to endometriosis infertility.<sup>8</sup> However, a research found that it's ability to increase blood plasma levels suggests that it plays a unique function in the treatment of endometriosis.<sup>8</sup> Some studies have also found that its may lower hyperplasia and cancer risk by reducing cellular proliferation and inducing apoptosis in cancer cells.<sup>9</sup>

This review investigates the role and effectiveness of vitamin D (25-OH-D serum) as a therapeutic option for endometriosis, particularly in alleviating chronic pain and infertility. We hypothesize that vitamin D supple-

mentation may improve clinical outcomes by reducing inflammation and disease symptoms. However, while several studies encourage the positive benefits of vitamin D in modulating inflammatory responses and improving endometriosis-related symptoms, other investigations have reported no significant clinical improvement, inconsistency in current findings and the need for further robust evidence.

## MATERIALS AND METHODS

### Literature searching

This current study involves a comprehensive review of the literature. For this investigation, we looked for relevant publications published in electronic databases such as PubMed, ScienceDirect, Research Gate, and Google Scholar. The combination of the search method between Medical Subject Headings (MeSH) and keyword search phrases for Vitamin D with MeSH and keyword search terms for Endometriosis Measurement Methods and Analysis or Endometriosis in the Gynecology. To improve results, search phrases were adjusted to the specific database. For this review, all articles from 2014 to 2024 were identified and analyzed. We adhered to the recommended Reporting Items for Systematic Review and also Meta-analysis (PRISMA) criteria.

### Eligibility criteria

The data for the present study were divided into two categories; inclusion criteria and exclusion criteria. All experimental studies, cohort studies, longitudinal studies, case report studies, social or pilot studies and observational studies – within the last ten years and with English as the language – were included in this study. The subjects of non-pregnancy and healthy women – with or without endometriosis, from any race, and especially those who have chronic pain and infertility – were selected to be included for the present study. Inclusion criteria also all studies need to have the same unit of measurement and if it is different, it was equated with a standardized calculation.

### Study selection and screening

The reviewers performed the screening procedure for the studies. All titles, abstracts, and keywords were examined. The reviewers assessed the quality of the studies in the current systematic review using the PRISMA technique and the Mixed Methods Appraisal Tool (MMAT). This tool included five items for each group, which were assessed as Y (YES = 1), N (NO =

0), or C (Cannot tell = 0). In other words, the favorable response was decided the final score.

### Data extraction

The methodology for this systematic review is based on several key components. This systematic review focuses on endometriosis, a chronic, hormone-dependent disorder causing pain and infertility due to the growth of endometrial tissue outside the uterus,<sup>7,10</sup> and vitamin D, particularly 25-hydroxyvitamin D (25-OH-D), which regulates calcium balance in the body.<sup>11</sup> The review includes experimental, cohort, review, and observational studies involving women of reproductive age (12-50 years). Furthermore, various biochemical methods were used throughout the studies, and factors such as the study period, country of origin, characteristics of intervention and control groups, outcome measures, and key findings—including the effectiveness of the intervention on psychological symptoms and any reported adverse events—were extracted for analysis.

## RESULTS AND DISCUSSION

A total of 1,000 one hundred and fifty-six studies were identified, and after deleting 710 duplicates, 446 articles were qualified for title and abstract evaluation. According to the selection criteria, 313 studies were eliminated. Then, 133 full-text papers and publications were assessed for eligibility, with 123 records discarded owing to unrelated outcomes, active control group designs, or non-English language. The qualitative synthesis concluded with the inclusion of 20 papers. [Figure 1](#) depicts the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis) flowchart of the research selection procedure.

In this review, the total number of participants included was 5,346 women and 60 female rats with and without endometriosis, aged 12-50 years. Most of these studies were conducted in Iran,<sup>7</sup> USA,<sup>3</sup> South Korea,<sup>2</sup> Russia,<sup>2</sup> Turkey,<sup>1</sup> Brazil,<sup>1</sup> Poland,<sup>1</sup> Italy,<sup>1</sup> Germany,<sup>1</sup> and Japan.<sup>1</sup>

[Table 1](#) presents descriptions of 20 primary articles that were included in this study.

Gynecological endometriosis is a painful and persistent inflammatory illness characterized by the development of endometrial glands and stroma, as well as endometrial-like tissue outside the uterine cavity or ectopic region.<sup>14,15</sup> This impacted around 6-10% of reproductive-age women, rising to 25-38% in women with persistent pelvic discomfort and 30-50% in infertile women.<sup>1,2,15</sup> Endometriosis is commonly linked to dysmenorrhea, dyspareunia, persistent pelvic discomfort, irregular uterine bleeding, and infertility.<sup>15</sup> Many endometriosis ideas include retrograde menstruation and metaplasia. However, it cannot stand alone; other variables, such as genetics and immunology, play a significant role in endometriosis.<sup>4</sup> According to an Iranian research, endometriosis mimics various autoimmune and malignant illnesses by boosting angiogenesis and endometrial tissue invasion into certain organs.<sup>5,7</sup> Several treatments have been suggested to improve the living conditions of the patient, such as hormonal and metabolic treatment, several surgeries, and also changing lifestyle, like exercise and dietary options, to change the physical condition.<sup>5</sup>

Vitamin D, sometimes known as the "secosteroid" vitamin, which is comparable to a steroid with a broken carbon ring, is essential for a variety of metabolic processes in the body, particularly in women's reproductive systems.<sup>6</sup> Some studies suggest that vitamin D has a function in appropriate cellular growth control.<sup>7</sup> This vitamin also regulates the inflammatory response, increasing anti-inflammatory cytokines while decreasing pro-inflammatory cytokines.<sup>6,7</sup> Vitamin D supplementation is crucial in endometriosis because it contains receptors and an enzyme necessary for production.<sup>6</sup> All of the studies in this review showed that compared to the general population, women with endometriosis had decreased serum levels of vitamin D. A study found that hypovitaminosis D3—specifically—is the risk factor for endometriosis.<sup>5</sup> However, vitamin D level was not significantly related to the severity of endometriosis, but a study examined that this vitamin (25-OH-D serum) correlated with gravidity.<sup>3,4</sup>

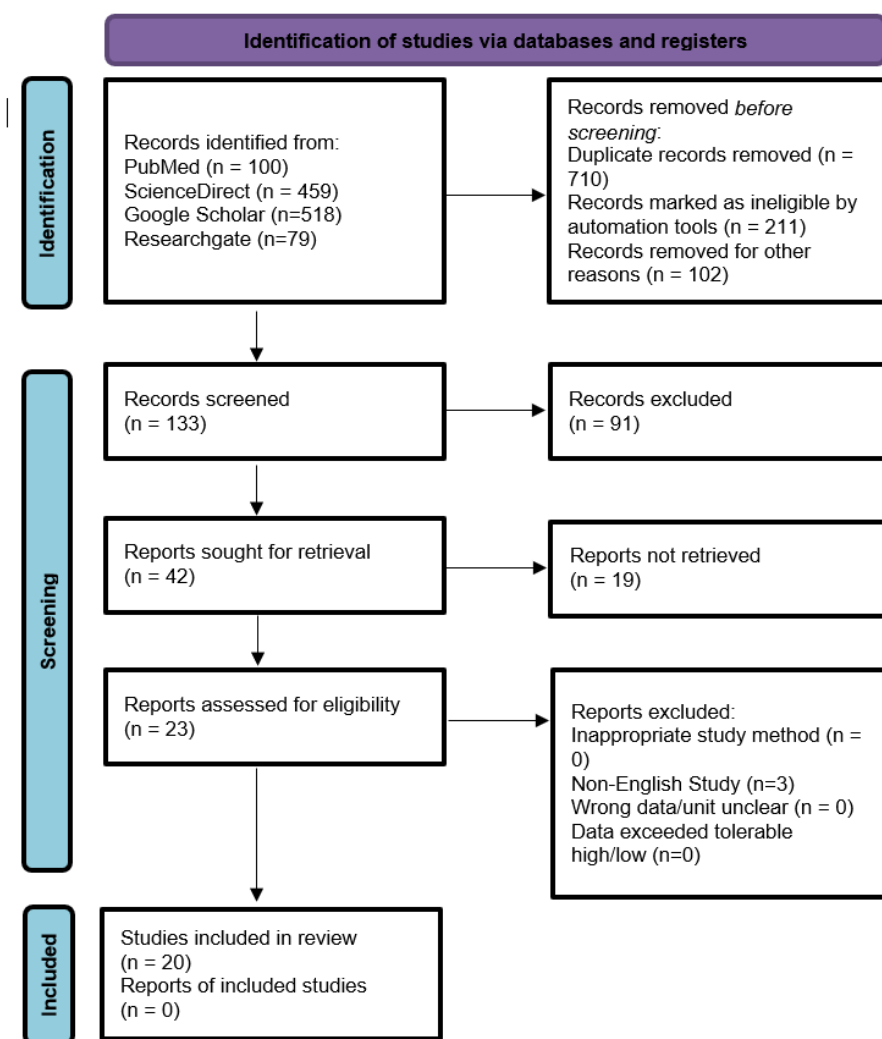


Figure 1. PRISMA flowchart of the literature selection

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 <sup>12</sup> ”	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 <sup>13</sup>	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 1 $\alpha$ -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, <sup>40</sup> 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 $\pm$ 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 studies in vitro and population studies in American women demonstrated that vitamin D serum levels may prevent the progression of endometriosis, which shows that the lower serum level of vitamin D is associated with the prevalence of endometriosis.<sup>16-19</sup> From some reports, vitamin D shows that it has an important role as an anti-proliferative and anti-neoplastic, which affects genomic and non-genomic ways. The genomic action through VDR is more important, as VDR is highly expressed in endometriosis. Vitamin D supplementation will be bonded to VDR so that this will decrease the progression of the disease.<sup>19</sup> A study in Russia explained the gene contribution in

vitamin D and endometriosis-associated infertility. The study demonstrated that 25-OH-D serum will decrease the level of this gene variation and play an important role in decreasing the progression of endometriosis.<sup>10</sup> Another study supported this hypothesis, which explained that the VDR haplotype—which is found in women's endometrial tissue—is the risk factor for endometriosis.<sup>8</sup> However, the study in Brazil shows that there is no significant correlation between vitamin D serum level and the infertility status of women with endometriosis. Therefore, there is a controversy about the relation between vitamin D and endometriosis.<sup>6</sup>

The use of vitamin D3 intake may be one possible, safe, and low-cost option for endometriosis treatment.<sup>19-20</sup> Vitamin D was also demonstrated to inactivate  $\beta$ -catenin in endometriosis patients. This shows that vitamin D may be used to decrease the progression of this disease.<sup>21</sup> Also, one study showed that vitamin D supplementation decreased the EF concentration of sCD44 in the endometriosis.<sup>22</sup> Some studies show an improvement in chronic pain of endometriosis after consuming vitamin D supplementation with surgical treatment. Another study supported that vitamin D intake will improve, resulting in chronic pelvic pain and another metabolic profile, such as total/HDL-cholesterol ratio, hs-CRP, and TAC levels.<sup>23</sup> However, a study in Iran showed that vitamin D supplementation was not effective in treating endometriosis-associated pain.<sup>7</sup> Explained in another study that vitamin D might just delay and regress the progression of endometriosis but not have much effect in treating the pain or infertility.<sup>9</sup>

This study provides a comprehensive overview of the relationship of vitamin D levels and the condition of endometriosis through a systematic review, thus providing an initial basis for understanding the potential role of vitamin D as one of the risk factors and therapeutic possibilities in the management of endometriosis. However, there are inconsistent findings between studies regarding the effectiveness of vitamin D supplementation on endometriosis treatment, making it difficult to draw strong conclusions. In addition, the absence of large-scale clinical trials is a major limitation in confirming the significant benefits of vitamin D supplementation.

## CONCLUSION

In conclusion, this review show that Vitamin D level in women with endometriosis found lower and the deficiency of Vitamin D condition explained as one of the risk factors of endometriosis. However, there is still a controversy for the correlation between Vitamin D supplementation to endometriosis treatment. Some studies clearly show the improvement, but some explain no significant correlation and benefit for treating endometriosis with Vitamin D supplementation. Larger trials might be needed to explore and indicate possible effects of the Vitamin D supplementation for endometriosis treatment.

## DISCLOSURES

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No recognition and/or acknowledgement is present.

## Conflict of interest

No conflicting interests are present in this research.

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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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