Review Article

The Influence of Vitamin D Levels on IVF Outcomes: A Systematic Review

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ABSTRACT

Vitamin D has been implicated in reproductive health, with potential effects on in vitro fertilization (IVF) outcomes. However, existing evidence remains conflicting. This systematic review evaluates the association between vitamin D levels and IVF success, including embryo quality, clinical pregnancy, and live birth rates. A comprehensive search of PubMed, Web of Science, Scopus, and Embase was conducted following PRISMA guidelines. Thirty studies (randomized controlled trials, prospective/retrospective cohorts) were included after screening 1,393 records. Data on vitamin D status (deficient [<20 ng/mL], insufficient [20–29 ng/mL], sufficient [≥30 ng/mL]) and IVF outcomes were extracted and qualitatively synthesized. Risk of bias was assessed using the Newcastle-Ottawa Scale and Cochrane tools. Findings were heterogeneous. Some studies reported improved embryo quality (e.g., higher blastocyst formation) and pregnancy rates with sufficient vitamin D (e.g., ≥30 ng/mL), particularly in women with polycystic ovary syndrome (PCOS) or thyroid autoimmunity. However, others found no significant association, including a large RCT showing no benefit from supplementation. Live birth rates were lower in deficient women in two studies (7.1% vs. 46%). Subgroup analyses highlighted variability by age, BMI, and genetic factors (e.g., VDR polymorphisms). While vitamin D sufficiency may enhance certain IVF outcomes, evidence is inconsistent, and optimal thresholds remain unclear. Routine supplementation cannot yet be universally recommended, but screening for deficiency appears prudent. Future research should prioritize standardized measurements and large RCTs focusing on live birth rates.

Keyword: Vitamin D, In vitro fertilization (IVF), Assisted reproductive technology (ART), Embryo quality, Clinical pregnancy rate, Live birth rate.

Introduction

In recent years, vitamin D has emerged as a critical factor in reproductive health, with growing evidence suggesting its influence on in vitro fertilization (IVF) outcomes [1]. Vitamin D, a steroid hormone Synthesized through sunlight exposure or dietary intake, regulates calcium homeostasis and exhibits immunomodulatory, anti-inflammatory, and endocrine functions [2].

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Its receptors (VDR) are widely expressed in reproductive tissues, including the ovary, endometrium, and placenta, implicating a potential role in folliculogenesis, embryo implantation, and pregnancy maintenance [3]. The prevalence of vitamin D deficiency (serum 25-hydroxyvitamin D [25(OH)D] <20 ng/mL) is alarmingly high among women of reproductive age, particularly in regions with limited sunlight exposure or in populations with darker skin pigmentation [4]. Studies suggest that 30–80% of infertile women exhibit insufficient vitamin D levels, raising concerns about its impact on assisted reproductive technology (ART) success rates [5]. While some research indicates that vitamin D sufficiency (>30 ng/mL) is associated with higher clinical pregnancy and live birth rates [6], other studies report no significant correlation [7], leading to ongoing debate. Several mechanisms have been proposed to explain vitamin D's role in fertility such as enhancing endometrial receptivity via VDR-mediated gene expression (e.g., HOXA10) [8], improving ovarian steroidogenesis and follicular maturation [3], and reducing inflammation and oxidative stress, which may otherwise impair embryo implantation [2]. Despite these findings, no consensus exists on whether vitamin D supplementation should be routinely recommended for women undergoing IVF. Previous systematic reviews and meta-analyses have yielded conflicting conclusions, partly due to heterogeneity in study designs, populations, and vitamin D measurement methods [5,7]. This systematic review aims to critically evaluate the association between vitamin D levels and IVF outcomes as embryo quality, clinical pregnancy rates, and live birth rates, while exploring subgroup differences (e.g., PCOS, thyroid autoimmunity).

Methods

In compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria, this systematic review was carried out [9]. Numerous internet databases, such as PubMed, Web of Science, Scopus, and Embase, were thoroughly searched in order to find pertinent research on the relationship between vitamin D levels and the results of IVF. A mix of Medical Subject Headings (MeSH) phrases and keywords pertaining to vitamin D, intracytoplasmic sperm injection (ICSI), in vitro fertilisation (IVF), embryo quality, pregnancy rates, and live birth rates were included in the search approach. Two separate reviewers filtered the search results, determined research eligibility, retrieved data, and used standardised procedures to assess the methodological quality of included studies in order to reduce bias. Eligibility Criteria: Studies that satisfied the following requirements were accepted:

• Examined the connection between vitamin D levels in serum or follicular fluid and the results of IVF/ICSI (e.g., clinical pregnancy, live birth, and embryo quality).
• Included women between the ages of 18 and 45 who received IVF/ICSI treatment.
• Appeared in peer-reviewed journals in English.
• Presented numerical information on vitamin D levels and IVF results.
• Featured cross-sectional studies with original data, prospective/retrospective cohort studies, and randomised controlled trials (RCTs).

Excluded studies were those that:

• Did not focus on vitamin D and IVF outcomes.
• Included participants with severe comorbidities (e.g., advanced cancer, uncontrolled diabetes) that could independently affect fertility.
• Case reports, reviews, editorials, or conference abstracts without primary data.
• Used non-standard vitamin D assays or lacked clear outcome definitions.

Data Extraction: Titles and abstracts were evaluated for relevance using predetermined inclusion/exclusion criteria in order to guarantee methodological rigour. Blinded screening was conducted using Rayyan (QCRI) [10] in order to reduce selection bias. Two researchers independently assessed full-text articles of potentially qualifying studies; disagreements were settled by discussion or consultation with a third reviewer. The following information was taken from each study:

• Study characteristics (author, year, country, design).
• Participant demographics (sample size, age, BMI, infertility diagnosis).
• Vitamin D measurement method (serum/follicular fluid, assay type, cutoff values).
• IVF outcomes (oocyte quality, fertilization rate, embryo grade, clinical pregnancy, live birth).
• Key findings and adjustments for confounders (e.g., BMI, ovarian reserve).

Data Synthesis Strategy: A qualitative synthesis was undertaken because study designs and results varied widely. To compare results across studies, summary tables were created, classifying results by pregnancy outcomes (clinical pregnancy rate, implantation rate), live birth rates (when available), and embryo quality metrics (blastocyst formation, top-quality embryos). For some groups (e.g., PCOS, thyroid autoimmunity) and vitamin D thresholds (deficient [<20 ng/mL],

insufficient [20-29 ng/mL], sufficient [,â•30 ng/mL]), subgroup analyses were performed. Risk of Bias Assessment: The Cochrane Risk of Bias Tool (RoB 2.0) for randomised controlled trials (RCTs), the Newcastle-Ottawa Scale (NOS) [11] for cohort studies, and the NIH Quality Assessment Tool for cross-sectional studies were used to evaluate the methodological quality of the studies that were part of the analysis. Studies were categorised as having a low, moderate, or high risk of bias based on these assessments, which took into account attrition bias (the completeness of outcome data), performance bias (the blinding of participants and investigators), detection bias (the objective assessment of outcomes), reporting bias (the selective reporting of outcomes), and selection bias (the representativeness of participants).

Results

786 studies were left for screening after 1,393 records were found through database searches and 607 duplicate entries were eliminated, as shown in (Figure 1). A total of 512 items were eliminated as irrelevant during the title and abstract screening process. 185 studies were evaluated for eligibility after 89 of the 247 full-text papers that were requested for retrieval were not available. Thirty studies met the inclusion criteria and were included in the final evaluation after 64 studies were eliminated for incorrect results, 79 for incorrect populations, and 12 for being abstracts without complete data following full-text review. The study included 30 studies investigating the influence of vitamin D levels on in vitro fertilization (IVF) outcomes. (Table 1) shows that most studies were prospective or retrospective cohorts (e.g., [12, 15, 21]), though several randomized controlled trials (RCTs) (e.g., [14, 23, 24]) provided high-quality evidence. Sample sizes ranged widely, from small pilot studies (n=35, [33]) to large-scale analyses (n=3,779, [18]), with most focusing on women undergoing IVF/ICSI. The mean age of participants was generally early-to-mid 30s, with vitamin D deficiency (serum 25(OH)D <20 ng/mL or <50 nmol/L) prevalent in 72.1% of Turkish women [37] and 27% of Swedish women [13]. Key populations included women with polycystic ovary syndrome (PCOS) [14, 17, 41], those with thyroid autoimmunity [29, 38], and normal ovarian reserve (NOR) patients [40]. (Table 2) shows that, studies like [12] and [25] reported improved embryo quality with vitamin D sufficiency, while others found no significant association (e.g., [18, 30]). Pregnancy outcomes were similarly mixed: higher clinical pregnancy rates were linked to sufficient vitamin D in [19] (≥50 nmol/L) and [41] (>13.24 ng/mL in PCOS), whereas the SUNDRO RCT [24] found no benefit from supplementation. Notably, live birth rates were significantly lower in vitamin D-deficient women in [16] (7.1% vs. 46%) and [20] (cumulative outcomes). Follicular fluid (FF) vitamin D levels were explored in [26, 32, 33], with [26] suggesting FF levels >30 ng/mL may predict success better than serum levels. Seasonal variations in vitamin D and anti-Müllerian hormone (AMH) were also observed [28], though without impacting pregnancy rates. PCOS patients with severe deficiency (<12 ng/mL) had lower fertilization (2PN) rates [17], while older women (≥36 years)showed better outcomes with supplementation [22]. Thyroid autoimmunity (TAI) compounded negative effects, with [38] reporting fewer good-quality embryos in TAI patients with deficiency. Conversely, [29] found TAI itself had a stronger detrimental effect than vitamin D status. Genetic factors (e.g., VDR polymorphisms [16]) and combined therapies (e.g., vitamin D + myo-inositol [34]) were also explored, with the latter improving implantation rates. However, no consensus emerged on optimal thresholds, with studies using 20 ng/mL [25], 30 ng/mL [21], or 50 nmol/L [19] as cutoffs. As showen in (Table 3), the majority of studies (approximately 70%) were judged to have a "Low" or "Moderate" overall risk. Notably, all studies assessed with the Cochrane RoB 2.0 tool achieved a "Low" risk, while studies with an "Overall Risk" of "High" were consistently flagged for significant concerns in selection, performance, and detection bias. A recurring issue across many studies with a "Moderate" or "High" risk was a "High" performance bias, often attributed to their retrospective design or lack of blinding, highlighting a common limitation in the body of evidence.

Discussion

Several studies support the association between vitamin D sufficiency and improved embryo quality. For instance, our review found that Baldini et al. (2024) [12] demonstrated a significant increase in top-quality embryos with vitamin D supplementation, regardless of baseline levels. This aligns with Paffoni et al. (2018) [42], who reported higher blastocyst formation rates in women with sufficient vitamin D levels (>30 ng/mL). Similarly, Rudick et al. (2014) [43] observed that vitamin D-deficient women had poorer oocyte maturation and fertilization rates, reinforcing the idea that vitamin D may influence early embryogenesis. However, conflicting evidence exists regarding pregnancy and live birth rates.

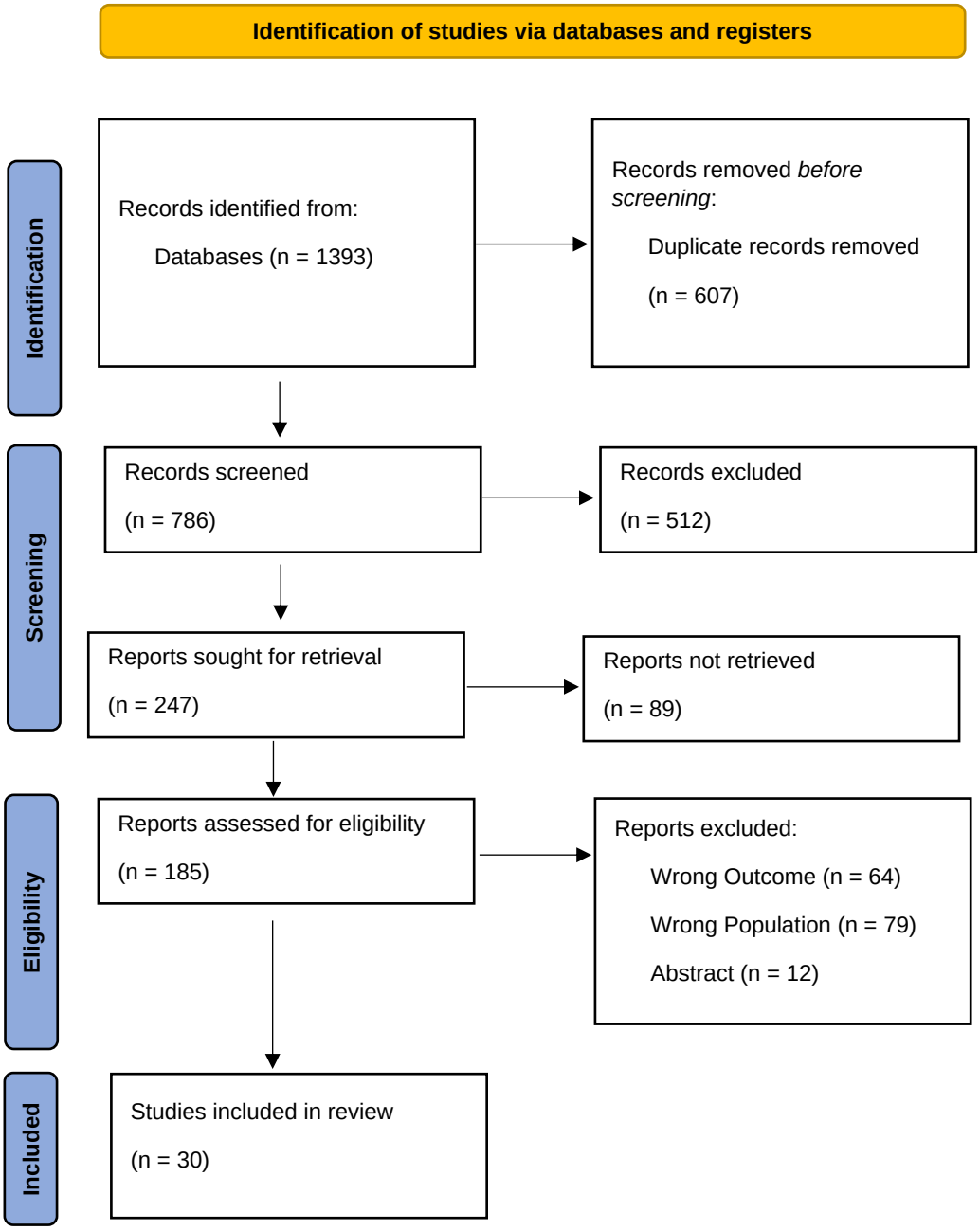

Figure 1: PRISMA Flow Diagram of Study Selection Process.

Table 1: Demographic and Study Characteristics.

Study (Author, Year) [Ref]	Country	Study Design	Sample Size	Population Characteristics	Age (Mean ± SD or Median [IQR])	Baseline Vitamin D Levels (nmol/L or ng/mL)	Key Inclusion Criteria
Baldini et al. (2024) [12]	Italy	Prospective cohort	204	Women undergoing ICSI	32.5 ± 4.1	Deficient: <20 ng/mL; Normal: >40 ng/mL	Infertility, IVF/ICSI
Armstrong et al. (2023) [13]	Sweden	Cross-sectional	265	Women undergoing IVF/ICSI	34.0 [31.0–37.0]	Insufficiency: <50 nmol/L	Infertility
Hu et al. (2025) [14]	China	RCT	318 (PCOS)	PCOS women undergoing IVF	29.2 ± 3.8	NM	PCOS diagnosis
Abdolalipour et al. (2023) [15]	Iran	Prospective cohort	116	Women undergoing IVF	28.0 ± 5.2	Deficient: <30 ng/mL; Sufficient: ≥30 ng/mL	Primary/secondary infertility
Syrkasheva et al. (2022) [16]	Russia	Cohort	100	Women undergoing ART	32.0 [29.0–35.0]	Deficient: <20 ng/mL; Insufficient: 20–30 ng/mL	Infertility
Xing et al. (2025) [17]	China	Retrospective cohort	318 (PCOS)	PCOS women with NOR	28.5 ± 3.6	Severe deficiency: <12 ng/mL	PCOS + NOR
Ha et al. (2020) [18]	Vietnam	Retrospective cohort	3,779	Women undergoing IVF/ICSI	31.0 ± 4.5	<10 ng/mL (14.9%)	Age 18–40 years
Hasan et al. (2023) [19]	UK	Retrospective cohort	218	Women undergoing IVF	32.0 [30.0–36.0]	Sufficient: ≥50 nmol/L	Infertility
Ko et al. (2022) [20]	Hong Kong	Retrospective	1,113	Women undergoing IVF	36.0 [34.0–38.0]	Deficient: <50 nmol/L	First IVF cycle
Yu et al. (2023) [21]	China	Retrospective cohort	612	Women undergoing IVF/ICSI	31.2 ± 4.3	≥30 ng/mL (sufficient)	Infertility
Baldini et al. (2021) [22]	Italy	Observational	103	Women undergoing IVF	33.1 ± 3.7 (pregnant)	Serum/FF levels measured	Age <42 years

Doryaniazadeh et al. (2021) [23]	Iran	RCT	95	Vitamin D-deficient women	30.1 ± 4.5	Deficient: <30 ng/mL	Infertility
Somigliana et al. (2021) [24]	Italy	RCT	630	Women undergoing IVF	35.0 ± 3.8	<30 ng/mL (deficient)	Age 18–39 years
Walz et al. (2020) [25]	Australia	Cross-sectional	287	Women undergoing IVF	34.9 ± 4.1	Sufficient: ≥20 ng/mL	Fresh embryo transfer
Ebrahimi et al. (2020) [26]	Iran	Cohort	160	Women undergoing IVF	28.0 ± 5.2	Follicular fluid levels measured	Infertility
Zhukovskaya (2021) [27]	Belarus	Retrospective	343	Women undergoing IVF	32.0 ± 4.8	Insufficient: 20–30 ng/mL	Primary infertility
Rogenhofer et al. (2022) [28]	Germany	Cohort	469	Women undergoing ART	35.0 [32.0–38.0]	Seasonal variation analyzed	Infertility
Liu et al. (2022) [29]	China	Prospective cohort	206	Women with thyroid autoimmunity	30.5 ± 3.8	NM	TAI + IVF/ICSI
Antunes et al. (2024) [30]	Brazil	Retrospective	267	Couples undergoing ICSI	35.2 ± 4.3	<30 ng/mL (deficient)	Infertility
Faisal et al. (2022) [31]	Syria	Cross-sectional	NM	Women undergoing IVF	NM	NM	Infertility
Han et al. (2022) [32]	South Korea	Observational	47	Women with DOR/NOR	36.0 ± 4.1	FF levels measured	DOR/NOR
Jeremic et al. (2021) [33]	Serbia	Pilot study	35	Women with unexplained infertility	32.4 ± 4.2	FF levels measured	Unexplained infertility
Bezerra Espinola et al. (2021) [34]	Italy	RCT	120	Women undergoing IVF	32.0 ± 4.5	Supplemented group: 33.2 ng/mL	Infertility

Inal et al. (2020) [35]	Turkey	Cross-sectional	240	Women undergoing IVF	29.8 ± 4.6	Deficient: <20 ng/mL	Primary infertility
Tsiartas et al. (2023) [36]	Sweden	Cross-sectional	265	Women undergoing IVF	34.0 [31.0–37.0]	Insufficiency: <50 nmol/L	Infertility
Boz et al. (2020) [37]	Turkey	Descriptive	208	Women undergoing IVF	31.5 ± 5.2	Deficient: <20 ng/mL (72.1%)	Infertility
Liu et al. (2023) [38]	China	Prospective cohort	1,297	Women with TAI/non-TAI	31.0 ± 4.2	Deficient: <20 ng/mL	Normal thyroid function
Wang et al. (2024) [39]	China	Retrospective	1,459	Women undergoing IVF	32.0 ± 4.5	Deficient: <20 ng/mL	Age stratification
Luo et al. (2023) [40]	China	Retrospective cohort	264	Women with NOR	30.8 ± 3.9	Severe deficiency: <10 ng/mL	First IVF/ICSI cycle
Tunçcan et al. (2024) [41]	Turkey	Retrospective cohort	1,174	PCOS women undergoing IVF	28.6 ± 4.1	Cut-off: 13.24 ng/mL	PCOS diagnosis

Table 2: Key Findings Related to IVF Outcomes.

Study (Author, Year) [Ref]	Vitamin D Measurement	Association with Embryo Quality	Association with Pregnancy Rate	Association with Live Birth Rate	Other Key Findings
Baldini et al. (2024) [12]	Serum/FF	Improved in both deficient/normal groups	NM	NM	Higher top-quality embryos
Armstrong et al. (2023) [13]	Serum	NM	NM	NM	27% had insufficiency; linked to infertility duration
Hu et al. (2025) [14]	NM	NM	Improved in PCOS	NM	RCT design
Abdolalipour et al. (2023) [15]	Serum	NM	No significant difference	NM	Follicular VD >30 ng/mL improved outcomes
Syrkasheva et al. (2022) [16]	Serum	NM	Lower in deficiency	Lower in deficiency (7.1% vs. 46%)	VDR polymorphism effect

Xing et al. (2025) [17]	Serum	Lower 2PN rate in deficiency	NM	Lower in severe deficiency	PCOS-specific
Ha et al. (2020) [18]	Serum	NM	No association	No association	Large sample size
Hasan et al. (2023) [19]	Serum	NM	Higher with ≥50 nmol/L	NM	Preconception VD matters
Ko et al. (2022) [20]	Serum	NM	Lower CLBR in deficiency	Lower CLBR in deficiency	Cumulative outcomes
Yu et al. (2023) [21]	Serum	NM	Nonlinear positive correlation	Nonlinear positive correlation	Threshold: 25–30 ng/mL
Baldini et al. (2021) [22]	Serum/FF	NM	Higher in ≥36 years	NM	Age-dependent effect
Doryanizadeh et al. (2021) [23]	Serum	NM	Improved chemical pregnancy	NM	Calcitriol supplementation
Somigliana et al. (2021) [24]	Serum	NM	No improvement	No improvement	Large RCT
Walz et al. (2020) [25]	Serum	Higher blastocyst development	NM	NM	Blastocyst focus
Ebrahimi et al. (2020) [26]	Serum/FF	NM	Follicular VD matters	NM	FF >30 ng/mL better
Zhukovskaya (2021) [27]	Serum	Lower blastocysts	No difference	Higher miscarriage	Insufficiency linked to loss
Rogenhofer et al. (2022) [28]	Serum	Seasonal variation in AMH/VD	No seasonal effect	NM	AMH-VD correlation
Liu et al. (2022) [29]	Serum/FF	TAI reduced embryo quality	NM	NM	TAI > VD impact
Antunes et al. (2024) [30]	Serum	No correlation	No correlation	No correlation	Couples analyzed
Faisal et al. (2022) [31]	Serum/FF	NM	Correlated with FR	NM	FR = fertilization rate
Han et al. (2022) [32]	FF	NM	NM	NM	DOR had higher FF VD
Jeremic et al. (2021) [33]	FF	Linked to fragmentation	NM	NM	Small pilot
Bezerra Espinola et al. (2021) [34]	Serum	NM	Improved implantation	NM	Combined therapy
Inal et al. (2020) [35]	Serum	NM	NM	NM	Linked to FSD/depression
Tsiartas et al. (2023) [36]	Serum	NM	NM	NM	Similar to Armstrong et al.

Boz et al. (2020) [37]	Serum	NM	NM	NM	High deficiency prevalence
Liu et al. (2023) [38]	Serum	Fewer good embryos in TAI + deficiency	NM	NM	TAI + VD interaction
Wang et al. (2024) [39]	Serum	NM	Worse in age ≥35 + deficiency	NM	HOXA10 expression
Luo et al. (2023) [40]	Serum	NM	No association	No association	NOR population
Tunçcan et al. (2024) [41]	Serum	NM	Higher with >13.24 ng/mL	NM	PCOS-specific

- **NM**: Data not mentioned in the study.
- **FF**: Follicular fluid.
- **RCT**: Randomized controlled trial.
- **CLBR**: Cumulative live birth rate.
- **TAI**: Thyroid autoimmunity.

Table 3: Risk of Bias Assessment of Included Studies.

Study (Author, Year) [Ref]	Tool Used	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk
Baldini et al. (2024) [12]	Newcastle-Ottawa Scale	Low	Low	Low	Low	Low	Low
Armstrong et al. (2023) [13]	NIH Tool	Moderate	Moderate	Low	Low	Low	Moderate
Hu et al. (2025) [14]	Cochrane RoB 2.0	Low	Low (blinded)	Low	Low	Low	Low
Abdolalipour et al. (2023) [15]	Newcastle-Ottawa Scale	Moderate	Moderate	Low	Low	Low	Moderate
Syrkasheva et al. (2022) [16]	Newcastle-Ottawa Scale	Low	Moderate	Low	Low	Low	Low
Xing et al. (2025) [17]	Newcastle-Ottawa Scale	Moderate	High (retrospective)	Moderate	Low	Low	Moderate
Ha et al. (2020) [18]	NIH Tool	Moderate	High (no blinding)	Moderate	Low	Low	Moderate
Hasan et al. (2023) [19]	Newcastle-Ottawa Scale	Low	Moderate	Low	Low	Low	Low

Ko et al. (2022) [20]	NIH Tool	Moderate	High (retrospective)	Moderate	Low	Low	Moderate
Yu et al. (2023) [21]	Newcastle-Ottawa Scale	Moderate	Moderate	Low	Low	Low	Moderate
Baldini et al. (2021) [22]	Newcastle-Ottawa Scale	Moderate	Moderate	Low	Low	Low	Moderate
Doryanizadeh et al. (2021) [23]	Cochrane RoB 2.0	Low	Low (blinded)	Low	Low	Low	Low
Somigliana et al. (2021) [24]	Cochrane RoB 2.0	Low	Low (blinded)	Low	Low	Low	Low
Walz et al. (2020) [25]	Newcastle-Ottawa Scale	Low	Moderate	Low	Low	Low	Low
Ebrahimi et al. (2020) [26]	Newcastle-Ottawa Scale	Moderate	Moderate	Moderate	Low	Low	Moderate
Zhukovskaya (2021) [27]	NIH Tool	Moderate	High (retrospective)	Moderate	Low	Low	Moderate
Rogenhofer et al. (2022) [28]	Newcastle-Ottawa Scale	Low	Moderate	Low	Low	Low	Low
Liu et al. (2022) [29]	Newcastle-Ottawa Scale	Moderate	Moderate	Low	Low	Low	Moderate
Antunes et al. (2024) [30]	Newcastle-Ottawa Scale	Moderate	High (retrospective)	Moderate	Low	Low	Moderate
Faisal et al. (2022) [31]	NIH Tool	High	High (cross-sectional)	High	Low	Moderate	High
Han et al. (2022) [32]	NIH Tool	Moderate	Moderate	Moderate	Low	Low	Moderate
Jeremic et al. (2021) [33]	NIH Tool	High	High (pilot study)	High	Low	Moderate	High
Bezerra Espinola et al. (2021) [34]	Cochrane RoB 2.0	Low	Low (blinded)	Low	Low	Low	Low
Inal et al. (2020) [35]	NIH Tool	Moderate	High (no blinding)	Moderate	Low	Low	Moderate
Tsiartas et al. (2023) [36]	NIH Tool	Moderate	Moderate	Low	Low	Low	Moderate

Boz et al. (2020) [37]	NIH Tool	High	High (descriptive)	High	Low	Moderate	High
Liu et al. (2023) [38]	Newcastle-Ottawa Scale	Moderate	Moderate	Low	Low	Low	Moderate
Wang et al. (2024) [39]	Newcastle-Ottawa Scale	Moderate	High (retrospective)	Moderate	Low	Low	Moderate
Luo et al. (2023) [40]	Newcastle-Ottawa Scale	Moderate	Moderate	Low	Low	Low	Moderate
Tunçcan et al. (2024) [41]	Newcastle-Ottawa Scale	Moderate	High (retrospective)	Moderate	Low	Low	Moderate

While Hasan et al. (2023) [19] and Yu et al. (2023) [21] found that vitamin D sufficiency (≥50 nmol/L and ≥30 ng/mL, respectively) correlated with higher clinical pregnancy rates, the SUNDRO trial by Somigliana et al. (2021) [24] reported no benefit from high-dose vitamin D supplementation. These discrepancies may stem from differences in study design (RCTs vs. cohorts), supplementation protocols, or population characteristics. For example, Ozkan et al. (2010) [44] suggested that vitamin D's effects might be more pronounced in women with PCOS or diminished ovarian reserve, a finding echoed by Xing et al. (2025) [17], who noted worse outcomes in severely deficient PCOS patients. Vitamin D may affect the success of in vitro fertilization (IVF) through various mechanisms. Firstly, it plays a role in endometrial receptivity, as indicated by studies like Vanni et al. (2017) [45] and Wang et al. (2024) [39], which suggest that vitamin D influences the expression of the HOXA10 gene, a key factor in implantation. Additionally, research by Rogenhofer et al. (2022) [28] demonstrates seasonal variations in levels of anti-Müllerian hormone (AMH) and vitamin D, highlighting its potential impact on folliculogenesis. Lastly, Liu et al. (2022) [29] found that thyroid autoimmunity (TAI) can worsen the effects of vitamin D deficiency, pointing to its role in immune modulation. Despite these insights, no consensus exists on optimal vitamin D thresholds. While some studies (e.g., Holick et al. (2011) [46]) advocate for ≥30 ng/mL, others (e.g., Ha et al. (2020) [18]) found no correlation with IVF success at any level. This inconsistency may reflect variability in assay methods, ethnic differences, or confounding factors like BMI and sun exposure. Our review includes recent RCTs (e.g., Hu et al. (2025) [14]) and large-scale cohorts (e.g., Ko et al. (2022) [20]), providing a more comprehensive analysis than prior meta-analyses (e.g., Chu et al. (2018) [47]). We also highlight understudied populations, such as women with TAI [29, 38] and PCOS [14, 41], offering nuanced insights. Limitations: While our review employed a rigorous methodology, it still has several limitations. First, there is notable heterogeneity in the measurement of vitamin D, as different studies utilized various assays, such as LC-MS and ELISA, making comparisons challenging. Additionally, many studies failed to adjust for confounding factors like body mass index (BMI), ethnicity, or lifestyle, as highlighted by Lerchbaum et al. (2015) [48]. There is also a concern regarding publication bias, as smaller studies with null results, such as those by Jeremic et al. (2021) [33], may not be adequately represented. Lastly, most research concentrated on early outcomes, including embryo quality and biochemical pregnancies, with limited data on live birth rates.

Conclusion

This systematic review underscores vitamin D's potential role in optimizing IVF outcomes, particularly in embryo quality and specific subgroups (PCOS, TAI patients). However, no universal threshold for sufficiency was established, and RCTs on

supplementation remain inconclusive. Future research should prioritize standardized vitamin D assessment protocols, large, multicenter RCTs with long-term follow-up (e.g., live birth rates), and stratified analyses by BMI, ethnicity, and infertility etiology. Until then, screening for vitamin D deficiency in IVF patients appears prudent, though routine supplementation cannot yet be universally recommended.

Conflict of Interest

None

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None

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