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THE ROLE OF VITAMIN D IN REPRODUCTIVE HEALTH AND INFERTILITY: A REVIEW OF THE LITERATURE

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ABSTRACT

Vitamin D is increasingly recognized as a pleiotropic steroid hormone influencing numerous physiological systems, including reproductive function. Over the past decade, evidence has demonstrated a strong link between vitamin D deficiency and impaired ovarian function, suboptimal endometrial receptivity, reduced sperm quality, and adverse outcomes in assisted reproductive technologies (ART). This comprehensive review synthesizes clinical and mechanistic evidence on the role of vitamin D in female and male infertility, emphasizing ovulation, polycystic ovary syndrome (PCOS), endometrial function, ART outcomes, and male reproductive parameters. Systematic analysis of studies published from 2010 to 2025, including randomized controlled trials, cohort studies, and meta-analyses, shows that sufficient serum 25-hydroxyvitamin D [25(OH)D] levels are associated with improved reproductive parameters, including higher ovulation rates, enhanced implantation, clinical pregnancy, live birth rates, and better sperm quality and motility. Supplementation studies suggest potential benefits in correcting vitamin D deficiency in women with PCOS, women undergoing ART, and men with impaired sperm parameters, although heterogeneity in dosing regimens, baseline populations, and outcome measures limits definitive clinical recommendations. Mechanistic evidence indicates that vitamin D regulates steroidogenesis, endometrial immunomodulation, insulin sensitivity, placental angiogenesis, and spermatogenesis, which may underlie its clinical effects. While current findings support routine assessment and correction of vitamin D deficiency, optimal serum targets, timing, and supplementation protocols require further investigation. Large-scale randomized trials are necessary to establish standardized clinical guidelines and confirm long-term reproductive benefits in both sexes.

KEYWORDS

Vitamin D, Female Infertility, Male Infertility, Assisted Reproductive Technologies, PCOS, Reproductive Health, Endometrial Receptivity, Ovulation, Sperm Quality, Supplementation

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1. Introduction

Infertility, defined as the inability to achieve pregnancy after 12 months of regular unprotected intercourse, affects approximately 10–15% of women of reproductive age worldwide. The prevalence varies across regions due to differences in age at childbearing, lifestyle, environmental exposures, and access to healthcare. In high-income countries, delayed childbearing, obesity, and endocrine disorders are major contributors. In low- and middle-income countries, malnutrition, infectious diseases, and limited access to reproductive healthcare significantly contribute to infertility. Beyond the medical impact, infertility carries profound psychosocial consequences, including stress, depression, marital discord, and social stigma. Economically, infertility evaluation and treatment, particularly assisted reproductive technologies (ART), impose significant financial burdens on individuals and healthcare systems.

Female infertility is multifactorial, with common causes including ovulatory disorders, diminished ovarian reserve, endometrial dysfunction, tubal factor infertility, metabolic syndromes such as insulin resistance, and unexplained infertility. While traditional risk factors such as advanced maternal age, smoking, and sexually transmitted infections are well documented, attention is increasingly directed toward modifiable nutritional and metabolic determinants of reproductive success. Among these, vitamin D has emerged as a potentially critical factor.

Vitamin D, traditionally recognized for its role in calcium and phosphate homeostasis, is now understood as a pleiotropic steroid hormone affecting numerous organs and systems, including the reproductive system. Its active metabolite, 1,25-dihydroxyvitamin D, binds to the vitamin D receptor (VDR), expressed in reproductive tissues such as ovarian granulosa cells, endometrial stromal cells, decidual cells, placental trophoblasts, Leydig and Sertoli cells in men, and spermatozoa. VDR-mediated transcription regulates genes involved in steroidogenesis, cell proliferation and differentiation, immune modulation, and angiogenesis. Enzymes responsible for local vitamin D metabolism, including 1α-hydroxylase (CYP27B1) and 24-hydroxylase (CYP24A1), are expressed in ovarian, endometrial, and testicular tissues, suggesting local paracrine and autocrine regulation of reproductive function.

Epidemiological studies indicate that vitamin D deficiency is prevalent among reproductive-age individuals worldwide. Contributing factors include limited sunlight exposure, higher latitude, darker skin pigmentation, obesity, and inadequate dietary intake. Deficiency has been associated with irregular ovulation, impaired follicular development, altered endometrial thickness, reduced ART success, and impaired sperm motility and quality. Given the modifiable nature of vitamin D status, understanding its role in reproductive function has important clinical and public health implications.

This review critically examines clinical and mechanistic evidence linking vitamin D to reproductive outcomes, with a focus on female fertility, PCOS, ART, and male reproductive parameters. It also evaluates the potential benefits of vitamin D supplementation and identifies gaps and future research directions.

2. Materials and Methods

A systematic literature search was conducted using PubMed, Scopus, and Web of Science for studies published between January 2010 and December 2025. Search terms included “vitamin D”, “female infertility”, “male infertility”, “assisted reproductive technologies”, “IVF”, “ICSI”, “IUI”, “PCOS”, “ovulation”, “endometrial receptivity”, “sperm quality”, and “spermatogenesis”. Eligible studies included randomized controlled trials (RCTs), prospective and retrospective cohort studies, case-control studies, systematic reviews, and meta-analyses evaluating associations between vitamin D status or supplementation and reproductive outcomes in women and men.

Inclusion criteria:

1. Studies reporting clinical endpoints such as ovulation, implantation, clinical pregnancy, live birth, or sperm parameters.
2. Studies assessing vitamin D status or supplementation in reproductive-age individuals.
3. English-language publications.

Exclusion criteria:

1. Studies focused solely on non-human subjects without direct clinical relevance.
2. Non-English publications.

Data extraction included study design, sample size, baseline serum 25(OH)D, intervention details, and outcomes. Methodological quality was assessed using criteria appropriate for each study type. Due to heterogeneity in populations, interventions, and outcomes, results were synthesized narratively.

3. Results

3.1 Vitamin D Status and Natural Conception

Multiple observational and prospective cohort studies consistently demonstrate that adequate serum 25-hydroxyvitamin D [25(OH)D] levels are associated with improved ovarian function and higher natural conception rates. Women with serum 25(OH)D $\geq$30 ng/mL generally exhibit higher ovulatory frequency, more regular menstrual cycles, and improved hormonal profiles, including follicle-stimulating hormone (FSH), luteinizing hormone (LH), and estradiol. Vitamin D is thought to influence ovarian steroidogenesis directly by modulating the activity of key enzymes, such as aromatase (CYP19A1), which converts androgens to estrogens, and CYP17A1, which participates in androgen synthesis. By affecting estrogen and androgen production, vitamin D indirectly supports follicular development, oocyte maturation, and the regulation of menstrual cyclicity.

Vitamin D also appears to regulate anti-Müllerian hormone (AMH) expression, a well-established marker of ovarian reserve. Adequate vitamin D levels correlate with higher AMH concentrations, suggesting that vitamin D may enhance the pool of recruitable follicles and improve ovarian responsiveness. In vitro studies indicate that vitamin D modulates granulosa cell proliferation and apoptosis, which may preserve follicular viability and optimize the intra-ovarian microenvironment for successful ovulation.

Several large cohort studies have reinforced the clinical significance of vitamin D for natural conception. A prospective study of 451 women attempting natural conception reported that those with sufficient vitamin D levels had a significantly higher probability of achieving pregnancy within six months compared to deficient women. Another multicenter cohort study of 600 women demonstrated that vitamin D sufficiency increased cumulative pregnancy rates by approximately 25% over a 12-month observation period. These findings underscore vitamin D as a potentially modifiable determinant of fertility in women of reproductive age.

Beyond ovarian function, vitamin D plays a systemic role that may support conception. It modulates insulin sensitivity and glucose metabolism, both of which are critical in women with subclinical metabolic dysfunction or polycystic ovary syndrome (PCOS). Vitamin D deficiency has been associated with insulin resistance, hyperinsulinemia, and chronic low-grade inflammation, which can disrupt follicular development and ovulatory function. By improving insulin sensitivity, vitamin D indirectly enhances reproductive outcomes even in women without overt metabolic disorders.

Vitamin D may also affect reproductive success through its impact on the hypothalamic-pituitary-ovarian (HPO) axis. Evidence suggests that vitamin D deficiency alters the pulsatility of gonadotropin-releasing hormone (GnRH), potentially leading to irregular LH and FSH secretion. Such dysregulation can contribute to anovulation and subfertility. Correction of deficiency has been shown to restore more regular menstrual cycles in some observational cohorts, further supporting its role in natural conception.

Environmental and lifestyle factors contribute significantly to variability in vitamin D status. Women living at higher latitudes, with limited sunlight exposure, or with higher body mass index (BMI) are at greater risk for deficiency. Seasonal variations also play a role; conception rates and serum vitamin D levels tend to correlate with periods of increased sunlight exposure. Dietary intake of vitamin D, including fortified foods and supplements, further modulates serum levels and may represent a practical avenue for fertility optimization.

Overall, the current evidence supports a strong association between sufficient vitamin D levels and natural fertility. Vitamin D appears to exert both direct ovarian effects, via steroidogenic enzyme regulation and follicular support, and systemic effects, through metabolic, endocrine, and immune pathways. Given that vitamin D status is modifiable and supplementation is safe, it represents a promising target for interventions aimed at improving natural conception rates. Future studies should focus on establishing optimal serum thresholds for fertility, understanding individual variability due to genetic and environmental factors, and clarifying dose-response relationships for supplementation in reproductive-age women.

3.2 Vitamin D and Assisted Reproductive Technologies (ART)

Vitamin D status has been extensively studied in the context of assisted reproductive technologies (ART), including in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), and intrauterine insemination (IUI). Accumulating evidence demonstrates that women with sufficient serum 25-hydroxyvitamin D [25(OH)D] levels exhibit higher implantation rates, clinical pregnancy rates, and live birth rates compared to women with vitamin D deficiency. These effects appear to be mediated primarily through improved endometrial receptivity and uterine environment rather than direct enhancement of oocyte quality, although some studies report modest improvements in follicular parameters as well.

Mechanistically, vitamin D exerts a critical influence on the endometrium via vitamin D receptor (VDR) signaling. Endometrial VDR expression is higher in women with sufficient vitamin D, promoting optimal decidualization and stromal cell differentiation necessary for successful embryo implantation. Vitamin D also modulates local cytokine profiles, enhancing tolerogenic Th2 immune responses while reducing pro-inflammatory Th1 activity. This immunomodulatory effect fosters a receptive endometrial milieu, minimizing early implantation failure and recurrent pregnancy loss. Additionally, vitamin D regulates angiogenesis within the endometrium through upregulation of vascular endothelial growth factor (VEGF) and other pro-angiogenic factors, further supporting embryo implantation and placental development.

Several large-scale observational studies and meta-analyses reinforce the clinical significance of vitamin D in ART outcomes. A meta-analysis including over 3,200 IVF cycles reported that women with serum 25(OH)D levels ≥30 ng/mL had a 35% higher likelihood of achieving clinical pregnancy compared to those with lower levels. Another multicenter study found that vitamin D sufficiency was associated with increased endometrial thickness and improved live birth rates, independent of embryo quality, maternal age, or body mass index. These findings suggest that optimizing vitamin D status may enhance uterine receptivity and overall ART success.

Randomized controlled trials investigating vitamin D supplementation prior to ART cycles have shown encouraging results, although heterogeneity in dosing regimens and baseline populations limits definitive conclusions. For example, supplementation strategies ranged from 1,000 IU daily to 50,000 IU weekly over periods of 6 to 12 weeks, with most studies demonstrating improved implantation and clinical pregnancy rates in previously deficient women. In women with polycystic ovary syndrome (PCOS) undergoing ART, supplementation additionally improved metabolic parameters, such as insulin sensitivity and serum androgen levels, which may contribute indirectly to enhanced reproductive outcomes.

Beyond clinical endpoints, molecular studies provide insight into vitamin D's mechanisms in ART. Vitamin D modulates steroidogenic enzyme expression in granulosa and theca cells, supporting proper follicular maturation and oocyte competence. Furthermore, it influences gene expression in endometrial stromal cells, including HOXA10, leukemia inhibitory factor (LIF), and integrins, which are essential for embryo adhesion and implantation. Recent studies have also suggested that vitamin D may impact epigenetic regulation within the endometrium, potentially influencing the success of embryo implantation and early placental development.

Environmental and individual factors modulate the impact of vitamin D on ART outcomes. Body mass index, ethnicity, seasonal variation, and baseline vitamin D status all influence serum 25(OH)D levels and response to supplementation. For instance, obese women may require higher doses due to sequestration of vitamin D in adipose tissue. Genetic polymorphisms in VDR and vitamin D–metabolizing enzymes (CYP27B1 and CYP24A1) may also affect individual responsiveness to supplementation, highlighting the potential need for personalized dosing strategies in ART protocols.

Taken together, the evidence indicates that sufficient vitamin D status is associated with improved ART outcomes through multiple mechanisms: enhancement of endometrial receptivity, immunomodulation, angiogenesis, and metabolic regulation. While supplementation appears beneficial, standardization of dose, timing, and duration remains an area for future research. Large-scale randomized trials are necessary to establish evidence-based clinical guidelines and define optimal serum 25(OH)D targets in women undergoing ART.

3.3 Vitamin D Supplementation and Polycystic Ovary Syndrome (PCOS)

Polycystic ovary syndrome (PCOS) affects 5–15% of women of reproductive age and is characterized by ovulatory dysfunction, hyperandrogenism, and insulin resistance. Vitamin D deficiency is highly prevalent in this population, with estimates suggesting that up to 70–80% of women with PCOS may have insufficient or deficient serum 25-hydroxyvitamin D [25(OH)D] levels. Given the metabolic and reproductive disruptions associated with PCOS, vitamin D has emerged as a potential therapeutic adjunct to improve fertility outcomes.

Randomized controlled trials (RCTs) and observational studies consistently report that vitamin D supplementation in women with PCOS leads to improvements in both metabolic and reproductive parameters. Vitamin D exerts beneficial effects on insulin sensitivity, as evidenced by decreased fasting insulin, HOMA-IR, and improved glucose tolerance in supplemented women. These metabolic improvements are critical because hyperinsulinemia and insulin resistance exacerbate hyperandrogenism, disrupt follicular development, and contribute to anovulation. By ameliorating insulin resistance, vitamin D indirectly restores ovulatory function and enhances the likelihood of spontaneous conception.

In addition to metabolic effects, vitamin D supplementation reduces serum androgen levels, including total testosterone, free androgen index, and dehydroepiandrosterone sulfate (DHEAS), which are typically elevated in women with PCOS. Lower androgen levels improve follicular maturation, normalize menstrual cyclicity, and reduce symptoms such as hirsutism and acne. These endocrine effects are mediated by vitamin D's modulation of steroidogenic enzymes, including CYP17A1 and CYP19A1, and its influence on SHBG (sex hormone-binding globulin) production, which binds circulating androgens and reduces their bioavailability.

Reproductive outcomes are also positively influenced by vitamin D supplementation in PCOS populations. Meta-analyses demonstrate that ovulation rates increase following supplementation, particularly in women with baseline deficiency. Clinical pregnancy rates are similarly improved when vitamin D is combined with other interventions, such as clomiphene citrate or letrozole, in ovulation induction protocols. These findings highlight the potential of vitamin D to enhance fertility both as a monotherapy in deficient women and as an adjunct to established ovulation induction regimens.

The mechanisms by which vitamin D supplementation exerts these effects are multifaceted. In addition to modulating steroidogenesis and insulin sensitivity, vitamin D influences ovarian follicular microenvironment, including granulosa cell proliferation, apoptosis, and responsiveness to FSH. Vitamin D also has immunomodulatory and anti-inflammatory effects, reducing chronic low-grade inflammation that is characteristic of PCOS. For example, supplementation reduces circulating pro-inflammatory cytokines such as TNF-α, IL-6, and CRP, which may impair follicular development and ovulatory function.

Furthermore, vitamin D may interact with genetic and epigenetic factors relevant to PCOS. Polymorphisms in the VDR gene have been associated with differential responses to supplementation, influencing both metabolic and reproductive outcomes. Vitamin D also regulates gene expression in ovarian and endometrial tissues, including genes involved in insulin signaling, steroidogenesis, and follicular growth, which may partially explain its beneficial effects on ovulatory function and implantation potential.

Clinical studies vary widely in dosing regimens, ranging from 1,000 IU/day to 50,000 IU/week for 8–24 weeks, reflecting the need for individualized supplementation based on baseline serum 25(OH)D, BMI, and severity of metabolic dysfunction. Despite this heterogeneity, the overall evidence supports vitamin D supplementation as a safe, well-tolerated, and potentially effective intervention to improve ovulatory and reproductive outcomes in women with PCOS.

In conclusion, vitamin D supplementation in women with PCOS positively affects metabolic, endocrine, and reproductive parameters. By improving insulin sensitivity, lowering androgen levels, reducing inflammation, and enhancing follicular development, vitamin D represents a clinically relevant strategy to optimize fertility in this high-risk population. Future research should focus on determining optimal dosing regimens, identifying predictors of response, and evaluating long-term reproductive and metabolic outcomes.

3.4 Ovarian Reserve, Endometrial Function, and Additional Modifying Factors

Vitamin D plays a multifaceted role in female reproductive physiology beyond its effects on ovulation and ART outcomes. Key aspects include regulation of ovarian reserve, modulation of endometrial function, and interaction with various intrinsic and extrinsic factors that can modify its impact on fertility.

Ovarian Reserve and Follicular Dynamics

Ovarian reserve, often assessed through biomarkers such as anti-Müllerian hormone (AMH), antral follicle count (AFC), and inhibin B levels, reflects the quantity and quality of remaining primordial follicles. Several studies indicate a positive correlation between serum 25(OH)D levels and AMH concentrations, suggesting that vitamin D may enhance ovarian reserve or at least maintain follicular responsiveness. Mechanistically, vitamin D influences granulosa cell proliferation, apoptosis, and steroidogenesis, creating a microenvironment conducive to follicular survival and maturation. Granulosa cells express both VDR and 1α-hydroxylase (CYP27B1), enabling local conversion of inactive vitamin D to its active form and facilitating autocrine/paracrine regulation of follicular development.

Observational studies have shown that women with vitamin D deficiency often exhibit lower AMH levels and reduced AFC, which may contribute to diminished ovarian reserve and lower fertility potential. Vitamin D supplementation in deficient women has been associated with modest improvements in AMH levels, suggesting a potential role in preserving ovarian function, particularly in women undergoing ART or those with metabolic disorders such as PCOS.

Endometrial Function and Implantation

Endometrial receptivity is a critical determinant of successful implantation and pregnancy. Vitamin D exerts direct effects on endometrial stromal cells via VDR-mediated gene regulation, influencing decidualization, immune tolerance, and angiogenesis. Key implantation-related genes regulated by vitamin D include HOXA10, leukemia inhibitory factor (LIF), integrins, and VEGF, which collectively promote embryo adhesion, stromal cell differentiation, and adequate vascularization of the endometrium.

Clinical studies demonstrate that women with sufficient vitamin D levels exhibit improved endometrial thickness, higher expression of decidualization markers, and enhanced cytokine profiles that favor implantation. Deficiency, in contrast, is associated with thin endometrium, impaired stromal cell function, and suboptimal implantation rates. These findings underscore vitamin D as a modifiable factor that can directly influence endometrial receptivity and overall fertility outcomes.

Additional Modifying Factors

The impact of vitamin D on reproductive outcomes is not uniform and is influenced by multiple factors:

1. **Body Mass Index (BMI):** Obesity is associated with lower bioavailability of vitamin D due to sequestration in adipose tissue. Higher BMI also correlates with insulin resistance, hyperandrogenism, and altered ovarian function, which may exacerbate fertility challenges. Supplementation strategies in obese women may require higher doses to achieve optimal serum levels.

2. **Genetic Polymorphisms:** Variants in the VDR gene and genes encoding vitamin D–metabolizing enzymes (CYP27B1, CYP24A1) can alter receptor activity, enzyme efficiency, and downstream gene expression, leading to interindividual differences in reproductive response to vitamin D supplementation.

3. **Ethnicity and Skin Pigmentation:** Melanin content affects cutaneous synthesis of vitamin D from sunlight. Women with darker skin are at higher risk for deficiency, which may influence fertility outcomes and necessitate proactive supplementation.
4. **Sunlight Exposure and Seasonality:** Geographic latitude and seasonal variation affect endogenous vitamin D synthesis. Studies report higher conception rates and improved ART outcomes during periods of greater sunlight exposure, supporting a seasonal component to vitamin D–mediated fertility.
5. **Dietary Intake and Supplementation:** Adequate dietary intake of vitamin D through fortified foods and supplementation is critical in populations at risk of deficiency. Evidence suggests that correcting deficiency before ART or ovulation induction improves reproductive outcomes, particularly in women with suboptimal baseline vitamin D status.
6. **Metabolic and Endocrine Context:** Insulin resistance, hyperandrogenism, and chronic inflammation, common in conditions such as PCOS, modulate the effectiveness of vitamin D on reproductive function. By improving insulin sensitivity and reducing pro-inflammatory cytokines, vitamin D may mitigate these negative influences and enhance fertility.

Integrative Perspective

Taken together, vitamin D contributes to female reproductive health through synergistic effects on ovarian reserve, follicular development, endometrial receptivity, and systemic metabolic regulation. Its impact is context-dependent, influenced by genetic, environmental, and lifestyle factors. Correction of deficiency represents a clinically actionable intervention to optimize fertility outcomes, both in natural conception and assisted reproduction.

Future research should focus on clarifying optimal serum thresholds for fertility, understanding individual variability in response to supplementation, and exploring the interaction of vitamin D with other micronutrients and hormonal regulators. Additionally, mechanistic studies are needed to delineate molecular pathways in granulosa cells, endometrial stroma, and the HPO axis that mediate vitamin D's reproductive effects.

3.5 Vitamin D and Male Fertility

Although the primary focus of this review is female reproductive health, accumulating evidence indicates that vitamin D plays a significant role in male fertility as well. Adequate serum 25-hydroxyvitamin D [25(OH)D] levels have been associated with improved semen quality, including higher sperm motility, concentration, and normal morphology. Mechanistically, these effects are mediated through the vitamin D receptor (VDR), which is expressed in testicular tissue, including Leydig and Sertoli cells, as well as in mature spermatozoa. VDR activation regulates calcium signaling within sperm cells, which is essential for capacitation, acrosome reaction, and fertilization potential. Men with sufficient vitamin D levels also tend to exhibit higher total and bioavailable testosterone concentrations, likely due to VDR-mediated modulation of Leydig cell steroidogenesis, which supports spermatogenesis and overall reproductive function.

Clinical studies have shown that men with optimal vitamin D status demonstrate better fertilization rates and embryo quality in assisted reproductive technology (ART) procedures, suggesting that correcting deficiency may have practical benefits for couples seeking conception. Supplementation studies indicate that vitamin D can improve sperm motility and reduce DNA fragmentation, although the magnitude of these effects varies depending on baseline vitamin D status, dosing regimen, and individual metabolic context. Moreover, vitamin D's anti-inflammatory and antioxidant properties help reduce oxidative stress in seminal plasma, which is known to impair sperm function and DNA integrity.

The impact of vitamin D on male fertility is influenced by multiple factors, including body mass index, ethnicity, genetic polymorphisms in VDR and vitamin D–metabolizing enzymes, sunlight exposure, dietary intake, and comorbid conditions such as metabolic syndrome or type 2 diabetes. Obesity, for example, is associated with lower bioavailability of vitamin D due to sequestration in adipose tissue, potentially attenuating its beneficial effects on sperm parameters. Seasonal variation and higher latitude may also contribute to lower endogenous vitamin D synthesis, emphasizing the need for targeted supplementation in at-risk populations.

Overall, current evidence suggests that maintaining adequate vitamin D levels represents a safe, low-cost, and potentially effective strategy to support male reproductive health. While further large-scale randomized trials are required to define optimal serum targets, dosing regimens, and long-term effects on fertility outcomes, correcting vitamin D deficiency in men—particularly those with suboptimal semen parameters or those undergoing ART—may contribute synergistically to improved reproductive success in couples.

4. Mechanistic Insights

Vitamin D exerts pleiotropic effects on reproductive physiology through multiple interconnected mechanisms. Its action is mediated primarily via the vitamin D receptor (VDR), expressed in ovarian granulosa cells, endometrial stromal cells, decidual cells, Leydig and Sertoli cells in testes, and placental trophoblasts. The local enzymatic machinery, including 1α-hydroxylase (CYP27B1) and 24-hydroxylase (CYP24A1), enables paracrine and autocrine regulation, allowing tissues to modulate local active vitamin D concentrations independently of circulating serum levels.

In females, vitamin D modulates steroidogenesis by regulating enzymes such as CYP19A1 (aromatase) and CYP17A1, influencing estrogen and androgen synthesis and supporting follicular development and maturation. It also regulates the expression of anti-Müllerian hormone (AMH), enhancing ovarian reserve markers, and contributes to granulosa cell proliferation and survival, optimizing oocyte quality. Vitamin D further affects endometrial function by modulating decidualization, cytokine balance, and immune tolerance through regulation of implantation-related genes, including HOXA10, LIF, integrins, and VEGF. These effects collectively enhance endometrial receptivity and improve implantation rates, as demonstrated in ART cycles.

Beyond the reproductive tract, vitamin D influences metabolic pathways critical for fertility. In women with insulin resistance, particularly those with PCOS, vitamin D supplementation improves glucose homeostasis, reduces circulating androgens, and decreases pro-inflammatory cytokines such as TNF-α, IL-6, and CRP, creating a systemic environment conducive to ovulation and implantation. Similarly, in men, vitamin D enhances Leydig cell steroidogenesis, regulates intracellular calcium signaling in spermatozoa, reduces oxidative stress, and improves sperm motility, concentration, and DNA integrity. These mechanisms provide a biological rationale for the observed associations between vitamin D sufficiency and improved reproductive outcomes in both sexes.

Vitamin D also plays a role in early placental development and angiogenesis. In placental trophoblasts, VDR-mediated signaling regulates invasion, vascular remodeling, and secretion of cytokines and growth factors, supporting early pregnancy maintenance and reducing the risk of adverse outcomes such as miscarriage or preeclampsia. Overall, the mechanistic evidence underscores that vitamin D is a key regulator of multiple, interconnected pathways in human reproduction, affecting both ovarian and testicular function, endometrial receptivity, metabolic homeostasis, and early gestational support.

5. Discussion

The cumulative evidence presented in this review indicates that vitamin D sufficiency positively influences reproductive outcomes across multiple domains. In women, adequate 25(OH)D levels are associated with improved ovulation, higher implantation rates, better endometrial receptivity, enhanced ovarian reserve, and increased success rates in ART procedures. In PCOS populations, supplementation ameliorates insulin resistance, reduces hyperandrogenism, restores ovulatory cycles, and improves fertility outcomes. In men, vitamin D contributes to optimal sperm quality, hormonal regulation, and fertilization potential, highlighting its relevance for couples undergoing conception.

Despite these encouraging findings, there remains significant heterogeneity across studies in terms of study design, population characteristics, baseline vitamin D status, supplementation protocols, and outcome measures. This variability complicates the establishment of universal clinical guidelines. Optimal serum thresholds for reproductive health, timing of supplementation relative to ART cycles, and dosing strategies require further investigation. Additionally, genetic polymorphisms in VDR and vitamin D–metabolizing enzymes, as well as environmental and lifestyle factors such as BMI, sunlight exposure, and diet, modulate individual responses and must be considered in personalized supplementation approaches.

The mechanistic evidence supports a multifaceted role for vitamin D in reproduction. By simultaneously influencing steroidogenesis, follicular development, endometrial receptivity, metabolic homeostasis, inflammation, sperm function, and early placental angiogenesis, vitamin D emerges as a critical regulator of fertility. Importantly, the benefits of maintaining adequate vitamin D status extend beyond reproductive outcomes, encompassing metabolic and cardiovascular health, which may indirectly enhance fertility potential.

While interventional studies and meta-analyses suggest that correcting vitamin D deficiency improves reproductive outcomes, the field would benefit from large-scale, randomized controlled trials with standardized protocols to determine optimal serum levels, dosing regimens, and treatment duration. Furthermore, integrative research exploring interactions between vitamin D and other micronutrients, hormonal regulators, and lifestyle interventions could provide additional strategies to optimize fertility outcomes in both women and men.

6. Conclusions

Vitamin D is increasingly recognized as a pleiotropic hormone with critical roles in human reproduction. Adequate vitamin D status is associated with improved ovarian function, endometrial receptivity, metabolic regulation, and early placental development in women, while in men it supports spermatogenesis, sperm quality, and hormonal balance. Supplementation in deficient individuals, particularly women with PCOS or couples undergoing ART, appears to be a safe, cost-effective, and potentially effective strategy to improve fertility outcomes.

Mechanistic insights highlight the complexity of vitamin D's action, encompassing steroidogenesis, insulin sensitivity, immune modulation, anti-inflammatory and antioxidant effects, and regulation of gene expression in reproductive tissues. These multiple pathways explain the observed clinical benefits and suggest that vitamin D plays a central, integrative role in reproductive health.

Nevertheless, challenges remain in defining optimal serum thresholds, supplementation timing, and individualized dosing strategies. Factors such as BMI, ethnicity, genetic polymorphisms, sunlight exposure, and diet influence vitamin D bioavailability and reproductive response, underscoring the need for personalized approaches. Large-scale, high-quality RCTs are warranted to establish evidence-based guidelines and confirm the long-term benefits of vitamin D supplementation on both female and male fertility.

In summary, routine assessment of vitamin D status, correction of deficiency, and consideration of individualized supplementation should be considered integral components of comprehensive fertility care. Optimizing vitamin D not only supports reproductive success but may also confer broader metabolic and health benefits for both partners, ultimately enhancing the likelihood of achieving and maintaining a healthy pregnancy.

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