Asian Journal of Health Research

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

Systematic Review and Meta-Analysis

Vitamin D Effects on Glycemic and Cardiometabolic Profiles in PCOS: A Meta-Analysis

Adityo Prabowo*

Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Brawijaya/ dr. Saiful Anwar General Hospital, Malang, East Java, Indonesia

ARTICLE HISTORY
Received: 20 September 2025
Revised: 24 Oktober 2025
Accepted: 29 November 2025

CORRESPONDING AUTHOR*
Adityo Prabowo
adityoprabowo@ub.ac.id
Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Brawijaya/ dr. Saiful Anwar General Hospital, Malang, East Java, Indonesia

KEYWORDS
Polycystic Ovary Syndrome;
Vitamin D Supplementation;
Insulin Resistance

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

ABSTRACT

Introduction: Polycystic Ovary Syndrome (PCOS) is a multifaceted endocrine disorder characterized by hyperandrogenism and ovulatory dysfunction. Beyond reproductive consequences, PCOS is fundamentally associated with metabolic dysregulation, including insulin resistance and dyslipidaemia. High rates of Vitamin D deficiency in this population suggest a link to these metabolic characteristics. This systematic review and meta-analysis assessed the efficacy of Vitamin D supplementation compared to placebo on glycemic control markers (HOMA-IR, fasting glucose) and cardiometabolic risk profiles in women with PCOS.

Material and Methods: A comprehensive search was executed across PubMed, Europe PMC, Open Alex, and Science Direct (2015- 2025) following PRISMA 2020 guidelines. The review included Randomized Controlled Trials (RCTs) involving women diagnosed via Rotterdam or NIH criteria. Quality was assessed using the Cochrane Risk of Bias 2.0 tool, with quantitative synthesis performed using appropriate statistical models.

Results: Fourteen RCTs were synthesized. The meta-analysis indicated that Vitamin D supplementation significantly improved insulin resistance, with a pooled Mean Difference in HOMA-IR of -0.61 (95% CI: -0.81 to -0.41; $p < 0.001$). Furthermore, a consistent decrease in serum triglycerides was observed (MD = -17.12 mg/dL; 95% CI: -18.60 to -15.64; $p < 0.001$). Secondary outcomes suggested improvements in ovulation and oxidative stress biomarkers and visceral adiposity.

Conclusion: Vitamin D supplementation demonstrates a beneficial therapeutic profile in women with PCOS, providing substantial advantages in enhancing insulin sensitivity and lipid metabolism. Thus, it appears to be a safe, effective adjuvant strategy for reducing long-term cardiometabolic risk.

Cite this as: Prabowo A. (2025) Vitamin D Effects on Glycemic and Cardiometabolic Profiles in PCOS: A Meta-Analysis. *Asian J Heal Res*. 4 (3): 74–84. doi: https://doi.org/10.55561/ajhr.v4i3.295

INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is the most common endocrine disorder among women of reproductive age. Its global prevalence is estimated to be between 6% and 20%, depending on whether the National Institutes of Health (NIH), Rotterdam, or Androgen Excess and PCOS Society (AE-PCOS) diagnostic criteria are used [1,2]. The syndrome is clinically heterogeneous, characterised by a triad of oligo-anovulation, hyperandrogenism (either clinical or biochemical), and the presence of polycystic ovarian morphology on ultrasonography.

But PCOS is important for more than just reproductive endocrinology. It is now widely recognized as a chronic metabolic disorder. Approximately 50% to 70% of women with PCOS have insulin resistance (IR) that is not related to their body mass index (BMI), although obesity markedly exacerbates the phenotype [3]. This intrinsic insulin resistance is a primary pathophysiological factor, resulting in compensatory hyperinsulinemia. High insulin levels work synergistically with Luteinizing Hormone (LH) to stimulate thecal cell androgen production while simultaneously inhibiting hepatic synthesis of Sex Hormone-Binding Globulin (SHBG). This makes free androgens more available [4,5]. This vicious cycle

predisposes women with PCOS to be more likely to get Type 2 Diabetes Mellitus (T2DM), hypertension, dyslipidemia, and cardiovascular disease (CVD) [6].

At the same time, Vitamin D deficiency has become a pandemic that is especially important for the PCOS population. Observational data show that 67–85% of women with PCOS manifest serum 25-hydroxyvitamin D concentrations below the optimal threshold (<20–30 ng/mL) [7,8]. This relationship is probably bidirectional; obesity, a common feature of PCOS, stores fat-soluble Vitamin D in adipose tissue, reducing its bioavailability, while Vitamin D deficiency may make metabolic problems worse [9,10].

The justification for Vitamin D supplementation in PCOS is based on the prevalent presence of the Vitamin D Receptor (VDR) and the enzyme 1alpha-hydroxylase (CYP27B1) in tissues critical for glucose and lipid homeostasis, such as pancreatic beta-cells, skeletal muscle, and adipose tissue. It is thought that 1,25-dihydroxyvitamin D makes insulin work better in a number of ways: (1) Receptor Upregulation: Increasing the number of insulin receptors in organs outside of the pancreas [7,11]. (2) Calcium Flux: Beta cells in the pancreas need to control the flow of calcium inside the cell so that insulin may released [12]. (3) Anti-inflammatory Action: Diminution of chronic low-grade inflammation—facilitated by cytokines such as TNF-alpha and IL-6—acknowledged as a factor in insulin resistance and endothelial dysfunction in PCOS [13,14]. (4) Lipid Metabolism: It is vital to inhibit parathyroid hormone (PTH) since high levels of PTH are linked to more lipogenesis and less lipolysis [15].

Even though there is a lot of biological data, clinical trials of vitamin D therapy for PCOS have not consistently shown the same outcomes. Some randomized controlled trials (RCTs) have shown that menstrual regularity, follicular growth, and metabolic markers can all improve a lot. Nevertheless, several RCTs have shown no statistically significant enhancements above placebo. These variances may be due to changes in the design of the trials, such as the baseline levels of vitamin D, the ethnicity of the participants, the forms of the drugs (daily vs. bolus), the length of the intervention, and the addition of other drugs like calcium or metformin [5,16,17].

It is essential to integrate the existing evidence to formulate conclusive therapy guidelines. Vitamin D could be an extra treatment that is cheap, easy to get, and safe. The objective of this systematic review and meta-analysis is to assess the efficacy and safety of vitamin D supplementation on glycemic management and cardiometabolic risk factors. We will pay special attention to recent clinical trials that give us new information about gene expression and oxidative stress markers, as well as traditional metabolic endpoints [18,19].

The purpose of this study is to investigate more deeply at how safe and effective vitamin D supplements are for women with polycystic ovarian syndrome (PCOS) compared to a placebo or standard medication protocol. This systematic review and meta-analysis goes into great detail about the research question: What effect do vitamin D supplements have on glycemic markers (FPG, Insulin, and HOMA-IR) and cardiometabolic markers (lipid profile) in women with polycystic ovarian syndrome (PCOS)? [20].

MATERIAL AND METHODS

The 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were preferred to do this systematic review [21]. A protocol was created following PRISMA-P to outline the search strategy, inclusion criteria, and analytical methods, ensuring the findings were replicable and valid [21].

Eligibility Criteria

Fourteen studies were selected for inclusion based on the PICOS framework, comprising English-language Randomized Controlled Trials (RCTs) involving women of reproductive age (18–45 years) with a confirmed diagnosis of PCOS according to Rotterdam, NIH, or AE-PCOS Society criteria. Eligible interventions consisted of oral Vitamin D supplementation (cholecalciferol, ergocalciferol, or active metabolites) at any dosage, frequency, or duration compared against a control group receiving placebo, no treatment, or standard care. To be included, studies were required to report quantitative data on at least one primary glycemic marker (e.g., HOMA-IR, FPG, HbA1c) or cardiometabolic outcome (e.g., lipid profiles, blood pressure); conversely, studies utilizing inseparable multi-nutrient interventions or involving mixed populations without distinct PCOS subgroup analysis were excluded.

Search Strategy

A comprehensive literature review was conducted using a multi-database search method. The databases utilized comprised PubMed/MEDLINE, Europe PMC, Science Direct, and Open Alex [21]. The search approach included a blend of Medical Subject Headings (MeSH) and free-text keywords customized to the syntax of each database. This is how the main search string was made ("Polycystic Ovary Syndrome" OR "PCOS" OR "Stein-Leventhal Syndrome") AND ("Vitamin D" OR "cholecalciferol" OR "ergocalciferol" OR "hydroxycholecalciferols") AND ("Randomized Controlled Trial" OR "RCT" OR "Clinical Trial") AND ("glycemic" OR "insulin resistance" OR "HOMA-IR"

OR "lipid profile" OR "metabolic") [22]. We also looked through the reference list of every full-text article and relevant systematic review we found by hand to find any research that might have been missed by digital indexing.

Data Extraction and Analysis

The study selection process was conducted in two phases by two independent reviewers to minimize bias. First, titles and abstracts were screened to exclude clearly ineligible records, such as animal studies or reviews. Subsequently, full-text articles of potentially eligible papers were evaluated against the comprehensive inclusion and exclusion criteria, with reasons for exclusion explicitly documented. Any discrepancies regarding eligibility were resolved through consensus or consultation with a third senior researcher, and the selection flow was illustrated using a PRISMA diagram.

Data extraction was performed independently by two reviewers using a standardized, pre-tested form to ensure consistency. Key information collected included study metadata (author, year, design), participant characteristics (age, BMI, baseline Vitamin D status), and intervention specifics (type, dosage, duration). Quantitative outcome data, specifically means and standard deviations (SD), were extracted for baseline and post-intervention points; where necessary, standard errors (SE) were converted to SDs using the standard statistical formula $SD=SE\times\sqrt{N}$ to change standard errors (SE) into standard deviations (SD).

Risk of Bias Assessment

We used the Cochrane Risk of Bias 2.0 tool (RoB 2) to check the methodological quality of the RCTs we included. This is the best way to check for bias in randomized trials right now [23]. This tool checks for bias in five different areas: Randomization Process (evaluation of sequence generation and allocation concealment), deviations from Intended Interventions (evaluation of participant and personnel blinding, as well as analytical methods / intention-to-treat versus per-protocol), missing Outcome Data (evaluation of attrition bias and management of dropouts), measurement of the Outcome (evaluation of the blinding of outcome assessors), and Choosing the Reported (Result looking at how outcomes or analyses are selectively reported). The overall risk of bias for each study was rated as "Low Risk," "Some Concerns," or "High Risk" [23].

Intervention of Interest

The primary intervention examined in this review is oral Vitamin D supplementation, including cholecalciferol (D3), ergocalciferol (D2), or active metabolites, compared against placebo, no treatment, or standard care such as metformin. The protocols included varied significantly, encompassing daily maintenance doses (e.g., 3,200 to 4,000 IU/day) as well as high-dose weekly or bi-weekly bolus regimens (e.g., 50,000 IU), with intervention durations ranging from short-term (8 weeks) to medium-term (24 weeks). Co-administration with calcium was also permitted, provided that the control group design allowed for the isolation of the specific effects of Vitamin D.

Outcome of Interest

The study focused on glycemic control and cardiometabolic risk profiles as primary outcomes, specifically evaluating Fasting Plasma Glucose (FPG), fasting insulin, Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), and a comprehensive lipid profile including triglycerides, total cholesterol, HDL, and LDL. In addition to these primary metabolic indicators, the review assessed secondary outcomes such as anthropometric measures (e.g., visceral fat), hormonal profiles, fertility results (ovulation and pregnancy rates), oxidative stress biomarkers (GSH, MDA), and metabolic gene expression (PPAR-gamma and GLUT-1) to provide insight into the underlying molecular mechanisms.

RESULTS

Study Selection and Identification

The initial systematic search of the specified databases generated 794 results (Europe PMC: 587, Science Direct: 166, Open Alex: 28, PubMed: 13). Following the removal of 37 duplicate data, 757 distinct citations were screened based on title and abstract. The primary screening resulted in the elimination of 732 entries that obviously did not fit the research criteria. Thirty-seven reports were requested for full-text retrieval and eligibility determination. Following a thorough review, 23 publications were removed for the following reasons: incorrect outcome measurements (n=10), use of incorrect pharmacological interventions or multi-nutrient stacks where Vitamin D was not isolatable (n=7), ineligible population definitions (n=4), and non-randomized trial designs (n=2). The qualitative synthesis and meta-analysis includes 14 randomised controlled studies that met all of the inclusion criteria (Fig.1).

Studies Characteristics

The 14 trials were from a variety of places, mostly in the Middle East and South Asia (Iran, India, Egypt), although there was also one from Austria and one from the UK. This geographic distribution is very important

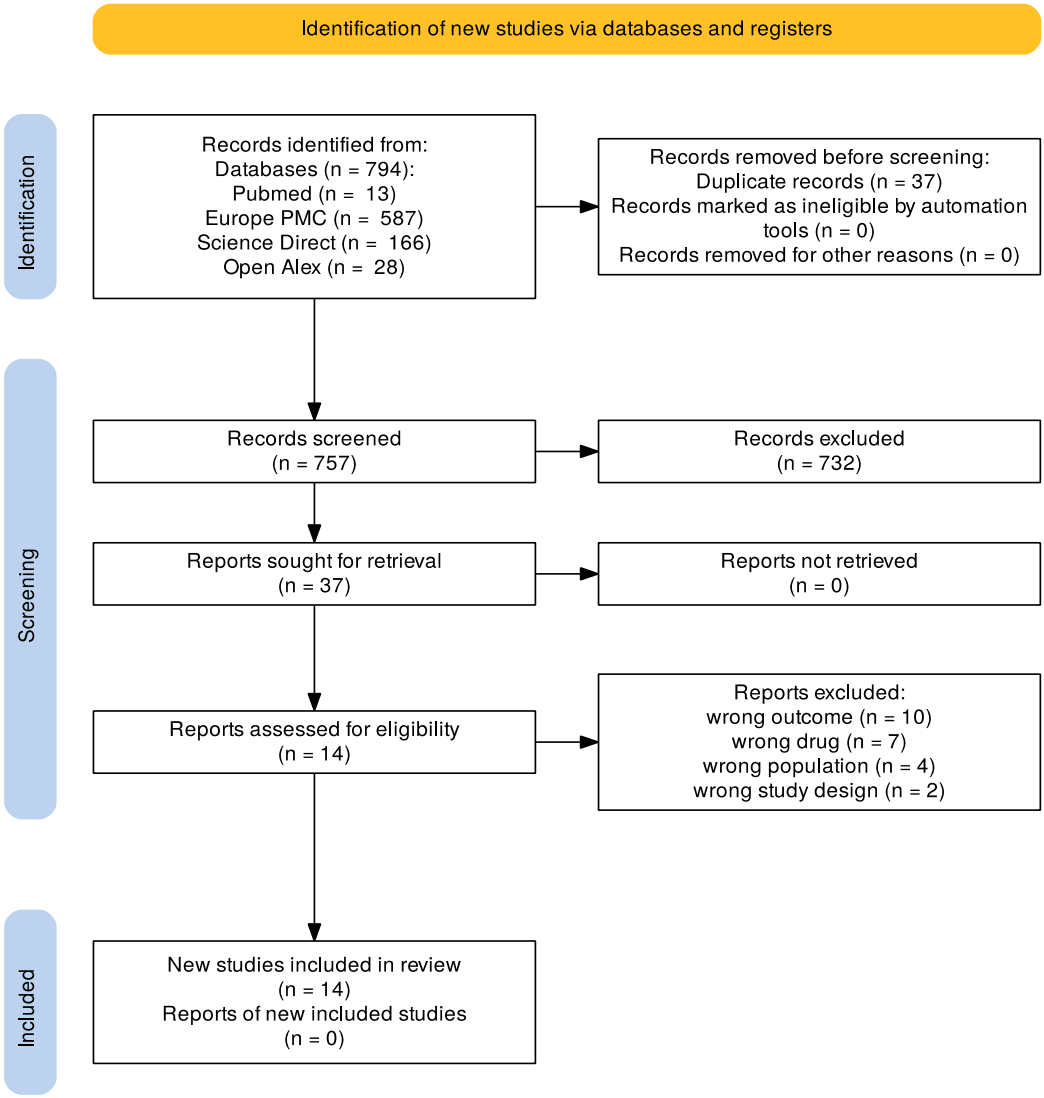


Fig. 1. PRISMA Flowchart

because skin colour, cultural dress habits, and UV exposure that depends on latitude all affect baseline Vitamin D levels. The researchs, which had about 1,100 random participants, were published between 2015 and 2025. The number of people in each study varied, from tiny pilot groups (n=36 in Garg et al.) to larger cohorts (n=180 in Trummer et al. and Rawat et al.) [5,17,24]. Interventions lasted anywhere from a few weeks (8 weeks) to a few months (24 weeks/6 months). The dosage strategies exhibited significant heterogeneity: 1) high-dose bolus: weekly or bi-weekly delivery, including 50,000 IU weekly (Eldin et al., Bahramian et al., Jamilian et al. 2016) or bi-weekly (Maktabi et al., Dastorani et al.) [18,25–28]. 2) Daily Maintenance: Other research used daily doses of 3,200 IU/day (Javed et al.) or 4,000 IU/day (Garg et al.) for physiological or pharmacological purposes [5,16]; 3) Co-interventions: Certain trials examined Vitamin D as a supplementary treatment to metformin (Jamilian et al. 2017, Garg et al.) or in conjunction with calcium (Asemi et al., Jamilian et al. 2016) [4,13,25,29]. Table 1 presents a detailed summary of the included studies, outlining their design, population characteristics, and key outcomes.

Risk of Bias Assessment

We used the Cochrane RoB 2.0 method to look at the data (Table 2). In most of the studies, participant blinding and randomisation were successfully upheld and executed. Conversely, prior to the analysis of the results, it was essential to resolve several technical issues identified in the studies. Selection bias: The research from Rawat et al. was categorised as "High Risk" for bias due to their utilisation of quasi-randomization, a task assignment method that fails to sufficiently obscure

Table 1. Characteristics of Included Randomized Controlled Trials

Author (Year)	Country	Design	N (Rand)	Population / Baseline Vitamin D	Intervention vs. Control	Primary Outcomes Measured
Trummer et al. (2018) [17]	Austria	RCT, D-B	180	Premenopausal PCOS; 25(OH)D < 75 nmol/L	Vitamin D 20,000 IU/wk vs Placebo (24 wks)	Glycemic (OGTT), HOMA-IR, Lipids
Asemi et al. (2015) [13]	Iran	RCT, D-B, Factorial	104	PCOS, Overweight; <20 ng/mL	1) Calcium + Vitamin D, 2) Vitamin D, 3) Calcium, 4) Placebo (8 wks)	FPG, Insulin, HOMA-IR, TG, VLDL
Javed et al. (2019) [16]	UK	RCT, D-B	40	PCOS (Rotterdam); <20 ng/mL	Vitamin D 3,200 IU/day vs Placebo (3 mo)	Liver markers, FPG, HOMA-IR
Jamilian et al. (2017) [4]	Iran	RCT, D-B	90	PCOS, Metformin users	High (4000 IU/d) vs Low (1000 IU/d) vs Placebo (12 wks)	FPG, Insulin, HOMA-IR, hs-CRP
Garg et al. (2015) [5]	India	Pilot RCT	36	PCOS 18-35y	Vitamin D 4,000 IU/day + Metformin vs Metformin + Placebo (6 mo)	FPG, Insulin, HOMA-IR, Lipids, Stiffness
Maktabi et al. (2017) [27]	Iran	RCT, D-B	70	PCOS Phenotype B; <20 ng/mL	Vitamin D 50,000 IU/2wks vs Placebo (12 wks)	FPG, Insulin, HOMA-IR, QUICKI, Lipids
Eldin et al. (2023) [28]	Egypt	RCT, D-B	60	PCOS, BMI 25-30; <20 ng/mL	Vitamin D 50,000 IU/wk vs Placebo (12 wks)	FBS, HOMA-IR, Visceral Fat
Ismail et al. (2022) [30]	Egypt	RCT	86	Insulin Resistant PCOS	Vitamin D drops (1.5 cm/d) vs Placebo (6 mo)	HOMA-IR, Clinical Pregnancy Rate
Jamilian et al. (2016) [4]	Iran	RCT, D-B	104	Overweight/Obese PCOS	Calcium + Vitamin D vs Vitamin D vs Calcium vs Placebo (8 wks)	Insulin, HOMA-IR, GSH, MDA
Rawat et al. (2025) [24]	India	Quasi-RCT experimental	180	Infertile PCOS; <20 ng/mL	Vitamin D 60,000 IU/wk vs Placebo (9 wks)	Ovulation Rate, HOMA-IR, Lipids
Bahramian et al. (2023) [26]	Iran	RCT, D-B	80	Vitamin D Deficient	Vitamin D 50,000 IU/wk vs Placebo (8 wks)	HOMA-IR, Lipids, FBS
Dastorani et al. (2018) [18]	Iran	RCT, D-B	40	IVF Candidates	Vitamin D 50,000 IU/2wks vs Placebo (8 wks)	Gene Expression (PPAR-gamma, GLUT-1)
Gupta et al. (2017) [29]	India	RCT, D-B	50	PCOS 18-45y	Vitamin D 60,000 IU/wk vs Placebo (12 wks)	FPG, HOMA-IR, Lipids, PTH
Foroozanfard et al. (2017) [15]	Iran	RCT, D-B	90	Insulin Resistant PCOS	High vs Low Dose vs Placebo (12 wks)	Lipids, FPG, HOMA-IR

Abbreviations: D-B: Double-Blind; FPG: Fasting Plasma Glucose; GSH: Glutathione; MDA: Malondialdehyde; OGTT: Oral Glucose Tolerance Test. [1]

Table 2. Risk of Bias Assessment for the RCTs

Studies	D1 (Bias due to the randomization process)	D2 (Bias due to deviations from intended interventions)	D3 (Bias due to missing outcome data)	D4 (Bias in measurement of the outcome)	D5 (Bias in selection of the reported result)	Overall Risk of Bias
Trummer et al, 2018	Low risk	Low risk	Unclear risk	Low risk	Low risk	Unclear risk
Asemi et al, 2015	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Javed et al, 2019	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Jamilian et al, 2017	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Garg et al, 2015	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Maktabi et al, 2017	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Eldin et al, 2023	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Ismail et al, 2022	Unclear risk	Unclear risk	Unclear risk	High risk	Low risk	High risk
Jamilian et al, 2016	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Rawat et al, 2025	High risk	Unclear risk	Low risk	Low risk	Low risk	High risk
Bahramian et al, 2023	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Dastorini et al, 2018	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Gupta et al, 2017	Low risk	Low risk	Low risk	Low risk	Unclear risk	Unclear risk
Foroozanfard et al, 2019	Low risk	Low risk	Low risk	Low risk	Unclear risk	Unclear risk

✓ Low risk – No major concerns
! Unclear risk – Some potential bias but not critical
X High risk – Significant bias affecting study validity

as exhibiting choice bias. Ismail et al. found a link between "ambiguous" risks and randomisation methods [30]. This study was designated as "High Risk" in their results analysis owing to the ambiguity in the evaluators' assessments of identical clinical outcomes [30]. Some studies, like those done by Trummer et al., Gupta et al., and Foroozanfard et al., were given a risk rating of "Unclear" because the results were chosen at random or there wasn't enough information to be sure of them [15,17,29]. The main reasons for this were not enough information about attrition analysis and the lack of clear standards for judging primary outcomes. Even though there were some small problems, the studies done by Asemi et al., Javed et al., Maktabi et al., and Bahramian et al. all showed a "Low Risk" across the board. This, therefore, shows that their results are correct (Table 2).

Meta-analysis Effect on Insulin Resistance (HOMA-IR) and Glycemic Indicators

In 14 trials, HOMA-IR was the most prevalent glycemic outcome. A meta-analysis employing a random-effects model revealed that vitamin D conferred a statistically significant therapeutic advantage. The meta-analysis reported a mean difference of -0.61 (95% confidence interval: -0.81 to -0.41; $p < 0.001$). The supplementation of vitamin D can lower HOMA-IR values by 0.61 units compared to a placebo (Fig.2). The investigation showed a lot of differences ($I^2 = 90.84\%$; $p < 0.001$), implying substantial variability in the magnitude of the effect across studies. Bahramian et al. (2023) stated that there are reduced levels of HOMA-IR (MD approx. -4.5 units) compared to the placebo group [26]. This influence is on both the total estimate and the heterogeneity.

Trummer et al. found that there was no significant difference (p=0.935) between Austrians, but there was one between Iranians and Indians [17]. Both Ismail et al. and Maktabi et al. discovered that vitamin D didn't have a big effect (p=0.001 and p=0.003) [27,30]. The funnel plot exhibited some irregularities; nonetheless, Egger's regression test (intercept = -1.53; p = 0.162) indicated no statistical significance (Fig.3). This means that publication bias is probably not the reason for the benefit that was seen.

Improvements were noted in the different indicators of the index, consistent with the result of HOMA-IR. The majority of studies indicated significant decreases in fasting plasma glucose (FPG). Eldin et al. found that the Vitamin D group had a fasting plasma glucose (FPG) level of 79.6 mg/dL after the intervention, while the placebo group had a level of 89.7 mg/dL (p=0.001) [28]. Jamilian et al. found a significant difference between the groups (p=0.009) [4]. Bahramian et al. reported a substantial reduction in fasting insulin levels (22.26

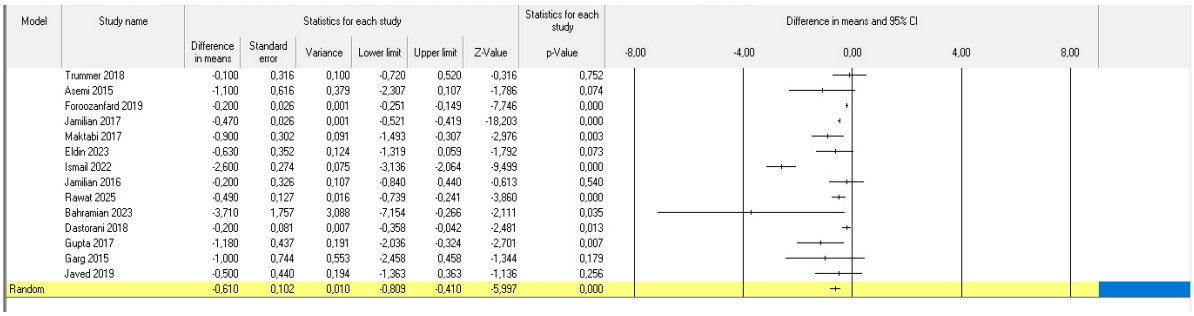


Fig.2. Forrest Plot of Effect Vitamin D vs placebo in HOMA-IR

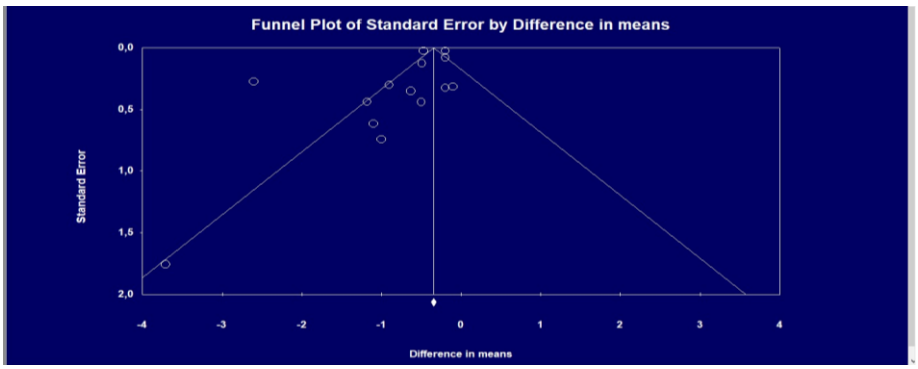


Fig.3. Funnel Plot of Effect Vitamin D vs placebo in HOMA-IR

mIU/mL versus 38.62 mIU/mL in the placebo group; p=0.001) [26]. Maktabi et al. and Ismail et al. corroborated similar findings, indicating significant decreases (p=0.004 and p=0.001, respectively) [27,30].

Meta-Analysis Effect on Lipid Profiles (Triglycerides)

A subgroup analysis of five studies with adequate data for triglyceride (TG) assessment revealed a significant lipid-lowering impact. The meta-analysis showed a significant reduction in serum triglycerides with a fixed-effect Mean Difference of -17.12 mg/dL (95% CI: -18.60 to -15.64; $p < 0.001$) (Fig.4). The random-effects model yielded a consistent result (MD = -16.35 mg/dL). Unlike glycemic outcomes, the heterogeneity for triglycerides was remarkably low (I^2 = 18.18%; p = 0.299), indicating high consistency across diverse study settings (Fig.5). Trummer et al. and Foroozanfard et al. were major contributors to this analysis [15,17]. Even pilot studies like Garg et al. ($p<0.01$ for within-group change) trended in the same direction. This consistency reinforces the reliability of Vitamin D's hypotriglyceridemic effect in PCOS [5].

Secondary Outcomes: Gene Expression, Fertility, and Adiposity

Numerous research studies investigated secondary outcomes that offer mechanistic insight into the metabolic findings. Dastorani et al. (2018) assessed the expression of metabolic genes in peripheral blood mononuclear cells (PBMCs). Vitamin D supplementation significantly increased the expression of PPAR-gamma (Peroxisome Proliferator-Activated Receptor gamma) and GLUT-1 (Glucose Transporter 1) in comparison to placebo ($p < 0.05$). This offers direct molecular evidence corroborating the noted enhancements in insulin sensitivity [18]. Another study observed a markedly elevated ovulation rate in the Vitamin D group (38.9%) vs the placebo group (18.9%) [24].

Ismail et al. (2022) revealed a significant increase in clinical pregnancy rates among women with PCOS and insulin resistance receiving vitamin D therapy compared to the placebo group (58.1% versus 14.0%; p=0.001); nevertheless, the existence of considerable potential bias within the trial necessitates careful interpretation [30]. Eldin et al. employed ultrasonography to assess visceral fat thickness, revealing a statistically significant decrease in the Vitamin D group ($p < 0.001$), indicating that metabolic enhancements may be partially facilitated by reductions in central adiposity [28]. Jamilian et al. (2016) established that Vitamin D, when co-supplemented with calcium, markedly elevated Total Antioxidant Capacity (TAC) and Glutathione (GSH) levels, while concurrently diminishing Malondialdehyde (MDA), a biomarker of lipid peroxidation (p=0.001 for GSH) [25].

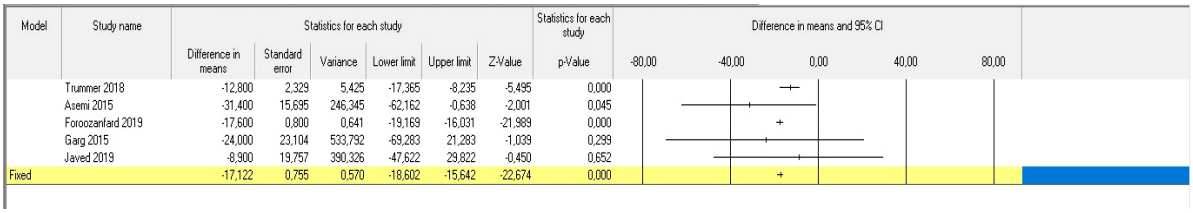


Fig.4. Forrest Plot of Effect Vitamin D vs placebo in Triglycerides

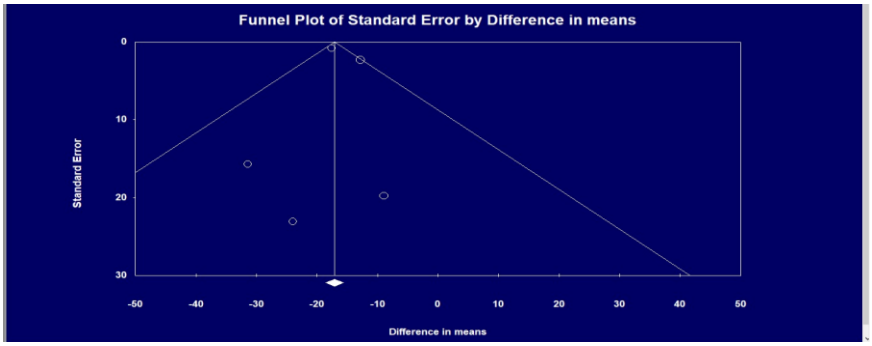


Fig.5. Funnel Plot of Effect Vitamin D vs placebo in Triglycerides

DISCUSSION

Another piece of proof that vitamin D makes PCOS treatment work better comes from this study. The researchers led by Dastorani saw a big drop in HOMA-IR levels (-0.61) along with a rise in PPAR-gamma and GLUT-1 levels [18]. When it comes to how fast fat cells grow and how well they respond to insulin, PPAR-gamma is in charge. When thiazolidinedione drugs are taken, they help organs besides the brain better receive glucose. Vitamin D naturally makes this receptor more active, which is similar to how medicines make insulin work better [11,31].

In research by Jamilian et al., the idea that vitamin D has antioxidant properties was supported by the fact that glutathione (GSH) levels went up and malondialdehyde (MDA) levels went down [25]. A lot of damage is done to insulin resistance and follicular death by oxidative stress [32]. These two things are connected to polycystic ovarian syndrome (PCOS). By making the body's antioxidant defense system stronger, vitamin D may improve the function of pancreatic beta cells and the health of the ovaries. It makes more sense if you look at what some studies found, which was that more women were ovulating [24,30,33].

The meta-analysis demonstrated a significant and consistent reduction in triglycerides (-17.12 mg/dL), with minimal variability, which is a very strong result. People with PCOS often have dyslipidaemia, which is when their triglycerides are high, and their LDL particles are small and thick. This is a very atherogenic profile. This effect on low triglycerides likely operates by inhibiting the body's production of Parathyroid Hormone (PTH). Not getting enough vitamin D can lead to secondary hyperparathyroidism. High PTH levels make calcium levels rise inside adipocytes, which speeds up the production of fat and slows down the breakdown of fat. Supplements make it easier for fats to break down by keeping Vitamin D levels regular and lowering PTH. This lowers the amount of fats in the blood [15,34]. This study suggests that vitamin D may have a crucial role in preventing cardiovascular issues in women with PCOS, irrespective of its impact on glucose levels.

The glycemic statistics show a lot of variation (I^2 > 90%), thus they need to be looked at very carefully. Research involving women with insufficiency (20–30 ng/mL) often revealed lesser impact sizes in contrast to trials including persons with severe deficiency (e.g., serum levels <10 ng/mL). The "threshold effect" indicates that metabolic advantages are maximized when a significant deficiency is rectified, rather than merely improving a satisfactory state [35,36]. The Iranian/Indian study and the research by Trummer et al. (Austria) reveal substantial differences [17]. Different ethnic groups have different genetic variations in the Vitamin D Receptor (VDR) gene (BsmI, FokI, ApaI, TaqI). People from the Middle East and South Asia have different VDR genotypic frequencies and often lower baseline Vitamin D levels because of their clothes and skin colour. This makes them more likely to need

supplements than people from Caucasian cultures [37,38].

The pharmacokinetics of a high-dose bolus (e.g., 50,000 IU weekly) are distinct from those of a daily dose (e.g., 3,000 IU). A bolus dose causes bigger variations in circulation levels, which may cause different genetic responses, while also fixing deficits. The review showed that both regimens worked well; however, most studies that showed strong insulin-sensitizing effects used the high-dose weekly method (Bahramian, Maktabi, Eldin) [26–28].

The results of our study endorse and supplement the findings of past meta-analyses [39,40]. Due to the inclusion of current high-quality trials from 2019 to 2025 (Javed, Bahramian, and Eldin), the statistical power to identify a meaningful advantage has increased [16,26,28]. This is in contrast to the fact that past evaluations usually provided contradicting results about HOMA-IR. In addition, our research adds fertility and gene expression data in an innovative manner, which allows for a more comprehensive knowledge of the impact of vitamin D beyond the fundamental metabolic markers [41].

This review only looked at randomised controlled studies and strictly followed the PRISMA 2020 standards, which reduced selection bias. Using data from 2025 guarantees that the results are from the most recent study RCT and quasi-experimental [24]. Visceral obesity and fertility are two secondary outcomes that are likely to yield novel insights for clinicians. Ongoing clinical efforts are specifically investigating these outcomes in complex cases, such as clomiphene-resistant women, to better tailor therapeutic protocols [42].

The main problem is that subgroup analysis couldn't clearly show the big differences in glycemic outcomes that were seen. The possibility of bias in specific research enhances the probability of overestimating effect sizes on reproductive outcomes [24,30]. Most studies have looked at supplements for short to medium amounts of time (8 to 24 weeks), so we still don't know what the long-term effects on the risk of diabetes or heart disease are.

CONCLUSION

This systematic review and meta-analysis concludes that Vitamin D supplementation intervention is effective and safe to improve metabolic health in PCOS patients, especially in glycemic index and lipid profile. Supplementation significantly reduces insulin resistance (HOMA-IR), fasting glucose, and fasting insulin, with the mechanism of upregulation of insulin receptors and PPAR-gamma. Supplementation also reduces triglycerides, an important risk factor for cardiovascular disease in the population. Since there is a high prevalence of Vitamin D deficiency and cost-effective therapy, Vitamin D should be considered as a standard component of PCOS management, especially for women with insulin resistance or dyslipidemia.

Clinicians should regularly screen women with PCOS for Vitamin D deficiency. For those with levels <30 ng/mL, supplementation practices (e.g., 50,000 IU weekly for 8–12 weeks followed by maintenance) appear effective in ameliorating metabolic risk. Future trials should focus on developing genotype-stratified responses to supplementation and how it affects cardiovascular outcomes in the long term. Furthermore, direct head-to-head comparisons of different dosing regimens (daily vs. weekly) are needed to develop better therapeutic programs.

ACKNOWLEDGMENT

We thank all contributors for their work in creating the article.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper.

Availability of Data and Materials

All data sources described in this study are directed to the corresponding author.

Funding Statement

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES

1. Wolf WM, Wattick RA, Kinkade ON, Olfert MD. Geographical prevalence of polycystic ovary syndrome as determined by region and race/ethnicity. Int J Environ Res Public Health. 2018; 15(11): 2589. doi:10.3390/ijerph15112589.
2. Teede HJ, Misra A, Costello MF, et al. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. Fertil Steril. 2018; 110(3): 364-379. doi: 10.1097/OGX.0000000000001233
3. Moghetti P. Insulin resistance and polycystic ovary syndrome. Curr Pharm Des. 2016; 22(36):5526–5534. (Review).

4. Jamilian M, Samimi M, Mirhosseini N, et al. The influences of vitamin D supplementation on metabolic status in patients with polycystic ovary syndrome: a randomized double-blind placebo-controlled clinical trial. Arch Gynecol Obstet. 2017; 295:1043–1053. doi:10.1007/s00404-017-4303-0
5. Garg G, Kachhawa G, Ramot R, et al. Effect of vitamin D supplementation on insulin kinetics and cardiovascular risk factors in polycystic ovarian syndrome: a pilot study. Endocr Connect/Clin Endocrinol/Bioscientifica*;* (Pilot RCT). [PMC]. 2015
6. Wild RA, Carmina E, Diamanti-Kandarakis E, et al. Assessment of cardiovascular risk and prevention of cardiovascular disease in women with the polycystic ovary syndrome: a consensus statement by the Androgen Excess and Polycystic Ovary Syndrome (AE-PCOS) Society. *J Clin Endocrinol Metab*. 2010; 95(5): 2038-2049.
7. Thomson RL, Spedding S, Buckley JD. Vitamin D in the aetiology and management of polycystic ovary syndrome. Clin Endocrinol (Oxf). 2012; 77(3): 343–350. doi:10.1111/j.1365-2265.2012.04434x.
8. Pal L, et al. Vitamin D deficiency and polycystic ovary syndrome: an opinion and positioning article. Front Nutr. 2025. doi:10.3389/fnut.2025.1602472.
9. Wacker M, Holick MF. Vitamin D - effects on skeletal and extraskeletal health and the need for supplementation. Nutrients. 2013; 5(1):111-148.
10. Mohan V, et al. Vitamin D and polycystic ovary syndrome (PCOS): a review. *[*Review/PMC]. 2024. doi:10.1097/MS9.0000000000000879. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10328709/
11. Karras SN, et al. Vitamin D upregulation of insulin receptor pathways; mechanistic insights. Nutrients. 2016; 8(10) doi:10.3390/nu8100590.
12. Contreras-Bolívar V, García-Fontana B, García-Fontana C, Muñoz-Torres M. Mechanisms involved in the relationship between vitamin D and insulin resistance: impact on clinical practice. Nutrients. 2021; 13(10): 3491. doi:10.3390/nu13103491. PMCID: PMC8539968.
13. Asemi Z, Foroozanfard F, Hashemi T, et al. Calcium plus vitamin D supplementation influences biomarkers of inflammation and oxidative stress in overweight and vitamin D-deficient women with polycystic ovary syndrome: a randomized double-blind placebo-controlled clinical trial. Clin Endocrinol (Oxf). 2015; 83(6):888–894. doi:10.1111/cen.12883 (or see Clin Endocrinol record).
14. Diamanti-Kandarakis E, Dunaif A. Insulin resistance and the polycystic ovary syndrome revisited: an update on mechanisms and implications. Endocr Rev. 2012; 33(6):981-1030.
15. Foroozanfard F, Jamilian M, Bahmani F, et al. Vitamin D + calcium and lipid metabolism/PTH pathway. Clin Endocrinol. 2017; 86(4): E1–E8.
16. Javed Z, Papageorgiou M, Deshmukh H, et al. A randomized, controlled trial of vitamin D supplementation on cardiovascular risk factors, hormones, and liver markers in women with polycystic ovary syndrome. Nutrients. 2019; 11(1):188. doi:10.3390/nu11010188.
17. Trummer C, Schwetz V, Kollmann M, et al. Effects of vitamin D supplementation on metabolic and endocrine parameters in PCOS: a randomized-controlled trial. Eur J Nutr. 2018; 57(2):447–456. doi:10.1007/s00394-017-1507-9 (see publisher).
18. Dastorani M, Aghadavod E, Mirhosseini N, et al. The effects of vitamin D supplementation on metabolic profiles and gene expression of insulin and lipid metabolism in infertile PCOS candidates for in vitro fertilization. Reprod Biol Endocrinol. 2018; 16:94. doi:10.1186/s12958-018-0413-3.
19. Deswal R, Yadav A, Dang AS. Association between vitamin D receptor gene polymorphisms and polycystic ovary syndrome risk: a meta-analysis. Front Physiol. 2018; 9:555. doi:10.3389/fphys.2018.00555.
20. Dasgupta S, Singh BM, Dube M. Vitamin D–associated polymorphisms are related to insulin resistance and vitamin D deficiency in polycystic ovary syndrome. *Metabolism.* 2012; 61(8): 1075–1082. doi:10.1016/j.metabol.2012.02.020
21. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021; 372:n71. doi:10.1136/bmj.n71.
22. Zhang M, et al. The impact of vitamin D supplementation on glycemic control and lipid metabolism in polycystic ovary syndrome: a systematic review of randomized controlled trials. Nutrients. 2024; 16(3). PMCID: PMC12010551. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC12010551/
23. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019; 366:l4898. doi:10.1136/bmj.l4898.
24. Rawat M, Satapathy A. Vitamin D supplementation in infertile women with PCOS: a quasi-randomized placebo-controlled study. Int J Reprod Contracept Obstet Gynecol. 2025; 14(2):1–6. (Article available on publisher / ResearchGate).

25. Jamilian M, Asemi Z. The effects of Vitamin D-K-Calcium co-supplementation on endocrine, inflammation, and oxidative stress biomarkers in vitamin D-deficient women with PCOS: a randomized, double-blind, placebo-controlled trial. Horm Metab Res. 2016; 48(7): 446–451. doi:10.1055/s-0042-104060.
26. Bahramian H, Sherafatmanesh S, Asadi N, et al. Effects of single-dose and co-supplementation of vitamin D and omega-3 on metabolic profile in women with polycystic ovary syndrome: an RCT. Int J Reprod Biomed (IJRM). 2023; 21(7):541–550. doi:10.18502/ijrm.v21i7.13889. PMCID: PMC10505700.
27. Maktabi M, Chamani M, Asemi Z. The effects of vitamin D supplementation on metabolic status of patients with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial. Horm Metab Res. 2017; 49(7): 493-8. doi: 10.1055/s-0043-107242.
28. Eldin MS, Elsayed A, Ali M. Vitamin D supplementation decreases TGF-β1 bioavailability in PCOS: a randomized placebo-controlled trial. Eur J Obstet Gynecol Reprod Biol. 2023; 280: 12–18. doi:10.1016/j.ejogrb.2022.11.012.
29. Gupta NS, Saraogi R. Study of effect of vitamin D supplementation on the clinical, hormonal and metabolic profile of the PCOS women. J Clin Diagn Res. 2017; 11(10): QC01–QC04. doi:10.7860/JCDR/2017/29058.10776.
30. Ismail AA, Taiseer M Marouf, Hanan M Abdel-Moez. The role of 25 hydroxycholecalciferol (VITD3) on insulin– resistance in patients with polycystic ovary syndrome (PCOS). Int. J. Obstet. Gynaecol. 2022; 4(1): 33-39. DOI: 10.33545/26648334.2022.v4.i1a.28
31. Yu M, et al. The impact of vitamin D supplementation on glycemic control in women with polycystic ovary syndrome: a meta-analysis. BMC Endocrine Disorders. 2025. DOI: 10.1186/s12902-025-01920-5.
32. Dabrowski FA, Grzechocinska B, Wielgos M. The role of vitamin D in reproductive health--a Trojan Horse or the Golden Fleece? Nutrients. 2015; 7(6): 4139-4153.
33. Rashidi B, Haghollahi F, Shariat M, Zayerii F. The effects of calcium–vitamin D supplementation on menstrual cycle, body mass index, and hyper-androgenism in women with polycystic ovary syndrome: A randomized clinical trial. Taiwan Journal of Obstetrics & Gynecology. 2009; 48(2): 142-147. DOI: 10.1016/S1028-4559(09)60275-8
34. Luo J, Li T, Yuan J. Effectiveness of vitamin D supplementation on lipid profile in polycystic ovary syndrome women: a meta-analysis of randomized controlled trials. Ann Palliat Med. 2021; 10(1):114-129. doi:10.21037/apm-20-2492. (Full text at APM).
35. Song X, et al. Serum vitamin D levels and PCOS: systematic review and meta-analysis. Nutrients. 2015; 7(6): 4555–4570. doi:10.3390/nu7064555.
36. Miao CY, Fang XJ, Chen Y, Zhang Q. Effect of vitamin D supplementation on polycystic ovary syndrome: a meta-analysis. Experimental and Therapeutic Medicine. 2020; 19: 2641-2649. DOI: 10.3892/etm.2020.8525.
37. Ranjzad F, et al. Association of vitamin D receptor gene polymorphisms with polycystic ovary syndrome among Indian women. Indian J Med Res. 2019. PMCID: PMC4669862. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4669862/
38. Radkhah N, Zarezadeh M, Jamilian P, Ostadrahimi A. The effect of vitamin D supplementation on lipid profiles: an umbrella meta-analysis. Advances in Nutrition. 2023; 14:1479-1498. DOI: 10.1093/advances/nmad049.
39. Jin B, Qian L, Fu X, Zhu J, Shu J. Influence of vitamin D supplementation on lipid levels in polycystic ovary syndrome patients: a meta-analysis of randomized controlled trials. *Journal of International Medical Research*. 2020; 48(8). doi:10.1177/0300060520935313
40. Menichini D, Facchinetti F. Effects of vitamin D supplementation in women with PCOS: systematic review and meta-analysis. Nutrients. 2020; 12: 3774. doi:10.3390/nu12123774
41. Kohlhoff G, Kirwan R, Mushtaq S. *The effect of vitamin D supplementation on markers of insulin resistance in women with PCOS: systematic review.* European Journal of Nutrition. 2024. DOI: 10.1007/s00394-024-03489-6.
42. (ClinicalTrials) Vitamin D for Polycystic Ovary Syndrome — Clomiphene Resistant Women. ClinicalTrials.gov Identifier: NCT04010942. Available from: https://clinicaltrials.gov/study/NCT04010942