DOI: https://doi.org/10.54393/pbmj.v9i10.1426

PAKISTAN BIOMEDICAL JOURNAL

https://www.pakistanbmj.com/journal/index.php/pbmj/index

ISSN (E): 2709-2798, (P): 2709-278X

Volume 9, Issue 10 (October 2026)

Systematic Review

Exploring the Role of Vitamin D in Female Infertility: Evidence from Biochemical, Physiological, and Reproductive Studies: A Systematic Review

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ARTICLE INFO

Keywords:
Vitamin D Deficiency, Female Infertility, Ovarian Reserve, Polycystic Ovary Syndrome, Assisted Reproductive Technology, Live Birth

How to Cite:
Khan, S., Khan, R., Muhammad, G., Fida, N., Yahya, S., & Cheema, N. N. (2026). Exploring the Role of Vitamin D in Female Infertility: Evidence from Biochemical, Physiological, and Reproductive Studies: A Systematic Review: Vitamin D in Female Infertility: Biochemical, Physiological, and Reproductive Studies. Pakistan BioMedical Journal, 9(10). https://doi.org/10.54393/pbmj.v9i10.1426

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Received Date: 23rd August, 2026
1st Revision Received: 22nd October, 2026
Acceptance Date: 29th October, 2026
Published Date:31st October, 2026

ABSTRACT

Vitamin D plays an important role in reproductive endocrinology, ovarian function, metabolic regulation, immune responses, and endometrial receptivity; however, its relationship with female infertility and assisted reproductive technology (ART) outcomes remains uncertain. **Objectives:** To evaluate associations between vitamin D status and biochemical, physiological, and reproductive outcomes among women with infertility. **Methods:** Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines, a qualitative synthesis without meta-analysis was conducted using original human studies published between January 2020 and December 2025 and identified through PubMed/MEDLINE, Web of Science, and Scopus. Twenty-two studies met the eligibility criteria. **Results:** Associations between vitamin D status and anti-Müllerian hormone (AMH), follicle-stimulating hormone (FSH), antral follicle count (AFC), ovulation, embryo quality, implantation, pregnancy, and live birth were inconsistent. Selected supplementation studies reported improvements in endocrine, metabolic, inflammatory, and ovarian reserve indicators, particularly among women with polycystic ovary syndrome or diminished ovarian reserve. **Conclusions:** Nevertheless, larger observational studies and randomized trials did not consistently demonstrate improved clinical pregnancy or live-birth outcomes. Vitamin D may influence female reproductive physiology through ovarian, endocrine, metabolic, immune, and endometrial pathways; however, current evidence does not establish a consistent fertility benefit from supplementation.

INTRODUCTION

Females have a complex reproductive system where multiple factors are involved, including ovarian reserve, reproductive ageing, metabolic abnormalities, endocrine dysfunction, and endometrial receptivity. Several underlying disorders, such as polycystic ovary syndrome (PCOS) and endometriosis [1]. Nutritional and hormonal factors have gained more importance since they are potential factors in reproductive function, such as vitamin D, which has biological activity beyond calcium metabolism and the skeleton [2]. Vitamin D is a fat-soluble secosteroid, which plays a role in various physiological pathways. Vitamin D receptors and metabolizing enzymes are present in reproductive tissues such as the ovary and endometrium, providing a possible role in follicular development, steroidogenesis, and in the maturation of the eggs, immune modulation, and implantation. These mechanisms can be used as a biological model to study the connection between vitamin D deficiency and female

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DOI: https://doi.org/10.54393/pbmj.v9i10.1426

reproductive impairment. But biological plausibility does not constitute clinical significance of the effect on fertility [3]. The main biochemical marker of vitamin D status is serum 25-hydroxyvitamin D [25(OH)D]. It has been studied together with other markers used in women with infertility, such as anti-Müllerian hormone (AMH); follicle-stimulating hormone (FSH); luteinizing hormone; antral follicle count (AFC); insulin resistance; inflammatory activity; and endometrial receptivity [3, 4]. Metabolic changes, hyperandrogenism, and/or ovulatory dysfunction may coexist with vitamin D deficiency, especially in PCOS. Women with low ovarian reserve and women with recurrent implantation failure have also been studied to see if there is some benefit to optimizing vitamin D in improving ovarian or endometrial functioning [4-6]. With this in mind, this systematic review was designed to collate original human studies and to summarize these findings. The published articles were between January 2020 and December 2025, and three specific objectives were addressed: (1) associations between vitamin D status and biochemical or ovarian reserve indicators; (2) associations between vitamin D status and ovulation, embryo development, embryo implantation, and pregnancy outcome; and (3) the effect of vitamin D supplementation on clinical pregnancy and live birth.

Evidence in the clinic is still inconclusive. Favorable vitamin D status is found with improvements in ovarian response, embryo characteristics, implantation, and pregnancy outcomes from some studies, while other studies show no or limited significant relationships. The results of supplementation trials have also been inconsistent regarding ovarian reserve markers, clinical pregnancy and live birth. These contrasting results may be explained by variations in the levels of vitamin D deficiency, in the characteristics of the participants, in the vitamin D supplementation regimens, and in the fertility-treatment protocols. Thus, the relevance of vitamin D status in female reproductive health and its role in infertility are still not well defined for women. The main research gap is that there is a lack of consistent evidence on the link between biochemical/physiological changes due to vitamin D status and clinically relevant reproductive outcomes. This review aimed to address the clinical importance of vitamin D and priorities for future fertility studies by critically comparing the results obtained using the different study designs and reproductive populations involved.

METHODS

The aim of the present systematic review was to investigate the relationship of vitamin D status with female infertility with respect to biochemical, hormonal, ovarian, and reproductive outcomes. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines were followed in the review. Due to the significant clinical and methodological heterogeneity among the studies included in the review, a qualitative review was performed without meta-analysis. Original studies published from January 2020 to December 2025 were searched for using the structured approach in PubMed/MEDLINE, Web of Science, and Scopus databases. The terms used were 'vitamin D', '25-hydroxyvitamin D', 'female infertility', 'subfertility', 'ovarian reserve', 'polycystic ovary syndrome', 'ovulation', 'in vitro fertilization (IVF)', 'intracytoplasmic sperm injection (ICSI)', 'implantation', 'pregnancy', and 'miscarriage', which were linked by Boolean AND and OR operators. Additional screening of reference lists of eligible articles was performed to identify relevant studies. Studies were included if they were original, human research that included women of reproductive age with infertility, subfertility, polycystic ovary syndrome (PCOS), diminished ovarian reserve, or women receiving fertility treatments. The following study designs were included: cross-sectional studies, case-control studies, cohort studies, randomized controlled studies, and non-randomized interventional. Studies needed to determine the level of 25-hydroxyvitamin D [25(OH)D] in the serum or follicular fluid, or supplement vitamin D levels, and its association with at least one biochemical, physiological, or reproductive outcome. Reviews (systematic and narrative), meta-analyses, case reports, case series, pilot studies, protocols, conference abstracts with insufficient primary data, animal studies, and exclusively in vitro studies were not included. The publications that were not in the specified period or did not show the reproductive outcomes were also not included. The database search identified 424 records (PubMed, 158; Web of Science, 126; Scopus, 140). Following removal of 96 duplicates, 328 records underwent title and abstract screening, of which 241 were excluded. Eighty-seven full-text reports were sought, five were unavailable, and 82 were assessed for eligibility. Subsequently, 60 reports were excluded, leaving 22 studies for qualitative synthesis. The study-selection process is presented in the PRISMA flow diagram (Figure 1).

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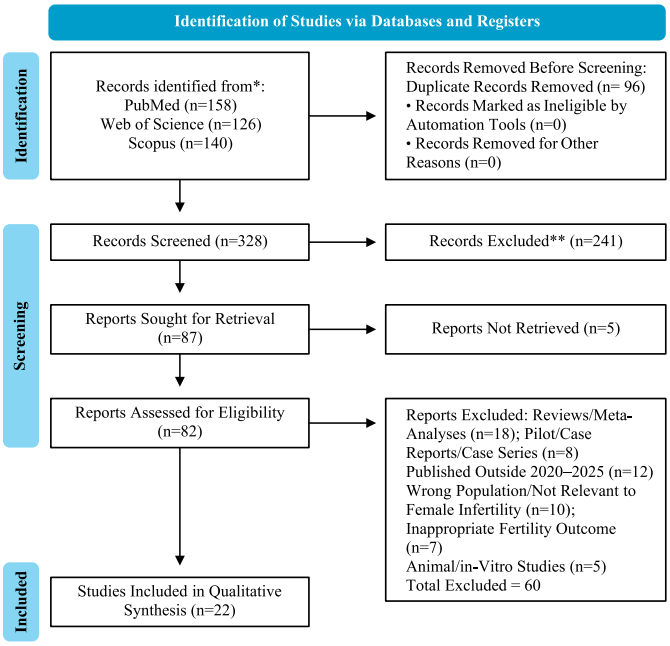


Figure 1: PRISMA 2020 Flow Diagram Showing the Identification, Screening, Eligibility Assessment, and Final Inclusion of Studies Evaluating the Association Between Vitamin D Deficiency and Female Infertility Outcomes

Extracted information included study design, sample size, participant characteristics, vitamin D assessment, supplementation regimen, ovarian reserve markers, reproductive hormones, metabolic and inflammatory indicators, and fertility outcomes. Ovarian parameters included anti-Müllerian hormone (AMH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and antral follicle count (AFC). Reproductive outcomes included ovulation, oocyte retrieval, embryo quality, implantation, biochemical and clinical pregnancy, miscarriage, and live birth. Study-specific vitamin D deficiency thresholds were retained because classification criteria varied across studies. Randomized controlled trials were assessed for methodological quality with the Cochrane Risk of Bias 2 (RoB 2) tool, and the relevant Joanna Briggs Institute (JBI) critical appraisal tools were used for non-randomized and observational studies. Confounding factors such as age, BMI, PCOS diagnosis, duration of infertility, season, sun exposure, supplement characteristics, and fertility-treatment protocols were taken into account for any associations reported. The studies were classified on the basis of their overall methodological weaknesses. The qualitative synthesis was broken down into biochemical and hormonal outcomes, ovarian and reproductive physiology, and clinical fertility outcomes. Where available, reported correlation coefficients, regression estimates, odds ratios, risk ratios, confidence intervals and p-values were extracted. Reported group percentages were used to calculate absolute risk differences, which were distinguished from adjusted effect estimates.

No statistical pooling was possible due to differences in population characteristics, outcome definitions, vitamin D thresholds, and intervention protocol. When interpreting the strength and clinical relevance of findings, potential residual confounding was taken into account, as were small sample sizes, incomplete reporting of confidence intervals, and multiple outcome testing.

RESULTS

Twenty-two studies published between 2020 and 2025 were included in the qualitative synthesis, comprising randomized controlled trials, observational studies, retrospective cohorts, and non-randomized interventions. Sample sizes ranged from 40 to 2,569 participants. Study populations included women with polycystic ovary syndrome (PCOS), diminished ovarian reserve, recurrent implantation failure, and those undergoing assisted reproductive technology (ART). Vitamin D exposure was assessed through serum or follicular-fluid 25-hydroxyvitamin D [25(OH)D] concentrations or supplementation. Considerable variation in study design, deficiency thresholds, interventions, and outcome definitions limited direct comparisons. Study characteristics are summarized (Table 1).

Table 1: Characteristics of Studies Included in the Systematic Review (n=22)

References	Design; Sample Size	Population and Vitamin D Assessment	Principal Outcome
[1]	Non-randomized intervention; 62	Diminished reserve; vitamin D replacement	AMH, FSH, AFC
[2]	Cross-sectional; 446	IVF; serum/follicular vitamin D	Oocyte and IVF outcomes
[3]	Retrospective cohort; 2,518 cycles	IVF; serum vitamin D	Cumulative live birth
[4]	Retrospective cohort; 306	IVF; preconception 25(OH)D	Pregnancy outcomes
[5]	Observational cohort; 2,569	IVF/ICSI; free and total 25(OH)D	Hormones, ovarian response
[7]	Cross-sectional; 287	Infertile women; serum 25(OH)D	AMH, AFC
[8]	RCT; 95 randomized, 74 analyzed	IVF; calcitriol versus placebo	Pregnancy
[9]	RCT/post-hoc; 330	PCOS/non-PCOS; vitamin D_3 versus placebo	Reproductive hormones
[10]	RCT; 630 randomized, 573 analyzed	IVF; high-dose vitamin D_3 versus placebo	Pregnancy, live birth
[11]	Before–after; 51	Diminished reserve; vitamin D supplementation	AMH

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DOI: https://doi.org/10.54393/pbmj.v9i10.1426

[12]	Cross-sectional; 199	Subfertility; serum 25(OH)D	Ovarian reserve
[13]	Retrospective cohort; 218	IVF; preconception 25(OH)D	Pregnancy
[14]	Observational; 265	Infertility; vitamin D, diet, sun exposure	Vitamin D insufficiency
[15]	RCT; 40	PCOS; vitamin D versus placebo	Metabolic biomarkers
[16]	Interventional; 204	ICSI; vitamin D-containing supplementation	Embryo quality
[17]	Retrospective; 267	IVF; serum vitamin D	Follicular response
[18]	Observational cohort; 1,459	IVF; vitamin D categories	Pregnancy, HOXA10
[19]	Retrospective cohort; 1,489	Frozen embryo transfer; serum 25(OH)D	Live birth
[20]	Cohort; 111	PCOS; pre-transfer 25(OH)D	Pregnancy, live birth
[21]	RCT; 112	Implantation failure; vitamin D/probiotics	Pregnancy, immune markers
[22]	Quasi-randomized; 180	PCOS; vitamin D versus placebo	Ovulation, metabolism
[23]	Retrospective cohort; 613	PCOS; IVF and vitamin D status	Oocytes, pregnancy

RCT, randomized controlled trial; IVF, in vitro fertilization; ICSI, intracytoplasmic sperm injection; AMH, anti-Müllerian hormone; FSH, follicle-stimulating hormone; AFC, antral follicle count; PCOS, polycystic ovary syndrome

Associations between vitamin D status and ovarian reserve markers were inconsistent. Supplementation studies reported improvements in selected hormonal markers, particularly among women with diminished ovarian reserve or PCOS. However, several interventions lacked concurrent controls, and most studies did not provide confidence intervals for their estimates. Findings relating to metabolic, oxidative-stress, and endometrial markers were similarly heterogeneous (Table 2).

Table 2: Association of Vitamin D with Biochemical, Hormonal, and Ovarian Physiological Outcomes

References	Outcome and Main Finding	Statistical Estimate
[1]	Increased AMH/AFC; decreased FSH	AMH p=0.001; AFC p=0.001; FSH p=0.002
[2]	Improved follicular/oocyte parameters	Follicles p=0.0043; oocytes p=0.0207; mature oocytes p=0.0233
[5]	Weak correlations with ovarian markers	AMH Spearman ρ=−0.057, p=0.004; AFC ρ=−0.053, p=0.007; FSH ρ=0.041, p=0.036
[7]	No significant association with AMH or AFC	AMH Spearman r=−0.083, p=0.161; adjusted p=0.182; AFC p=0.133
[9]	Increased FSH; reduced LH/FSH ratio in PCOS	FSH mean treatment effect 0.94 (95% CI 0.087 to 1.799), p=0.031; LH/FSH mean treatment effect −0.335 (95% CI −0.621 to −0.050), p=0.022
[11]	AMH increased after supplementation	AMH 0.50→0.79 ng/mL; p=0.02
[12]	No significant AMH/FSH differences	AMH p=0.904; FSH p=0.075; vitamin D–AMH r=−0.068, p=0.342
[14]	Vitamin D insufficiency common	Approximately 27%
[15]	Improved selected inflammatory/oxidative markers	Significant changes reported; numerical effects not available in extracted summary
[18]	Lower HOXA10 expression with deficiency	Deficient 0.58±0.11 versus replete 2.15±0.39; p=0.029
[22]	Improved endocrine/metabolic profile	Adjusted β: LH/FSH −1.28; testosterone −7.4; HOMA-IR−1.53

Values are reproduced from the previously extracted study results. Confidence intervals are not added where unavailable; numerical β estimates require confirmation of units and model specifications. Statistical significance does not necessarily indicate clinical significance. Clinical reproductive outcomes varied across studies

Several selected observational studies identified favorable pregnancy associations, particularly among women with PCOS. These differences were not consistently supported by adjusted estimates, and the evidence did not demonstrate a uniform improvement in live-birth outcomes (Table 3).

Table 3: Vitamin D Status, Supplementation, and Reproductive Outcomes

References	Reproductive Outcome	Effect Estimate/Statistical Result
[2]	Follicular/oocyte response	Follicles p=0.0043; oocytes p=0.0207; mature oocytes p=0.0233
[3]	Cumulative live birth	No significant independent association reported
[4]	Hypertensive pregnancy disorders	Adjusted OR 0.190 (95% CI 0.042– 0.852); p=0.030
[5]	Oocyte and implantation outcomes	Weak associations; clinically substantial effects not established
[8]	Biochemical and clinical pregnancy	Biochemical pregnancy 31.4% vs 18.2%; RD +13.2 pp; p<0.05. Clinical pregnancy 25.5% vs 13.6%; RD +11.9 pp; p>0.05
[10]	Clinical pregnancy	37% vs 40%; RD −3.0 pp; RR 0.91 (95% CI 0.75–1.11), p=0.37
[13]	IVF pregnancy	25(OH)D 56.4 vs 47.9 nmol/L; p=0.001
[16]	Embryo quality	Favorable changes in selected embryo parameters
[17]	Ovarian response	No consistent significant association
[18]	Implantation and pregnancy	Unfavorable association with deficiency, particularly at age ≥35 years

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DOI: https://doi.org/10.54393/pbmj.v9i10.1426

[19]	Live birth after frozen embryo transfer	30.9% vs 34.2%; RD −3.3 pp; OR 0.861 (95% CI 0.683–1.086); p=0.205
[20]	Clinical pregnancy/live birth in PCOS	Vitamin D 65.28 vs 52.22 nmol/L; p<0.001. Live birth 75.0% vs 52.1%; RD +22.9 pp; p=0.049
[21]	Pregnancy after implantation failure	Combination 46.4%, vitamin D 17.8%, probiotics 14.2%,control 10.7%; combination vs vitamin D p=0.002
[22]	Ovulation	Favorable association with supplementation; numerical effect unavailable
[23]	Oocyte/embryo outcomes	Oocytes 10.18 ± 4.27 vs 10.42 ± 4.22; p=0.48; mature oocytes 8.70 ± 3.93 vs 8.90 ± 3.84; p=0.48

RD, absolute risk difference; pp, percentage points; RR, risk ratio; OR, odds ratio; CI, confidence interval. Absolute differences are calculated from the published percentages and are not adjusted estimates. For studies reporting only p-values or qualitative findings, missing effect estimates and confidence intervals have not been fabricated

Nonetheless, randomized placebo-controlled trials typically showed reduced bias of the study compared to uncontrolled interventions and quasi-randomized studies. Most of the observational studies had moderate methodological limitations due to residual confounding, exposure misclassification, and retrospective selection. Some of the factors were not standardized, such as age, BMI, PCOS status, duration of infertility, seasonal variations in vitamin D levels, and treatment characteristics. Less precise estimates were also obtained in smaller studies (40-70 participants) for pregnancy outcomes. Multiple outcomes where a variety of isolated statistically significant observations were reported but not frequently examined with multiplicity adjustments (Table 4).

Table 4: Risk-of-Bias and Methodological Quality of Included Studies

References	Assessment Framework	Overall Risk	Main Methodological Concern
[1]	JBI	High	Non-randomized intervention
[2]	JBI	Moderate	Observational design
[3]	JBI	Moderate	Exposure classification/confounding
[4]	JBI	Moderate	Selection and lifestyle factors
[5]	JBI	Moderate	Residual confounding
[7]	JBI	Moderate	Cross-sectional design, residual confounding
[8]	RoB 2	Low	Reduced final analytical sample
[9]	RoB 2	Moderate	Post-hoc analysis
[10]	RoB 2	Low	No major concern identified
[11]	JBI	High	No concurrent control
[12]	JBI	Moderate	Cross-sectional design
[13]	JBI	Moderate	Retrospective design
[14]	JBI	Moderate	Exposure-related confounding
[15]	RoB 2	Low	Small sample
[16]	JBI	Moderate	Unclear randomization
[17]	JBI	Moderate	Retrospective grouping
[18]	JBI	Moderate	Observational confounding
[19]	JBI	Moderate	Non-randomized exposure
[20]	JBI	Moderate	PCOS-related confounding
[21]	RoB 2	Low– moderate	Multiple treatment arms
[22]	JBI	High	Quasi-random allocation
[23]	JBI	Moderate	Retrospective confounding

JBI, Joanna Briggs Institute critical appraisal tools; RoB 2, Cochrane risk-of-bias tool for randomized trials

Overall, the evidence suggests that vitamin D status may be associated with selected biochemical, endocrine, and ovarian responses; however, improvements in these intermediate outcomes were not consistently accompanied by higher clinical pregnancy or live-birth rates. Heterogeneous effect measures, incomplete confidence-interval reporting, residual confounding, and limited statistical precision prevented quantitative pooling and reduced certainty in the clinical interpretation.

DISCUSSION

The present systematic review confirms the link between vitamin D status and female infertility, published earlier is biologically plausible, but not clearly established. In the 22 studies included, serum 25(OH)D was studied in relation to ovarian reserve, reproductive hormones, metabolic abnormalities, endometrial receptivity, ovulation, embryo development, embryo implantation, pregnancy, miscarriage, and live birth. Biochemical results were inconsistent, with some studies

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DOI: https://doi.org/10.54393/pbmj.v9i10.1426

showing increased AMH, AFC, FSH, LH/FSH ratio, insulin resistance, decreased oxidative stress, or decreased inflammation after vitamin D supplementation. Mechanistic evidence from outside supports this pattern. Pazhohan *et al.* and Mousavi Salehi *et al.* showed that vitamin D supplementation had the effect of modifying the activity of β-catenin in the endometrium of infertile women with stage III–IV endometriosis, with a significant decrease in the active form of β-catenin, indicating the ability of vitamin D to modify pathways in abnormal endometrial physiology [24, 25]. Given these findings, there is a possibility that endocrine and immunological pathways may be involved, but the findings do not prove causation with regard to fertility outcomes. The relationship between vitamin D and reproductive function seems especially important in women with polycystic ovary syndrome (PCOS). Piao *et al.* reported that supplementation led to improved hormonal profiles and reproductive outcomes [26], and Swadi *et al.* reported favorable ovulatory response when vitamin-D deficient women were given letrozole [27]. In addition, Azhar *et al.* found links between vitamin D deficiency and poor lipid profiles in women suffering from PCOS [28]. Further randomized studies by Wen *et al.* showed that vitamin D supplementation has an effect on metabolic parameters of women with PCOS, suggesting its use in metabolic regulation but not necessarily in fertility [29], although the magnitude and clinical significance of these effects are unknown because ovarian, metabolic, and pregnancy outcomes were not always assessed by the same methods. Another potential pathway from vitamin D to reproductive function is endometrial receptivity. In the studies included, reduced HOXA10 expression was found in vitamin-D deficient women, indicating the potential for impaired processes of implantation. Similarly, Kuroshli *et al.* have demonstrated changes in markers of decidualization in the endometrium of women with recurrent implantation failure, such as expression of the vitamin D receptor and HOXA10 [6]. Thus, the present findings indicate that vitamin D could participate in implantation through mechanisms that differ from those of the classical markers of the ovarian reserve, such as differentiation of the endometrium and regulation of the immune system. But the clinical relevance is still unknown, and serum vitamin D level does not reliably correlate with endometrial receptivity or reproductive outcomes. The outcomes of ART are still inconclusive. Some studies indicated that there was a non-linear relationship between vitamin D and the pregnancy outcomes [30], while other studies found no significant effect on major IVF outcomes from supplementation [31, 32]. In a systematic review and meta-analysis, Meng *et al.* found that vitamin D may increase clinical pregnancy (OR=1.70, 95% CI 1.24–2.34); however, there was significant heterogeneity [33]. In contrast, Eller *et al.* showed that the majority of studies they included did not reveal a significant association between serum vitamin D levels and IVF success [34]. Hu *et al.* data from more recent randomized evidence also contribute to this debate [35]. These results, taken together, suggest that improved potential reproductive indicators should not be taken as definitive evidence of higher probability of a live birth.

The discrepancies between studies may be due to varying vitamin D deficiency criteria, supplementation protocols, baseline metabolic status, age of participants, BMI, infertility diagnosis, and/or assisted reproduction protocols. In addition, there was residual confounding in observational studies and less precision in smaller interventions. Multiple outcome testing and lack of consistency when reporting confidence intervals added to this, interpreting a challenge. The overall evidence is suggestive of a possible role for vitamin D in fertility, but not enough to make vitamin D supplementation a routine fertility-enhancing intervention. The main strengths of this systematic review are that it is located in a new area of research, but it has several limitations, including the fact that the studies were not all of the same design, the biological cutoff for vitamin D deficiency varied considerably, and definitions for reproductive outcomes were variable, making meta-analysis impossible. Some of the studies were small, had limited statistical reporting, and lacked adequate controls to assess for potential confounders. Evidence coverage may also be limited to studies and publications in English between 2020 and 2025. Multicenter randomized trials in the future should focus on using standardized methods to replace vitamin D, report adjusted effect estimates (with 95% confidence intervals), and use cumulative live birth as the primary outcome. Special emphasis needs to be given to women with PCOS, low ovarian reserve, and recurrent implantation failure.

CONCLUSIONS

There are at least 5 pathways in which Vitamin D could influence female reproductive function: Ovarian, Endocrine, Metabolic, Immunological and Endometrial. While supplementation appears to enhance some biochemical and physiological parameters, the existing evidence shows no clear evidence of enhanced clinical pregnancy or live-birth outcomes.

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DOI: https://doi.org/10.54393/pbmj.v9i10.1426

Authors' Contribution

Conceptualization: SK
Methodology: SK
Formal analysis: SK
Writing and Drafting: SK, RK, GM, NF, SY, NNC
Review and Editing: SK, RK, GM, NF, SY, NNC

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflict of Interest

All the authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

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