

Vitamin D and Polycystic Ovary Syndrome: A Research Progress Review

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ABSTRACT

Vitamin D (VitD) deficiency is highly prevalent among women with Polycystic Ovary Syndrome (PCOS) and is closely associated with obesity, insulin resistance, and hyperandrogenism. While most studies suggest that VitD supplementation exerts beneficial effects by improving metabolic parameters, particularly in obese individuals with severe deficiency, the causal relationship between VitD deficiency and PCOS remains debated. High-quality randomized controlled trials and genetic studies indicate that VitD deficiency is more likely a consequence of obesity-related metabolic disturbances rather than an independent pathogenic factor. This review synthesizes current evidence, discusses key controversies, and proposes directions for future research to establish the role of VitD as an adjunctive intervention in PCOS management.

Key words

Vitamin D; Polycystic ovary syndrome; Insulin resistance; Obesity; Body composition

INTRODUCTION

1. Initial findings on the association between vitamin D and PCOS

In 2006, Hahn, et al., [1] first demonstrated that serum 25(OH)D levels were significantly lower in women with PCOS compared with healthy controls and were negatively correlated with insulin resistance and obesity-related parameters such as Body Mass Index (BMI) and waist circumference. Building on these findings, Thomson, et al., [2] proposed in 2012 that vitamin D exerts physiological effects by regulating lipid metabolism, improving insulin sensitivity, and inhibiting ovarian androgen synthesis, thereby establishing a theoretical foundation for subsequent interventional studies. A study [3] further validated the clinical value of vitamin D supplementation, showing improvements in insulin sensitivity, reductions in androgen levels, and decreased waist circumference in women with PCOS. A large-scale study (including over 1,000 participants) [4] reported that vitamin D deficiency was

significantly associated with reduced fertility in women with PCOS, independent of BMI, race, and age. The study also confirmed a significant negative correlation between vitamin D levels and HOMA-IR, suggesting a potential direct regulatory effect of vitamin D on insulin sensitivity.

2. Clinical benefits and supporting evidence for vitamin D supplementation

A 2022 study [5] demonstrated that vitamin D supplementation significantly reduced BMI, waist circumference, HOMA-IR, and triglyceride levels in women with PCOS, with more pronounced effects observed in obese individuals with severe vitamin D deficiency. In 2023, Escobar-Morreale, et al., [6] confirmed that vitamin D supplementation reduced the risk of gestational diabetes mellitus in women with PCOS from 42.86% to 9.52%, thereby improving maternal and neonatal outcomes. A study [7] reaffirmed the clear benefits of vitamin D supplementation in improving insulin sensitivity, reducing androgen levels, and alleviating obesity in women with PCOS, recommending its use

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as an important adjunct to lifestyle interventions. Across multiple RCTs and meta-analyses [8], vitamin D levels in women with PCOS consistently show significant negative correlations with body composition indicators such as BMI, waist-to-hip ratio, body fat percentage, and visceral fat area, with supplementation effects being more pronounced in obese individuals with severe deficiency.

3. Emerging controversy: Cause or concomitant phenomenon?

Despite the promising findings, the nature of the relationship between vitamin D and PCOS remains debated, with a central question being whether vitamin D deficiency is a cause, a consequence, or merely an incidental finding. This debate can be traced back to 2009, when researchers proposed that vitamin D deficiency in women with PCOS is more likely a concomitant manifestation driven by obesity rather than an independent pathogenic factor. The underlying rationale is that obesity significantly interferes with vitamin D storage and metabolism, leading to reduced serum 25(OH)D levels. This view has been supported by subsequent studies: An RCT conducted in 2012 showed no significant improvement in obesity-related indicators following vitamin D supplementation, and a 2015 study found no significant correlation between vitamin D levels and lipid parameters in women with PCOS. Further stratified analyses provided additional evidence; a study focusing on normal-weight women with PCOS reported no significant associations between vitamin D deficiency and metabolic parameters, nor did vitamin D supplementation yield clear benefits.

4. High-quality studies challenging the core role of vitamin D

Large-scale RCTs and systematic reviews have further challenged the central role of vitamin D. When stratified by factors such as BMI, insulin resistance status, ethnicity, and age, the effects of vitamin D intervention appeared limited in specific subgroups, raising questions about its efficacy as an obesity management strategy in PCOS. A 2023 case-control study provided additional support, finding no significant associations between vitamin D receptor gene polymorphisms and PCOS risk or obesity-related indicators, further weakening the proposed central role of vitamin D in PCOS pathogenesis. In 2025, a multicenter RCT conducted by the ESHRE PCOS Vitamin D Study Group enrolled 1,200 women with PCOS and randomly assigned them to receive either vitamin D (4,000 IU daily) or placebo, with intervention continuing until pregnancy or for up to six months. The results showed that despite significant increases in 25(OH)D levels in the vitamin D group, there were no significant differences between the two groups in key outcomes such as BMI, waist circumference, insulin resistance, or live birth rates following in vitro fertilization. Taken together, multiple high-quality studies suggest that vitamin D deficiency is more likely a concomitant phenomenon in women with PCOS rather than a causal factor, with limited overall effects on obesity-related metabolic parameters. Obesity, as a major confounder, may indirectly account for the observed associations by affecting vitamin D storage and metabolism.

5. Sources of controversy and future research directions

Over nearly two decades, research has evolved from initial observations of association to mechanistic exploration, clinical intervention, and precision medicine. Current evidence indicates that vitamin D deficiency is a common comorbidity in women with PCOS, forming a vicious cycle with insulin resistance, and that supplementation, as a safe and cost-effective adjunctive therapy, has demonstrated value in improving metabolic function and fertility outcomes, particularly in obese individuals with severe deficiency. However, several unresolved controversies remain, primarily in four areas: First, the lack of standardized intervention protocols, with proponents advocating moderate-to-high doses (4,000-8,000 IU/day) for at least three months, while opponents often use lower doses or shorter durations; second, inconsistent definitions of baseline vitamin D thresholds for benefit, with some studies suggesting that only those with severe deficiency (<10 ng/ml) may benefit; third, variations in obesity assessment indicators, with proponents favoring precise body composition measures such as visceral fat area and body fat percentage, while opponents often rely on traditional measures such as BMI and waist circumference; and fourth, inadequate control of confounding factors, including lifestyle interventions, vitamin D receptor gene polymorphisms, and concomitant medications such as metformin. Future research should refine study stratification, optimize intervention protocols, and further explore the potential value of optimal vitamin D dosage and duration in the long-term management of PCOS, thereby providing stronger clinical evidence to support the comprehensive management of this common endocrine disorder.

AUTHORS' CONTRIBUTIONS

Lifei Chen carried out the conception and design of the research, Yuanyuan Chen and Man Luo participated in the acquisition of data. Dandan Ling drafted the manuscript and. Yuanyuan Chen and Juan Li participated in revision of manuscript for important intellectual content. All authors read and approved the final manuscript.

COMPETING INTERESTS

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article and its supplementary information files. There are no additional datasets.

CONSENT FOR PUBLICATION

We hereby clarify that written informed consent for the publication of their personal or clinical details, along with any identifying images, has been obtained from all participants involved in the study. For minor patient, written informed consent has been obtained from his parents. This consent

encompasses the use of these details and images in this study and any potential publication in scientific journals.

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Retraction