Asian Journal of Health Research
Journal Homepage: https://a-jhr.com
Published by Ikatan Dokter Indonesia Wilayah Jawa Timur

Original Research

Association between Vitamin D 1,25 (OH)2 D3 Serum with Endometriosis-Related Pelvic Pain and Infertility Condition in Endometriosis

I Wayan Arsana Wiyasa, Daniel Alexander Suseno, Febie Putra Suwana*

Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Brawijaya/Saiful Anwar General Hospital, Malang, East Java, Indonesia

ARTICLE HISTORY
Received: 16 May 2025
Revised: 23 June 2025
Accepted: 28 July 2025

CORRESPONDING AUTHOR*
Febie Putra Suwana
Febieppds@gmail.com
Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Brawijaya/Saiful Anwar General Hospital, Malang, East Java, Indonesia

KEYWORDS
Endometriosis; Pelvic Pain; Infertility; Vitamin D

This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/)

ABSTRACT

Introduction: Endometriosis is an estrogen-dependent chronic inflammatory disease characterized by the growth of endometrial tissues outside the endometrium or in the pelvic area. This condition is usually found in reproductive women, 15 – 49 years old. Chronic pelvic pain related to endometriosis is one of the major symptoms that makes women come to the clinic, besides dysmenorrhea and dyspareunia. This condition also affects the fertility of women, which, in some reports, shows that 30 – 50% women with endometriosis are also infertile. Vitamin D is a type of vitamin that is popular for treating reproductive problems. Vitamin D (1,25 (OH)2 D3) serum is important in inflammation and implantation, which supports overcoming endometriosis symptoms.

Material and Methods: The Present study performed a cross-sectional study. A total of ninety-one women were included in this study, which was divided into three groups: the normal group, the pelvic pain group, and the infertility pain group. The results were confirmed by ANOVA and a LSD 95% test.

Results: There is a difference in Vitamin D (1,25 (OH)2 D3) serum level in the chronic pelvic pain group and/or infertility group. This significantly shows that there is a correlation between those variables.

Conclusion: There is a significant difference in Vitamin D (1,25 (OH)2 D3) serum levels between the control group and the pelvic pain or infertility group. This show sthat there is a significant correlation between Vitamin D serum with chronic pelvic pain related-endometriosis and/or infertility related-endometriosis. However, this correlation score remains low and is considered insignificant.

Cite this as: Wiyasa IWA, Suseno DA, Suwana FP (2025) Association between Vitamin D 1,25 (OH)2 D3 Serum with Endometriosis-Related Pelvic Pain and Infertility Condition in Endometriosis. *Asian J Heal Res.* 4 (2): 39–43. doi: 10.55561/ajhr.v4i2.253

INTRODUCTION

As one of the gynecological problems, commonly affecting reproductive women, Endometriosis is a condition characterized by the endometrial tissues growing outside the uterus, but still inside the pelvis and around the organs close by. Since 1600 BC, this disease still well known as "disease of theory" [1]. From the report in 2014, this disease can affect any population and races, 6-10% women of reproductive age globally. It shows that endometriosis affects every 1 in 10 productive women aged 15 – 49 years, or around 176 million women worldwide [2].

There are various studies to observe clinical and biomolecular theories for endometriosis and its etiopathogenesis, but it remains unclear. Nowadays, new studies show that the inflammation theory is the most rational theory to explain the pathogenesis of this disease [2,3]. This theory explains that the tissue that grows ectopic will trigger the expression of macrophages, cytokines, and growth factors in the peritoneal fluid, which will stimulate the growth even more [1].

Major symptoms of endometriosis are pain. Three types of pain correlate with endometriosis involve dysmenorrhea, dyspareunia, and chronic pelvic pain.

Usually, the patient will complain about these three types of pain [4]. Pain is a subjective and very complex experience, which the patient needs to describe. Furthermore, the endometriosis questionnaire is used to diagnose endometriosis. The total severity consists of 4 elements, including pelvic pain, dysmenorrhea, dyspareunia, pelvic tenderness, and induration, which every elements consists of 4 grades; 0 means nothing, 1 means mild, 2 means moderate, and 3 means severe.

The correlation between endometriosis and infertility remains unclear. Women with infertility have 6 – 8 times higher risk of getting endometriosis than normal women [5,6]. From previous studies, 25 – 50% women diagnosed with endometriosis 30 – 50% also diagnosed as infertile. Some theories submitted for the association between endometriosis and infertility such as the abnormality of pelvic anatomy, abnormalities of endocrinology and ovulation, hormonal changes, and mediator cells in the endometrium. Popular theory for this correlation is that the inflammatory process in endometriosis can damage the ovum and sperm [6].

Vitamin D is one kind of vitamin that has a useful effect. Nowadays, this vitamin keeps being studied and developed for its function in reproduction. These studies focused on the anti-inflammatory function of Vitamin D, anti-proliferation, and anti-invasive effect of Vitamin D, which were documented in an in-vitro study in synovial fibroblasts case of rheumatoid arthritis in 2012, dendritic cells in psoriasis in 2017, and its effect for cancer treatment in 2015 [7,8]. Previous studies suggested that the immunomodulatory effect of Vitamin D (1,25(OH)2 D3 will inhibit the activation and proliferation process of T cells and suppress the production of IL-2 and Interferon in Th1, which this mechanism will reduce the symptoms of endometriosis. [9,10,11].

This study will focus on evaluating Vitamin D (125 (OH)2 D3) serum concentration in women diagnosed with endometriosis. This study will show the deficiency of Vitamin D serum in endometriosis and its clinical spectrum. It will also show the correlation between serum Vitamin D concentration with pelvic pain and infertility in endometriosis. The knowledge from this study, in the short term, can be included in patient consultation, those suspected with endometriosis. Furthermore, this study can be used as consideration for developing Vitamin D (1,25 (OH)2 D3) serum prototype addition to endometriosis therapy. [12].

MATERIAL AND METHODS

A cross-sectional study was carried out to examine the association between Vitamin D (125 (OH2) D3) Vitamin D serum with Pelvic Pain and Infertility in Endometriosis in dr. Saiful Anwar General Hospital Malang, in the period from February to July 2020. The total sample consists of 93 women who are divided into 3 groups consist of 31 normal women as controls, 31 women with chronic pelvic pain, and 31 women with infertility. The sample was taken by inclusion criteria only, without exclusion criteria. The inclusion criteria is women who are diagnosed with endometriosis and confirmed with the Pathology Anatomy Laboratory result, where the sample is chosen by two additional criteria, such as (1) women diagnosed with endometriosis and chronic pelvic pain, and (2) women with endometriosis and infertility. The sample size was determined using the correlation coefficient from a study conducted [5,10,11,13], and the formula for correlation calculation was used to establish the sample size.

The concentration of Vitamin D (1,25 (OH)2 D3) serum was measured by the Central Laboratory of RSUD dr. Saiful Anwar Malang used the ELISA method using the blood sample up to 5 mL drawn from the cubital fossa vein. The result is divided into three categories: normal if the concentration is between 30-100 ng/mL, insufficiency if 20 – 29,9 ng/mL, and deficiency if the concentration is less than 20 ng/mL. The degree of pelvic pain is measured by anamnesis and physical examination based on the Biberoglu and Behrman score (Questionnaire of Endometriosis) [4]. The total score is based on 5 elements, consisting of pelvic pain evaluation score, dysmenorrhea, dyspareunia, pelvic tenderness, and induration. The scores were categorized into 0: nothing, 1: mild, 2: moderate, 3: severe. Infertility is measured by anamnesis based on the definition, which means the failure of pregnancy at least 12 weeks after normally having sexual intercourse (primary infertility), and/or inability to become pregnant or maintain the pregnancy (secondary infertility) [10,14].

The statistical analysis was conducted using SPSS version 20.0 for Windows. This study used ANOVA (Analysis of Variance), a one-way test. If the H_0 is rejected, then continued by an LSD 95% test.

RESULTS

A total of ninety-one women participated in this study, divided into 3 groups consist of 31 normal women as controls, 31 women with chronic pelvic pain, and 31 women with infertility. To analyze the correlation between Vitamin D (1,25 (OH)2 D3) serum with pelvic pain and infertility in endometriosis, Table 1 shows the result of the correlation between Vitamin D serum with pelvic pain and infertility in endometriosis using the ANOVA test. Table 1 shows that Sig. is 0,000 less than $\alpha = 5\%$. Therefore, at the real level = 5% we reject Ho, so the conclusion obtained is that there is a significant difference in the average vitamin D levels of the three

Table 1. Correlation between Vitamin D (1,25 (OH)2 D3) Serum with Pelvic Pain and Infertility in Endometriosis

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	26691.332	2	13345.666	124.110	.000
Within Groups	9677.749	90	107.531		
Total	36369.081	92			

Table 2. Correlation between Vitamin D Serum Levels with Pelvic Pain and Infertility in Endometriosis

(I) Vitamin D Serum	(J) Vitamin D Serum	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Normal	Pelvic Pain	33.96129*	2.63390	.000	28.7286	39.1940
	Infertility	37.63226*	2.63390	.000	32.3995	42.8650
Chronic Pelvic Pain	Normal	-33.96129*	2.63390	.000	-39.1940	-28.7286
	Infertility	3.67097	2.63390	.167	-1.5617	8.9037
Infertility	Normal	-37.63226*	2.63390	.000	-42.8650	-32.3995
	Pelvic Pain	-3.67097	2.63390	.167	-8.9037	1.5617

*. The mean difference is significant at the 0.05 level.

Table 3. Correlation Between Vitamin D (1,25 (OH)2 D3) Serum Levels with Chronic Pelvic Pain in Endometriosis and Symptoms Variation

		Pelvic Pain Symptoms	Vitamin D Serum Levels
Pelvic Pain	Pearson Correlation	1	.125
	Sig. (2-tailed)		.502
	N	31	31
Vitamin D Serum Levels	Pearson Correlation	.125	1
	Sig. (2-tailed)	.502	
	N	31	31

groups (normal patients, pelvic pain, and infertility). Since the ANOVA shows there is a significant difference in Vitamin D, to identify which group has the difference, the data was analyzed using the LSD test.

Based on Table 2, showed the correlation between Vitamin D levels in normal patients (control group) and Vitamin D levels in the chronic pelvic pain group, the score is Sig. 0,000 significant in real level 5%. The score explained that there is a significant difference in Vitamin D serum levels in the control group and the patients with chronic pelvic pain. For Vitamin D serum levels in the control group and infertility group, Table 2 showed Sig. 0,000 significant in real level 5%. Based on the score, summarized that there is a significant difference in Vitamin D serum levels in the control group and the patients with infertility.

Based on Table 3, it can be analyzed that the correlation score between Vitamin D serum levels with symptoms variation of pelvic pain is 0,125, with a significant score is 0,502. The correlation score 0,125 shows that there is a positive correlation between Vitamin D serum levels and pelvic pain symptoms, which means that the higher the level of Vitamin D serum will increase in pelvic pain symptoms. However, this correlation is still very low and considered insignificant, as shown in a significant score of 0,502, that bigger than the real level of 0,05.

DISCUSSION

This study found that from ANOVA test and LSD 95% tests, the results show that there is a significant difference between Vitamin D (1,25 (OH)2 D3) serum level in the normal group and patients with chronic pain level and/or infertility in endometriosis. Based on the correlation score found that there is a correlation between the increased levels of Vitamin D serum with the pelvic pain symptoms in endometriosis. According to theories, endometriosis is one of the estrogen-dependent inflammatory conditions, which the major symptom reported globally is chronic pelvic pain. This symptom occurs because the endometrium tissue presented grows outside endometrium, in the pelvic cavity or organs around. The endometrium tissue will then trigger the inflammatory response [15].

Dietary is one of the keys to controlling endometriosis, which it is believed that diet contributes to some regulators for inflammation, associated with smooth muscle contractility, the immune system, and it estrogenic effect [16]. Endometriosis has a very complex

etiology, which involves genetic factors, hormonal, immunologic, and other environmental factors [17]. Recently, endometriosis has shown immunology disorders, also mimicking tumor and malignancy problems. Base on pathophysiology, this condition influence inflammatory mediators, which the place of tissue grow and it will giving the pelvic pain symptoms. [16].

From this perspective, previous studies show that Vitamin D (1,25 (OH)2 D3) serum will significantly work to reduce the pelvic pain level, by decreasing prostaglandin synthesis and increasing the prostaglandin inactivation, 1,25(OH)2 Vitamin D will decrease the pelvic pain [16]. Sadly, Vitamin D deficiency is found to be high nowadays [17]. Although the role of Vitamin D serum in endometriosis treatment is still unclear and debated, some studies with mice and rats induced endometriosis samples reported that the Vitamin D dosage given to animals with endometriosis is higher than the normal group. However, on the contrary, a study in women with endometriosis found that Vitamin D serum levels is higher [17]. There may be an association between Vitamin D (1,25 (OH)2 D3) serum level with endometriosis-related pelvic pain in some previous research, but until now, this association remains controversial. Some studies have not shown any difference or low difference in the result, just like this study.

Specifically in fertility studies, reported that 25 – 50% infertile women have endometriosis, and it supported by reports that show among endometriosis women, 30 – 50% are infertile. This strongly linked that the condition is caused by pelvic anatomy, altered peritoneal function, abnormality of the ovulation process, and failure of implantation. A lot of studies show that Vitamin D plays an important role in implantation, in which 1,25 (OH)2 D3 is involved in activation of the HOXA10 gene. This gene is potentially important in stimulating the expression of RNA [16]. Only one cohort study about fertility-related endometriosis, which the results show that there is a similar cumulative pregnancy rate between the Vitamin D and placebo group [18–20].

The low population size in this study is a main limitation. Another limitation presented in the sample which not all can be presented the population of endometriosis, which not all pelvic pain and infertility patients are confirmed diagnosed by endometriosis. The majority of the population only have the symptoms but are not diagnosed with endometriosis. Endometriosis is a disease with multifactorial symptoms. Lastly, the Vitamin D correlation remains unclear with pelvic pain-related endometriosis and infertility-related endometriosis, which this study only focuses on the difference in serum level and considers insignificant.

CONCLUSION

Endometriosis is a disease well known for its correlation with estrogen-dependent chronic inflammatory disease, which this disease characterized by endometrial tissues that grow in the pelvic cavity. The symptoms of this condition include chronic pelvic pain or dysmenorrhea and dyspareunia. Laparoscopy can be performed to diagnose this condition. According to theories, nutritional support will help the progress and outcome of this condition. Vitamin D (1,25 (OH)2 D3) serum is one of the dietary treatments that can support this condition. This study shows that there is a significant difference in Vitamin D (1,25 (OH)2 D3) serum levels between the control group and the pelvic pain or infertility group. This shows that there is a significant correlation between Vitamin D serum with chronic pelvic pain related-endometriosis and/or infertility related-endometriosis. However, this correlation score remains low and is considered insignificant.

ACKNOWLEDGMENT

We thank all the authors of the articles reviewed in this article.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

1. Parasar, P., Ozcan, P. and Terry, K. L. (2017) 'Endometriosis: Epidemiology, Diagnosis and Clinical Management', *Current Obstetrics and Gynecology Reports*. doi: 10.1007/s13669-017-0187-1.
2. Sopiyudin Dahlan, M. (2016) *Besar Sampel dalam Penelitian Kedokteran dan Kesehatan*, *Sagung Seto*.
3. Burney, R. O. and Giudice, L. C. (2012) 'Pathogenesis and pathophysiology of endometriosis', *Fertility and Sterility*. doi: 10.1016/j.fertnstert.2012.06.029.
4. Irani, M. and Merhi, Z. (2014) 'Role of vitamin D in ovarian physiology and its implication in reproduction: A systematic review', *Fertility and Sterility*. Elsevier Inc., 102(2), pp. 460-468.e3. doi: 10.1016/j.fertnstert.2014.04.046.
5. Liu, T. *et al.* (2017) 'NF-κB signaling in inflammation', *Signal Transduction and Targeted Therapy*. doi: 10.1038/sigtrans.2017.23.

6. Gilmore, T. D. (2006) 'Introduction to NF-κB: Players, pathways, perspectives', *Oncogene*. doi: 10.1038/sj.onc.1209954.
7. Donnez, J. *et al.* (2016) 'Endometriosis and infertility', *Panminerva Medica*. doi: 10.1007/978-1-4471-4953-8_3.
8. Mehedintu, C. *et al.* (2014) 'Endometriosis still a challenge', *Journal of medicine and life.*
9. Bourdel, N. *et al.* (2015) 'Systematic review of endometriosis pain assessment: How to choose a scale?', *Human Reproduction Update*. doi: 10.1093/humupd/dmu046.
10. Barrea, L. *et al.* (2017) 'Vitamin D and its role in psoriasis: An overview of the dermatologist and nutritionist', *Reviews in Endocrine and Metabolic Disorders*. doi: 10.1007/s11154-017-9411-6.Riccio, L. da G. C. *et al.* (2018) 'Immunology of endometriosis', *Best Practice and Research: Clinical Obstetrics and Gynaecology*. doi: 10.1016/j.bpobgyn.2018.01.010.
11. Schoenmakers, I. and Jones, K. S. (2017) *Pharmacology and Pharmacokinetics*. Fourth Edi, *Vitamin D: Fourth Edition*. Fourth Edi. Elsevier Inc. doi: 10.1016/B978-0-12-809965-0.00037-9.
12. Stratton, P. and Berkley, K. J. (2011) 'Chronic pelvic pain and endometriosis: Translational evidence of the relationship and implications', *Human Reproduction Update*. doi: 10.1093/humupd/dmq050.
13. Jakobsen, J. and Jäpelt, R. B. (2012) 'Vitamin d', in *Handbook of Analysis of Active Compounds in Functional Foods*. doi: 10.1201/b11653.
14. Harada, T. (2014) *Endometriosis: Pathogenesis and treatment*, *Endometriosis: Pathogenesis and Treatment*. doi: 10.1007/978-4-431-54421-0.
15. Adamson, G. D. and Pasta, D. J. (2010) 'Endometriosis fertility index: The new, validated endometriosis staging system', *Fertility and Sterility*. doi: 10.1016/j.fertnstert.2009.09.035.
16. Somigliana, E. *et al.* (2007) 'Vitamin D reserve is higher in women with endometriosis', *Human Reproduction*, 22(8), pp. 2273–2278. doi: 10.1093/humrep/dem142.
17. Facchin, F. *et al.* (2015) 'Impact of endometriosis on quality of life and mental health: Pelvic pain makes the difference', *Journal of Psychosomatic Obstetrics and Gynecology*. doi: 10.3109/0167482X.2015.1074173.
18. Vilarino, F. L. *et al.* (2011) 'Analysis of vitamin D receptor gene polymorphisms in women with and without endometriosis', *Human Immunology*. Elsevier Inc., 72(4), pp. 359–363. doi: 10.1016/j.humimm.2011.01.006.
19. Morotti, M., Vincent, K. and Becker, C. M. (2017) 'Mechanisms of pain in endometriosis', *European Journal of Obstetrics and Gynecology and Reproductive Biology*. doi: 10.1016/j.ejogrb.2016.07.497.
20. Mormile, R. and Vittori, G. (2014) 'Vitamin D intake and endometriosis: The good and the bad', *European Journal of Obstetrics and Gynecology and Reproductive Biology*. Elsevier Ireland Ltd, 177(2014), pp. 152–153. doi: 10.1016/j.ejogrb.2014.02.023.