



The Role of Vitamin D in Endometrial Receptivity for Successful Implantation

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Abstract

Successful embryo implantation depends on endometrial receptivity during the implantation window, which involves gene regulation, decidualization, and local immune modulation. Vitamin D has received attention due to the expression of the vitamin D receptor (VDR) in the endometrium and its role in regulating receptor gene transcription. To review the scientific evidence regarding the association of vitamin D levels with endometrial receptivity and implantation outcomes in assisted reproductive technology (ART). A literature review was conducted through a systematic search of PubMed, Google Scholar, and ScienceDirect (2020–2026). Observational human studies assessing vitamin D levels on endometrial parameters or pregnancy outcomes were included; eight studies met the criteria. Vitamin D plays a role in the regulation of HOXA10, HAND2, decidualization, and the tolerogenic immune balance. However, clinical outcomes are heterogeneous; some studies show benefits primarily in deficiency states, while others find no significant associations with implantation rate or live birth rate. Vitamin D has the potential to be a permissive factor in endometrial receptivity, but it is not a primary determinant of implantation success.

Keywords:

Vitamin D;
Endometrial Receptivity;
Embryo Implantation;
Assisted Reproductive
Technology.

INTRODUCTION

Infertility is the inability of a couple to achieve pregnancy after having regular sexual intercourse without contraception for at least 12 months, and is a global reproductive health problem that impacts 10-15% of couples of childbearing age in many countries including Indonesia (Simanjuntak et al., 2025). The success of conception is not only influenced by the quality of the embryo, but also by endometrial receptivity, which is the ability of the endometrium to support the adhesion and invasion of the embryo during the window of implantation, which is a transient period in the mid-luteal phase that depends on local molecular and immune changes (Cai et al., 2021; Baldini et al., 2024; Jiang et al., 2025). Infertility globally places a significant burden. Recent epidemiological studies estimate that tens of millions of couples worldwide experience infertility, with an increasing trend especially in developing countries and urban populations. In Indonesia itself, the prevalence of infertility is estimated to reach 12-15% among reproductive couples, leading to an increase in demand for fertility services and the use of assisted reproductive procedures such as IVF/ICSI. Despite advances in assisted reproductive techniques, recurrent implantation failure (RIF) remains a major obstacle to achieving clinical pregnancy because it involves maternal, embryonic, or endometrial factors that are not yet fully understood (Rostami et al., 2025).

Various observational studies in the last five years have shown that vitamin D status correlates with biological aspects of the endometrium that favor implantation; for example, vitamin D is associated with higher expression of HOXA10 and other endometrial receptivity parameters, while vitamin D deficiency is often found in infertile women with RIF or subgroups such as PCOS (Wang et al., 2024). In addition, in vitro and observational studies in humans have shown that vitamin D affects uterine immune cell function and the expression of key genes that contribute to endometrial readiness, although the exact mechanism is still under investigation (Ko et al., 2022). The existence of vitamin D receptors (VDRs) in reproductive tissues including the endometrium, and modulation of the expression of genes related to endometrial receptivity such as HOXA10, play a role in the differentiation of endometrial cells that favor implantation (Ha et al., 2020).

However, the association between vitamin D levels, molecular endometrial receptivity parameters, and clinical success implantation through ART (Assisted Reproductive Technology) still shows mixed results in recent retrospective and prospective studies, requiring a thorough literature review (Octavia et al., 2025). Inconsistency in the effect of vitamin D on ART outcomes, some studies found a positive relationship between vitamin D status and clinical pregnancy rate and live birth rate, while other studies found no meaningful relationship and showed a knowledge gap in understanding how vitamin D contributes to implantation failure or success through systemic or local mechanisms in the endometrium (Xu et al., 2025). Population differences, study design, vitamin D assessment methods, and focus on clinical outcomes versus endometrial molecular parameters are some of the factors that make the interpretation of this scientific evidence complicated, so a comprehensive review of vitamin D, endometrial receptivity, and implantation success is critical to providing research direction and clinical recommendations sharper.

This inconsistency reveals a clear research gap. Existing studies vary substantially in design, population characteristics, timing of vitamin D measurement, biological specimens used, and outcomes assessed. Some studies emphasize clinical endpoints such as pregnancy rate and live birth, whereas others focus on molecular markers of receptivity such as HOXA10, HAND2, decidualization markers, and inflammatory balance. As a result, there is still limited integrative understanding of whether vitamin D acts as a direct determinant of implantation success, an indirect modulator of endometrial competence, or merely a permissive factor whose effect is most visible in deficiency states.

The urgency of this research therefore lies in the need to bridge molecular evidence and clinical outcomes. Endometrial receptivity cannot be adequately explained by morphology alone, because normal endometrial thickness does not always guarantee implantation success. Vitamin D has been linked to key mechanisms such as decidualization, regulation of prolactin and HAND2, modulation of HOXA10, suppression of excessive Th1/Th17 inflammation, enhancement of regulatory T-cell activity, and support of vascular remodelling. Clarifying these interconnected pathways is important for identifying which patients may truly benefit from vitamin D assessment or supplementation in fertility practice.

The novelty of this research lies in its attempt to position vitamin D not simply as a general nutritional factor, but as a biologically active reproductive modulator that may shape the permissive endometrial environment required for implantation. Unlike earlier studies that often examined only serum vitamin D levels or only pregnancy outcomes, this study emphasizes

the integration of molecular, immunological, and clinical perspectives. Such an approach offers a more comprehensive framework for understanding how vitamin D may influence embryo–endometrium dialogue and why its effects appear heterogeneous across different ART populations.

Based on that rationale, the purpose of this research is to examine and synthesize scientific evidence regarding the role of vitamin D in endometrial receptivity and implantation success, especially in the setting of assisted reproductive technology. More specifically, the research seeks to identify how vitamin D is associated with receptivity-related genes, decidualization processes, immune tolerance, and implantation-related outcomes, while also evaluating whether current evidence supports vitamin D as a clinically meaningful predictor or intervention target in infertility management.

The expected contribution of this research is both theoretical and practical. Theoretically, it enriches reproductive medicine literature by clarifying the multidimensional role of vitamin D in implantation biology and by highlighting the unresolved relationship between mechanistic plausibility and clinical effectiveness. Practically, the findings may help clinicians, fertility researchers, and policy makers refine screening strategies, improve individualized infertility management, and design future studies that integrate molecular biomarkers with ART outcomes. In that sense, the objective and benefit of this study are to provide a stronger scientific basis for decision-making, generate more focused recommendations for future research, and ultimately support better reproductive outcomes for infertile couples

RESEARCH METHODS

This study was prepared as a literature review that aims to comprehensively review the scientific evidence regarding the role of vitamin D on endometrial receptivity and implantation success based on observational studies in humans. The literature search is carried out systematically through major international databases, namely PubMed, Google Scholar and ScienceDirect, with publication coverage between 2020-2026. The search strategy used a combination of relevant keywords, including vitamin D, 25-hydroxyvitamin D, endometrial receptivity, endometrial function, embryo implantation, and pregnancy outcome, which were associated with Boolean AND and OR operators according to the characteristics of each database. Inclusion criteria include original research with cross-section, case-control, or cohort designs involving human subjects, either on natural conception or assisted reproductive technologies such as ART or IVF, as well as explicitly assessing the effect of vitamin D levels on endometrial receptivity parameters or implantation outputs.

Included articles were limited to English or Indonesian publications with full-text access, while literature reviews, meta-analyses, editorials, case reports, animal studies, in vitro studies, as well as articles with inadequate data were excluded from the analysis. The total livelihood was obtained 1,257 and 8 studies were included in the criteria. Data from studies that meet these criteria are extracted in a standardized manner and summarized in the form of a table including the study design, sample count and characteristics, vitamin D indicators, endometrial receptivity evaluation methods, and implantation or pregnancy outcomes. The synthesis was carried out in a descriptive-narrative manner by emphasizing the consistency, direction of

relationship, and variation of findings between studies to gain a comprehensive understanding of the contribution of vitamin D to the endometrial environment that supports implantation.

RESULTS AND DISCUSSION

Table 1. Data Extraction

Author (Year)	Design	Sample	Definition of Vitamin D	Endometrial Parameters	Other parameters	Implantation Outcome / Pregnancy	Effect Size	Key Conclusions
Cai et al., 2020(6)	Prospective cohort	2,569 fresh IVF/ICS I cycles	Total & free 25(OH)D measured 1 day before embryo transfer; Analyzed by quintile & category guideline	The thickness of the endometrium is recorded before embryo transfer as a baseline; not analyzed as the primary mediator	AMH, estradiol, embryo quality	Implantation rate, clinical pregnancy, ongoing pregnancy	Insignificant (p>0.05 multivariate)	Vitamin D is not associated with implantation or pregnancy success
Baldini et al., 2024(7)	Retrospective controlled study	204 ICSI cycles	Serum & Follicular Fluid 25(OH)D; vitamin D3 supplementation 2000 IU/day for 3 months	Endometrial thickness increased in the deficiency group after supplementation	Oocyte count, top-quality embryo	Implantation rate, pregnancy rate, abortion rate	Implantation is insignificant; Embryo quality significantly improves	Vitamin D improves embryo quality; effects on the endometrium especially in the deficiency group
Jiang et al., 2025(8)	Cohort Retrospective	188 cycles of IVF/ICS I	Serum 25(OH)D is analyzed as a continuous variable	Endometrial thickness on the day of administration of hCG was higher in the pregnant group	AMH, antral follicle count, oocyte count	Clinical pregnancy rate	OR 1.46	Vitamin D is an independent predictor of pregnancy and is associated with endometrial thickness
Ha et al., 2020(9)	Cohort Retrospective	3,779 IVF/ICS I cycles	Serum 25(OH)D categorized (<10, 10–30, ≥30 ng/mL)	Not analyzed as a primary variable	Number of oocytes, number of embryos	Ongoing pregnancy rate	Insignificant	Vitamin D is not significantly associated with pregnancy outcomes
Ko et al., 2022 (CLBR) (10)	Cohort Retrospective	1,113 IVF cycles	Serum 25(OH)D; deficiency <50 nmol/L	Not reported as a primary variable	Ovarian stimulation response, embryonic stage	Cumulative live birth rate	p=0.021	Vitamin D deficiency is associated with a decrease in cumulative live birth rate
Ko et al., 2025 (FET) (11)	Cohort Retrospective	1,489 cycles of frozen embryo transfer	Serum 25(OH)D; deficiency <50 nmol/L	Endometrial preparation protocol analyzed; Endometrial	Embryonic stage (blastocyst/c leavage)	Live birth rate	OR 0.861	There is no significant association between

					thickness is not a major variable				vitamin D and live birth rate
Tian et al., 2022(12)	Observational Foresight	2,569 IVF/ICS I cycles	Free & total 25(OH)D measured before embryo transfer	&	The thickness of the endometrium is not specifically analyzed	FSH, AMH, oocyte count	Implantation rate, clinical pregnancy	Correlation is very weak	Vitamin D does not play a major role in successful implantation
Hosseinisadat et al., 2022(13)	Cross-sectional	102 IVF cycles	Serum follicular fluid 25(OH)D	&	Not analyzed	Number of oocytes, number of embryos	Implantation rate, clinical pregnancy	Insignificant	No association was found between vitamin D and ART outcomes

Embryo implantation is a highly complex biological process and demands precise synchronization between blastocyst development and maternal endometrial readiness during the window of implantation. During this period, there are changes in gene analysis, molecular adhesion activation, cytokine secretion, and regulation of growth factors that allow for attachment and invasion of trophoblasts (Sehring et al., 2022). It is estimated that most implantation failures in assisted reproductive technology stem from the suboptimal receptivity of the endometrium compared to the quality of the embryo alone. Endometrial receptivity itself is a dynamic functional state characterized by successful desidualization, vascular remodeling, and the creation of maternal immune reconciliation. In addition, the differentiation of stromal cells into decidua cells plays an important role in regulating maternal-embryonic communication, controlling local inflammation, and supporting adequate angiogenesis (Okada, 2018). Disruptions in this process have been linked to infertility, repeated implantation failure, and poor pregnancy outcomes. In clinical practice, endometrial thickness (ET) is often used as an indirect indicator of receptivity. A thicker endometrium is thought to reflect adequate proliferation and an optimal hormonal response. However, these parameters are morphological and not always parallel to the molecular or immunological readiness of the tissues, so patients with normal ET may still experience implantation failure (Saxtorph et al., 2020).

The study of vitamin D in reproduction increased after the discovery of the expression of vitamin D receptors (VDR) and its metabolic enzymes in the ovaries and endometrium. Vitamin D is known to have pleiotropic roles in cell differentiation, regulation of progesterone target genes, angiogenesis, and modulation of the maternal immune system (Fichera et al., 2019). The activation of this pathway is thought to strengthen the embryo-endometrial dialogue so as to support the success of implantation. Vitamin D (especially the active form of 1,25-dihydroxyvitamin D or 1,25(OH)₂D/calcitriol) is increasingly understood as a reproductive hormone because of its receptors, vitamin D receptors (VDRs), as well as vitamin D metabolic enzymes such as CYP27B1 are expressed in female reproductive tissues including the endometrium, thus enabling local action through autocrine and paracrine mechanisms in the window of implantation phases (Farhangnia et al., 2024; Yi et al., 2025; Guo et al., 2020). At the molecular level, vitamin D acts as a transcription regulator by modulating the expression of various genes involved in cell differentiation, immune regulation, and reproductive tissue function. Endometrial receptorship itself is the result of complex integration between ovarian steroid signals, the formation of a tolerogenic immune environment, the process of stromal remodeling through desidualization, as well as the regulation of adhesion molecules necessary

for successful embryo-endometrial interactions, and vitamin D is thought to play a role in modulating important nodes in these biological networks.

At the transcription level, the 1,25(OH)₂D-vitamin D receptor (VDR) complex binds to the vitamin D response element in DNA and regulates the expression of various genes involved in cell differentiation and reproductive tissue function. This genomic role makes vitamin D an important regulator in endometrial maturation and readiness for decidualization. Experimental evidence suggests that changes in VDR activity directly affect the ability of endometrial stromal cells to execute decidual programs, where manipulation of VDR expression can alter differential responses to hormonal stimulation. In addition, vitamin D is also reported to modulate the expression of key genes such as HAND2 and prolactin which are important markers in the desidualization process (Yoshida et al., 2024). Vitamin D deficiency models show disruption in decidual induction, suggesting that vitamin D deficiency can shift the molecular state of the endometrium towards a phenotype that is less conducive to implantation. These findings reinforce that vitamin D status not only represents systemic levels, but also reflects the functional capacity of the endometrium to carry out a gene regulation-based receptivity program.

One of the key components of endometrial receptivity is the decidualization of stromal cells, a differentiation process classically characterized by increased expression of prolactin (PRL) and insulin-like growth factor binding protein-1 (IGFBP1) as functional markers of cellular phenotype changes. These markers reflect the activation of transcriptional programs that support the formation of decidua and the readiness of the endometrium for interaction with trophoblasts. Experimental evidence suggests that the vitamin D pathway plays a role in modulating this differentiation process, where changes in vitamin D receptor (VDR) activity can affect the capacity of stromal cells to carry out the desidualization program. In populations with recurrent implantation failure (RIF), vitamin D deficiency is often found in conjunction with disturbances of the endometrial molecular environment and increased inflammatory processes, which can collectively inhibit the achievement of optimal receptive conditions. Thus, vitamin D is conceptually seen to contribute to the stromal transformation necessary to improve the readiness of the endometrium to receive an embryo. In addition to the classical marker of desidualization, the vitamin D pathway is also thought to affect an important mediator of endometrial receptivity that links progesterone signaling with stromal maturation processes in the luteal phase. Vitamin D is known to play a role in the regulation of immune function and differentiation of reproductive tissues, thus potentially modulating the endometrial response to hormonal signals. In vitro studies show that vitamin D₃ is able to increase the expression of heart and neural crest derivatives expressed 2 (HAND2) in endometrial stromal cells, a key regulator involved in progesterone response and tissue maturation required for implantation. At the clinical level, women with recurrent implantation failure (RIF) reported having endometrial steroid receptor expression disorders related to lower vitamin D levels as well as increased inflammatory markers. This association suggests that vitamin D may contribute to endometrial sensitivity to steroids, rather than just through changes in systemic hormone levels, but also through modulation of the local molecular environment.

At the receptivity gene level, HOXA10 is a transcription factor that has a central role in uterine development and the formation of endometrial receptive competence, so that changes in its expression can have a direct impact on implantation success (Pirlog et al., 2025). HOXA10

is involved in the regulation of stromal cell differentiation, adhesion molecular expression, as well as various molecular pathways required during the window of implantation. A number of studies on the network

Human endometrium shows that circulating vitamin D levels are related to HOXA10 expression levels, and exposure to 1,25(OH)₂D is reported to be able to increase the expression of the gene, providing a biological basis that vitamin D may improve endometrial readiness. In a clinical context, especially in women with polycystic ovary syndrome (PCOS) undergoing ovulation induction or assisted reproductive technologies (ART), vitamin D is associated with modulation of HOXA10 expression and may contribute to variations in reproductive output in such populations (Shilpasree et al., 2022).

The immunological dimension is an important component of successful implantation, as this process requires targeted immune tolerance to the embryo without eliminating the body's ability to defend itself against pathogens. An imbalance in the immune response is known to contribute to impaired endometrial receptivity and recurrent implantation failure (RIF). Vitamin D is widely positioned as an immunomodulator that is able to suppress the dominance of pro-inflammatory responses, including the Th1 and Th17 patterns, while promoting the formation of a tolerogenic environment through the increase of regulatory T cells (Treg) and regulation of uterine natural killer (NK) cell activity so that it is not cytotoxic excessive. In line with this concept, clinical studies show that women with RIF often have lower vitamin D levels accompanied by increased systemic and local inflammatory markers, indicating a link between vitamin D deficiency and endometrial immune balance disorders. Thus, vitamin D interventions could theoretically help decrease inflammatory activity and improve the immunological "set-points" required for controlled adhesion as well as trophoblast invasion.

The success of implantation is also highly dependent on vascular remodeling and the quality of endometrial perfusion, since trophoblasts in the early phase require angiogenic support as well as hemodynamic adaptation of decidua tissue. Disruption in this process can inhibit the development of embryo-maternal interaction optimally. Recent literature places vitamin D as a regulator that has the potential to influence various aspects of endometrial function, including cell differentiation, immune regulation, and tissue maturation, which collectively contribute to an environment that supports implantation. Experimental models suggest that vitamin D deficiency can disrupt the molecular networks that regulate the decidual response, thereby affecting the overall readiness of the endometrium. Thus, the influence of vitamin D on implantation success is likely to be multi-pathway or pleiotropic, not limited to a single biomarker, but rather involves complex interactions between the endocrine, immune, and vascular systems.

Although the biological basis for vitamin D's role in endometrial receptivity appears strong, clinical evidence on assisted reproductive technologies (ART) still shows mixed results. A recent meta-analysis reported that higher vitamin D levels were associated with an increased chance of clinical pregnancy and live birth, but the association was not always consistent across all reproductive parameters such as implantation rate and miscarriage risk. In addition, dose-response analyses showed the presence of a non-linear pattern, where adverse effects were more pronounced in deficiency conditions, while increasing levels above a certain threshold did not necessarily result in significant additional benefits.

The absence of associations in some ART studies is likely influenced by the typical conditions of the IVF cycle, where an increase in estradiol during ovarian stimulation may increase levels of vitamin D-binding protein (DBP) so that the proportion of vitamin D available physiologically changes. Total levels of 25(OH)D measured in serum may not fully reflect the biologically active components of vitamin D and are able to interact with receptors in endometrial tissue (Chen et al., 2024). In addition, confounding factors such as embryo quality, age, BMI, and ovarian response were controlled in multivariate analysis, the contribution of vitamin D to implantation outcomes can be statistically insignificant (Ko et al., 2025). The variability of tissue responses can also be influenced by host factors, including the polymorphism of the VDR gene, so the same vitamin D levels do not always produce equivalent biological effects between individuals (Moradkhani et al., 2024). These findings suggest that the influence of vitamin D is likely highly dependent on the clinical context, including the initial status of 25(OH)D, the patient's characteristics, as well as the underlying endometrial factors.

Embryo implantation is a complex biological process and requires precise synchronization between blastocyst development and maternal endometrial readiness during the window of implantation. In this phase, there is molecular adhesion activation, cytokine secretion, regulation of growth factors, as well as changes in gene expression that allow attachment and invasion of trophoblasts. Although implantation failure in ART is multifactorial, impaired endometrial receptivity remains an important component that contributes to suboptimal reproductive output. This receptivity reflects a dynamic functional condition characterized by successful desidualization, vascular remodeling, and the creation of maternal immune tolerance. Differentiation of stromal cells into decidua cells plays a central role in maternal-embryonic communication, local inflammatory control, as well as the support of angiogenesis. Clinical parameters such as endometrial thickness (ET) are often used as indirect indicators of receptivity, but their morphological nature does not always reflect the molecular and immunological readiness of tissues, so normal ET does not guarantee implantation success.

Studies of vitamin D in reproduction increased after the discovery of the expression of vitamin D receptors (VDRs) and their metabolic enzymes, including CYP27B1, in female reproductive tissues (18–20). Biologically, vitamin D has a pleiotropic role in cell differentiation, regulation of progesterone target genes, angiogenesis, and maternal immune modulation. Through VDR activation, vitamin D acts as a transcriptional regulator that modulates the expression of genes involved in desidualization, immune regulation, and endometrial function. Thus, vitamin D has the potential to strengthen the embryo-endometrial dialogue through modulation of the biological tissues underlying receptivity.

At the molecular level, the 1,25(OH)₂D-VDR complex binds to vitamin D response elements in DNA and regulates the expression of genes involved in endometrial differentiation as well as maturation. Changes in VDR activity have been shown to affect the capacity of stromal cells to carry out a desidualization program in response to hormonal stimulation (Hosseinisadat et al., 2022). Vitamin D also reportedly increases the expression of key genes such as HAND2 and prolactin, which are important markers of decidua differentiation. Vitamin D deficiency models show disruption in decidual induction and changes in molecular profiles towards conditions that are less favorable for implantation. These findings confirm that vitamin

D status not only represents systemic levels, but also relates to the functional capacity of the endometrium to carry out a gene regulation-based receptivity program.

In women with recurrent implantation failure (RIF), vitamin D deficiency is often found along with disturbances of the endometrial molecular environment as well as increased inflammatory processes. Vitamin D is thought to contribute to endometrial sensitivity to progesterone through the regulation of mediators such as HAND2, while balancing the immune response by suppressing the dominance of the Th1/Th17 pattern and supporting the formation of regulatory T cells. In addition, vitamin D has the potential to influence vascular remodeling and hemodynamic adaptation of desidua tissues, so its contribution to implantation is multi-pathway and involves endocrine, immune, and vascular interactions.

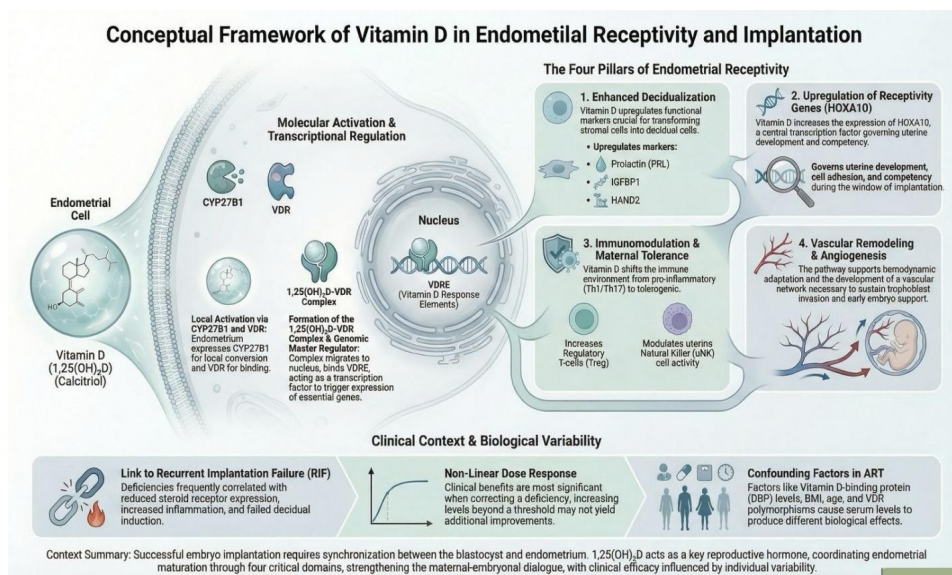


Figure 1. Conceptual framework of the pleiotropic role of vitamin D in endometrial receptivity and implantation.

Although the biological rationale is strong, the clinical evidence on ART still shows a heterogeneity of outcomes. Meta-analyses reported an association between higher vitamin D levels and an increased chance of clinical pregnancy and live birth, but the association was inconsistent on other parameters such as implantation rate and miscarriage risk. Dose–response analysis showed a non-linear pattern, where the most pronounced impact was seen on deficiency conditions, while increasing levels above the adequacy threshold did not necessarily result in additional benefits.

The absence of associations in some studies may be influenced by the characteristics of the IVF cycle, including increased estradiol during ovarian stimulation that increases levels of vitamin D-binding protein (DBP) thereby modifying the proportion of physiologically available vitamin D; as a result, total serum 25(OH)D levels may not fully reflect the biologically active component of the target tissue. In addition, once confounding factors such as age, BMI, ovarian response, as well as embryo quality were controlled in a multivariate analysis, vitamin D's contribution to implantation outcomes may become statistically insignificant (Tian et al., 2022). The variability of host factor-influenced tissue responses, including the polymorphism of the VDR gene, also has the potential to cause the same vitamin

D levels not to necessarily produce equivalent biological effects between individuals. Thus, the influence of vitamin D on implantation success is likely highly dependent on the clinical context and the patient's initial status, thus acting as a permissive factor rather than a primary determinant.

CONCLUSION

The findings of this study indicate that vitamin D has a potentially important role in influencing endometrial receptivity and implantation success in the context of assisted reproductive technology. The presence of vitamin D receptors and metabolic enzymes in endometrial tissue suggests that vitamin D participates in various biological processes involved in implantation, including decidualization, immune regulation, angiogenesis, and the expression of implantation-related genes such as HOXA10 and HAND2. Although several studies demonstrate a positive association between adequate vitamin D levels and improved reproductive outcomes, other studies report inconsistent or insignificant relationships. These differences indicate that the effect of vitamin D on implantation success is likely influenced by multiple factors, including patient characteristics, vitamin D status, study design, and clinical protocols used in fertility treatment. Thus, the evidence suggests that vitamin D may contribute to the establishment of a receptive endometrial environment, but its clinical significance still requires further clarification. Based on these findings, future research is recommended to conduct large-scale prospective studies and well-designed randomized controlled trials to better understand the causal relationship between vitamin D and implantation outcomes. Further investigations should also explore the molecular mechanisms through which vitamin D regulates endometrial receptivity, particularly its interaction with immune modulation, gene expression, and hormonal pathways during the implantation window. In addition, future studies should consider standardized measurement of vitamin D levels, control for potential confounding variables, and examine different populations of infertility patients. Such approaches will help generate more consistent evidence and may support the development of evidence-based clinical guidelines regarding vitamin D assessment or supplementation in fertility treatment programs.

REFERENCES

- Baldini, G. M., Russo, M., Proietti, S., Forte, G., Baldini, D., & Trojano, G. (2024). Supplementation with vitamin D improves the embryo quality in in vitro fertilization (IVF) programs, independently of the patients' basal vitamin D status. *Archives of Gynecology and Obstetrics*, 309(6), 2881–2890.
- Cai, S., Li, J., Zeng, S., Hu, L., et al. (2021). Impact of vitamin D on human embryo implantation — a prospective cohort study in women undergoing fresh embryo transfer. *Fertility and Sterility*, 115(3), 655–664. <https://doi.org/10.1016/j.fertnstert.2020.09.005>
- Chen, H., Yao, J., Hu, L., Liu, Y., Hocher, J. G., Zhang, X., et al. (2024). Vitamin D binding protein correlates with estrogen increase after administration of human chorionic gonadotropin but does not affect ovulation, embryo, or pregnancy outcomes. *Frontiers in Endocrinology*, 15.
- Farhangnia, P., Noormohammadi, M., & Delbandi, A. A. (2024). Vitamin D and reproductive disorders: A comprehensive review with a focus on endometriosis. *Reproductive Health*, 1–19. <https://doi.org/10.1186/s12978-024-01797-y>
- Fichera, M., Török, P., Tesarik, J., Della Corte, L., Rizzo, G., Garzon, S., et al. (2019). Vitamin D, reproductive disorders and assisted reproduction: Evidences and perspectives. *International Journal of Food Sciences and Nutrition*, 1–10. <https://doi.org/10.1080/09637486.2019.1661978>
- Guo, J., Liu, S., Wang, P., Ren, H., & Li, Y. (2020). Characterization of VDR and CYP27B1 expression in the endometrium during the menstrual cycle before embryo transfer: Implications for endometrial receptivity. *Reproductive Biology and Endocrinology*, 18(1), 1–11.
- Ha, A. N., Pham, T. D., & Vuong, L. N. (2020). Association between vitamin D levels and fertility outcomes in patients undergoing IVF/ICSI. *Journal of Reproductive Medicine*, 2(3), 85–92.
- Hosseinisadat, R., Saeed, L., Ghasemirad, A., Habibzadeh, V., & Heidari, S. S. (2022). Assessment of the effect of serum and follicular fluid vitamin D and glucose on assisted reproductive technique outcome: A cross-sectional study. *International Journal of Reproductive Biomedicine*, 20(3), 221–230.
- Jiang, S., Chen, Z., & Li, L. (2025). Pregnancy success: A predictive. 1–7. <https://doi.org/10.3389/frph.2025.1510484>
- Ko, J. K. Y., Shi, J., Li, R. H. W., Yeung, W. S. B., & Ng, E. H. Y. (2022). Effect of serum vitamin D level before ovarian stimulation on the cumulative live birth rate of women undergoing in vitro fertilization: A retrospective analysis. *Endocrine Connections*, 11(2).
- Ko, J. K. Y., Lam, M. T., Lam, K. K. W., Chan, T. O., Li, R. H. W., & Ng, E. H. Y. (2025). Association of serum vitamin D level and live birth rate in women undergoing frozen embryo transfer — A retrospective cohort study. *Journal of Assisted Reproduction and Genetics*, 42(2), 509–523.
- Moradkhani, A., Azami, M., Assadi, S., Ghaderi, M., Azarnezhad, A., & Moradi, Y. (2024). Association of vitamin D receptor genetic polymorphisms with the risk of infertility: A systematic review and meta-analysis. *BMC Pregnancy and Childbirth*, 24(1).
- Octavia, L., Andhika Panjarwanto, D., Nabila, P., Geany, P. L., Javier, R. M., Rahman, A. A., et al. (2025). The relationship between initial vitamin D levels and in vitro fertilization (IVF) outcomes in PCOS patients: A systematic review. *Frontiers in Medicine*, 12.
- Okada, H. (2018). Decidualization of the human endometrium. 1–8.
- Pirlog, L. M., Pătrășcanu, A. A., Ona, M. D., & Cătană, A., Rotar, I. C. (2025). HOXA10 and HOXA11 in human endometrial benign disorders: Unraveling molecular pathways and their impact on reproduction. *Biomolecules*, 15(4).
- Rostami, R., Jahanbakhsh, J., Mahdinia, E., Rezaei, A., Yarahmadi, S., Omidiani, N., et al. (2025). Endometrial steroid receptor dysregulation and its association with vitamin D, AMH, and

- inflammation in recurrent implantation failure: A case-control study. *International Journal of Fertility and Sterility*, 19(4), 411–420.
- Saxtorph, M. H., Hallager, T., Persson, G., Petersen, K. B., Eriksen, J. O., Larsen, L. G., et al. (2020). Assessing endometrial receptivity after recurrent implantation failure: A prospective controlled cohort study. *Reproductive Biomedicine Online*, 1–9. <https://doi.org/10.1016/j.rbmo.2020.08.015>
- Sehring, J., Beltsos, A., & Jeelani, R. (2022). Human implantation: The complex interplay between endometrial receptivity, inflammation, and the microbiome. *Placenta*, 117, 179–186. <https://doi.org/10.1016/j.placenta.2021.12.015>
- Shilpasree, A. S., Kulkarni, V. B., Shetty, P., Bargale, A., Goni, M., Oli, A., et al. (2022). Induction of endometrial HOXA10 gene expression by vitamin D and its possible influence on reproductive outcome of PCOS patients undergoing ovulation induction procedure.
- Simanjuntak, L., Susanti Pasaribu, R., & Novita Sari, S. (2025). Faktor-faktor penyebab terjadinya infertilitas pada pasangan usia subur di Desa Purwodadi Kecamatan Sunggal Tahun 2023. *Quantum Wellness: Jurnal Ilmu Kesehatan*, 13–21.
- Tian, M., Zeng, S., Cai, S., Reichetzedder, C., Zhang, X., Yin, C., et al. (2022). 25(OH) VitD and human endocrine and functional fertility parameters in women undergoing IVF/ICSI. 1–7.
- Wang, K., Dong, F., Ma, S., & Bu, Z. (2024). The association between vitamin D deficiency and clinical pregnancy rate in IVF patients with different age. *Frontiers in Endocrinology*, 15, 1–10.
- Xu, C., An, X., Tang, X., Yang, Y., Deng, Q., Kong, Q., et al. (2025). Association between vitamin D level and clinical outcomes of assisted reproductive treatment: A systematic review and dose–response meta-analysis. *Reproductive Sciences*, 32(5), 1446–1458.
- Yi, M., Montague Redecke, S. G., Wang, T., Bell-Hensley, A., Li, S., Massri, A. J., et al. (2025). Impact of vitamin D deficiency on defective endometrial decidualization and the repressive role of vitamin D receptor (VDR) in the epigenomic network. *bioRxiv*. <http://www.ncbi.nlm.nih.gov/pubmed/41292920>
- Yoshida, N., Takaki, K., Tanaka, A., & Tanaka, S. (2024). Vitamin D3 regulates HAND2 expression in endometrial stromal cell decidualization. 1–7.