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Research Article

The Interplay between Vitamin D deficiency and Polycystic Ovary Syndrome (PCOS)

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Abstract

PCOS is the most common endocrine disorder in the reproductive age group of women, and its prevalence is believed to range between 6-12% globally [1]. It has a broad range of clinical signs and symptoms, characterized by oligo and anovulation, hyperandrogenism, and polycystic ovaries morphologically, being is a complicated disorder with extensive effects on the reproductive, metabolic, and psychological systems [2]. To date, the exact etiology of PCOS is unknown, and multiple factors are assumed to be involved in the pathogenesis of PCOS, including genetic, environmental and hormonal factors [3].

In the past ten years, research has shown that low levels of vitamin D may increase the risk of developing polycystic ovary syndrome (PCOS) and can worsen its symptoms.

This is particularly important because vitamin D is a fat-soluble vitamin, a pro-hormone involved in various physiological aspects of the body, such as calcium balance, immune system function, and insulin level stability (4). It is well known that the biologically active form of vitamin D accomplishes its biological activities through the VDR, which is shown to be highly expressed in various tissues, including ovarian tissues [5]. This has, therefore, led to heightened concern in trying to determine the role of vitamin D in reproductive health with a focus on PCOS.

According to recent studies, low serum vitamin D levels have been linked to a major impact on the pathophysiology of polycystic ovarian syndrome (PCOS). Vitamin D insufficiency is common in women with PCOS, according to research by Karadağ et al. [6], and it is associated with harmful metabolic consequences like insulin resistance and hyperandrogenism. According to their research, vitamin D supplementation may help deficient PCOS patients' insulin sensitivity and androgen levels, which may reduce some symptoms. Similarly, vitamin D administration improves insulin resistance in PCOS-affected women by regulating hormonal imbalances such increased androgen levels, according to a meta-analysis by Łagowska et al. [7] When Cander et al. [8] examined the connection between vitamin D levels and insulin resistance, they discovered a substantial correlation between the two. This reinforces the idea that vitamin D deficiency may exacerbate PCOS, suggesting that addressing it could be crucial for effective management.

Vitamin D's effects on PCOS are claimed to operate through several pathways. Low vitamin D status has been suggested to be linked to a rise in insulin resistance, a feature of PCOS, since it is well known to have altered insulin sensitivity [9]. In addition, it has been evidenced that vitamin D has apparent effects on modulating the inflammatory processes, which are, by and large, abnormally activated in PCOS and lead to the state of chronically low-grade inflammation. There is also increasing data showing that vitamin D influences androgen synthesis and secretion [10]. Some of the evidence, like the work by Subashree et al. [11], suggests that vitamin D supplementation may be beneficial to reduce the high circulating levels of androgens in women and regulate the intermittent menstrual cycle in PCOS.

Keywords: vitamin D deficiency; polycystic ovary syndrome; PCOS; Vitamin D receptor; insulin resistance; inflammation; menstrual irregularities; hyperandrogenism; genetic factors; environmental factors; molecular mechanisms

Introduction

Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder in women of reproductive age, primarily characterized by metabolic and reproductive abnormalities. Ample evidence has established vitamin D deficiency as a factor that widely exacerbates standard features in PCOS, such as insulin resistance, hormonal imbalance, and low-grade chronic inflammation. Gaining insight into such a relationship is also crucial for developing effective management Methods: PubMed, Google Scholar, Science Direct, and ResearchGate were used to conduct a systematic literature review, with data selection based on articles published between 2016 and 2024. The targeted criterion of the human studies on this association between vitamin D and PCOS has been clinical, molecular, genetic, and environmental aspects; the articles written in English involve animals and endocrine disorders that do not directly relate to the current subject. Discussion: A comparison of the literature reveals that there is a very high prevalence of vitamin D deficiency in women with PCOS that may worsen the conditions of insulin resistance, irregular menstrual cycles, hyperandrogenism, and systemic inflammation. Thus, vitamin D directly influences significant molecular processes related to insulin signaling, hormone synthesis, and immune regulation; these findings make this vitamin deficiency central to the disease's development. It has been found that several studies have demonstrated that the supplementation of vitamin D can enhance metabolic and reproductive performance. Nonetheless, the best ways to administer the doses and how long they should be taken are still unknown. Genetic and environmental factors with customized therapeutic approaches are needed to moderate the vitamin D predisposition for PCOS. Conclusion: Thus, another way of ensuring the promotion of vitamin D deficiency is through the enhancement of the management of PCOS. In further studies, the development of supplementation strategies and the identification of personal treatment regimens should be the focus. When optimized as a form of treatment, vitamin D could rank among the best approaches fit for enhancing the quality of life of women with PCOS and reducing the many health risks that come with this disease.

Methods

This systematic review used a systematic search strategy to identify studies on the association between vitamin D deficiency and PCOS. The primary rationale of this paper was to compile and synthesize the most current and relevant research findings to develop an advanced understanding of mechanisms, implications, and possible therapeutic approaches linked with this interaction.

Search Strategy and Keywords

Four major academic databases were searched for this review: PubMed, Google Scholar, ScienceDirect, and ResearchGate. The extensive coverage of peer-reviewed literature in the scientific and medical domains was a contributing factor in this selection. To make sure the papers obtained were current and indicative of the most recent advancements in this field, the search was limited to articles published between 2016 and 2024. The following keywords, when combined with Boolean operators, formed the basis of the search strategy: "vitamin D deficiency," "polycystic ovary syndrome," "PCOS," "Vitamin D receptor," "insulin resistance," "inflammation," "menstrual irregularities," "hyperandrogenism," "genetic factors," "environmental factors," and "molecular mechanisms." The search results were restricted to research that thoroughly examined the connection between vitamin D and PCOS using Boolean operators.

Inclusion and Exclusion Criteria

A strict approach was undertaken to select relevant studies based on high-quality research on the inclusion criteria. Emphasis was placed on studies relating vitamin D deficiency to PCOS in human populations and studies following recognized diagnostic criteria, such as the Rotterdam criteria, in diagnosing women with PCOS. This ensures that the findings are applicable to human health and clinically useful. In addition, only research published in English were taken into consideration in order to preserve the review's quality and dependability. For appropriate data interpretation and analysis, this criterion is necessary. Studies not directly relevant to the issue of interest, animal models, abstract-only publications, and other endocrine illnesses or conditions that potentially change the relationship between vitamin D and PCOS were among the exclusion criteria. By omitting additional cases, this strategy allowed the review to remain focused on the particular connection between vitamin D insufficiency and PCOS.

The sensitive search was followed by the meticulous application of inclusion and exclusion criteria to yield studies that best contribute to deepening the understanding of the role of vitamin D in PCOS. The literature review highlights the most relevant recent research. It thus provides critical insights into the possible mechanisms by which vitamin D influences the pathophysiology of PCOS and aspects related to therapy by addressing vitamin D deficiency in women with PCOS. These selected studies lay the groundwork for considering the integration of vitamin D supplementation in the clinical management of PCOS and may contribute to improved outcomes among those affected.

Discussion

This review emphasises the common link between vitamin D insufficiency and women's polycystic ovarian syndrome (PCOS), emphasising how the shortage may worsen the disease's course. A worsening of the main symptoms of PCOS, such as insulin resistance, irregular menstruation, and hyperandrogenism, is associated with the deficit. In addition, the study examines the therapeutic potential of vitamin D supplementation and the complex interaction between vitamin D and insulin resistance in the context of PCOS.

1. Vitamin D and Insulin Resistance

Insulin resistance is quite common in patients with PCOS, and this is one of the aspects of the syndrome. This insensitivity is one of the factors that leads to obesity, dyslipidemia, and a higher risk of type 2 diabetes in women suffering from PCOS. The effect of vitamin D on insulin sensitivity has also initiated interest amongst many. Studies have found that women with insufficient vitamin D are likely to be more insulin resistant which will affect them negatively metabolically since they already have the PCOS health condition [6,7]. A review of the literature demonstrates that vitamin D has a role in gene expression and metabolic signaling pathways associated with insulin sensitivity, which has implications on metabolic health. The study conducted by Dastorani et al [9], suggests that vitamin D supplementation may enhance the metabolic status of women with PCOS to a relatively large extent. In this study, it has been determined that vitamin D supplementation improves insulin sensitivity and the pattern of lipid metabolism in infertile PCOS candidates for IVF. These results indicated that vitamin D supplementation has enhanced insulin sensitivity, and it goes further to reach a metabolic health domain of lipid profiles. Similarly, Zhao et al (12), showed that vitamin D supplementation interrupts insulin resistance in PCOS patients. Their studies noted that vitamin D helped increase insulin receptors and activity, which is crucial in glucose acceptance and metabolism.

These findings are further supported by Karadağ et al [6], who showed that in vitamin-D-deficient women with PCOS, insulin sensitivity was significantly improved after supplementation with vitamin D. In this context, plausible mechanisms for this favorable effect of vitamin D include modulation of calcium homeostasis and a reduction of inflammation. Chronic low-grade inflammation, which often accompanies PCOS, has been known to play a recognizable role in insulin resistance. The anti-inflammatory action of vitamin D is relevant in that context and may contribute to the attenuation of the inflammation processes, further promoting insulin resistance in women with PCOS.

Łagowska et al. [7], in their systematic review and meta-analysis, underlined the most relevant strategy for PCOS management, especially regarding

insulin resistance, was related to modifications in lifestyle that aimed at increasing vitamin D levels. Indeed, their analysis underlined that an integrated approach, which includes dietary changes, increased sunlight exposure, and vitamin D supplementation, might have a cumulative effect on improving insulin sensitivity and metabolic health in PCOS patients. The community-based management of PCOS involves a comprehensive treatment strategy that focuses on addressing the syndrome at the grassroots level. This holistic method encompasses the management of vitamin D deficiency as part of a wider therapeutic framework.

Cander et al. [8], showed excellent evidence of the interaction between vitamin D and insulin resistance in PCOS. They demonstrated that lower levels of vitamin D in serum were significantly related to higher levels of insulin resistance, thus indicating a direct relationship between vitamin D status and metabolic health in women with PCOS. These findings support that proper vitamin D levels are necessary for metabolic homeostasis and could contribute to reducing the risk of associated complications such as type 2 diabetes. Collectively, these investigations indicate that supplementation and behavioral interventions for vitamin D deficiency could offer a novel, promising strategy for the pharmacological administration of insulin resistance in women with PCOS. These studies suggest that vitamin D can potentially reverse staging and management of metabolic syndrome in terms of different diabetes complications such as type 2 diabetes.

2.Menstrual Irregularities and Hyperandrogenism

Menstrual irregularities and hyperandrogenism are the hallmark features of PCOS, which significantly affect the reproductive health and quality of life of the affected individual. The role of vitamin D in such symptom management has thus become one of interest, for which many studies look onward to its effect on menstrual regularity and androgen levels.

A systematic review and meta-analysis were conducted by Guraya and Alzobydi [13], addressing the association between hypovitaminosis D and PCOS. Their findings emphasized the role of vitamin D in ameliorating menstrual disturbances and hyperandrogenism, a deficiency that could further aggravate these two essential features of PCOS. Similarly, Karadağ et al. [6], in their research article, demonstrated that supplementation with vitamin D significantly improved insulin sensitivity and androgen levels among vitamin D-deficient women with PCOS. The study justifies the argument that supplementation with vitamin D may present a new therapeutic strategy for menstrual irregularities and hyperandrogenism in PCOS.

In addition, Subashree et al. [11] assessed the correlation between serum calcium and vitamin D and hormonal status in females with PCOS. They also pointed out that such a level was significant in women with this condition, and their results suggest that increased serum calcium and vitamin D levels are associated with improved hormonal profiles. This finding suggests vitamin D could play a role in the symptomatic management of PCOS. A cross-sectional study by Shan et al. [14], demonstrates that subnormal vitamin D levels are linked with hyperandrogenaemia among women affected by PCOS - an essential component of the relationship between vitamin D status and levels of androgens. This would, therefore, point to the fact that vitamin D might be centrally involved in the regulation of hyperandrogenism in women with PCOS.

3. Inflammation and Immune Modulation

One of the hallmarks of PCOS is chronic, low-grade inflammation, which is considered a significant factor in its pathogenesis. On the other hand, vitamin D deficiency is common among patients with PCOS and tends to promote an inflammatory state toward further metabolic and reproductive derangements. Vitamin D is well-recognized for its immunomodulatory effects, which play a critical role in modulating immune responses via suppression of inflammation. Hussein [15], performed a systematic review that underlined the supplementation with vitamin D as a strategy that might mitigate systemic inflammation and improve metabolic outcomes among women with PCOS.

The results support that vitamin D could help minimize chronic inflammation associated with the condition, providing a promising therapeutic option to help manage this complex condition. In this context, Guo et al. [10], pointed out the anti-inflammatory role of vitamin D. They suggested that supplementation with this vitamin may modulate the immune response and reduce oxidative stress, which is all part of the hallmark feature of PCOS pathophysiology.

Vitamin D supplementation, among other nutritional supplementation, on oxidative stress and hormonal balance was assessed by Sidabutar et al. [17], among PCOS women. The results indicated significant reductions in oxidative stress markers, coupled with an improvement in metabolic health following supplementation with vitamin D, thus pointing to the potential of vitamin D in countering inflammation processes associated with PCOS. These findings are essential since chronic inflammation enhances insulin resistance-a cardinal feature of the syndrome-and increases the risk for cardiovascular complications. The role of vitamin D in the pathophysiology may thus be essential for improving both metabolic and reproductive outcomes in women with PCOS through its anti-inflammatory and antioxidant effects [5,10,12]. While the data to date are encouraging, further research is needed to clarify, first, the actual mechanisms of the anti-inflammatory action of vitamin D and, second, the establishment of optimal treatment protocols that would result in reasonable control of the inflammatory process in PCOS patients [1,3].

4. Genetic and Environmental Factors

In parallel to inflammation, the vitamin D status of women with PCOS is determined by the combination of genetic profile and environmental factors. In this regard, Shi et al. [19], carried out a meta-analysis investigating the correlation between variations in the vitamin D receptor gene and polycystic ovarian syndrome (PCOS). They emphasized how some VDR gene variations, including VDR ApaI (rs7975232) and VDR BsmI (rs1544410), are connected to an increased risk of PCOS via pathways including metabolic dysregulation and insulin resistance. These polymorphisms may also impact blood parathyroid hormone and 25-hydroxyvitamin D levels via influencing the PTH-vitamin D axis. Significantly, the correlation differed by ethnicity, showing that environmental variables and VDR polymorphisms combine to cause PCOS in Asian populations but not in Caucasian ones.

Additionally, Morgante et al. [20], talked about the complex nature of PCOS, noting that it affects between 10 and 15 percent of women of reproductive age, with prevalence varied depending on geographic circumstances and diagnostic criteria. They emphasized the importance of lifestyle and environmental factors in obesity and insulin resistance (IR), which is an essential hallmark of PCOS, particularly in obese people. Geographical location influences the synthesis of vitamin D (VD), which is produced by exposure to UV radiation, and may have an effect on vitamin D levels in women with PCOS. The scientists also noted elevated oxidative stress markers in PCOS patients, which are impacted by diet and lifestyle. They discovered a negative relationship between serum vitamin D levels and body mass index (BMI), suggesting that obesity, which is frequently made worse by environmental factors, is associated with reduced vitamin D status and increased insulin resistance in women with PCOS[20].

Again, this highlights the importance of taking into account both hereditary and environmental factors when managing PCOS because of their interplay in determining the severity of symptoms and the effectiveness of treatment.

5. Molecular Mechanisms

Studies also show the presence of biochemical pathways that connect vitamin D insufficiency to PCOS. Subashree et al. (11) point out that 4–16% of women of reproductive age have PCOS, which frequently coexists with insulin resistance and compensatory hyperinsulinemia. According to their research, vitamin D plays a key role in controlling important genes linked to inflammation, steroidogenesis, and insulin signaling, which greatly contributes to the pathophysiology of PCOS. The results indicate that in addition to its regulatory function in calcium metabolism, which is necessary

for efficient insulin release, vitamin D may also affect insulin secretion through processes like the activation of insulin gene transcription. Furthermore, the immunomodulatory properties of vitamin D help reduce inflammatory reactions, which are known to put people at risk for insulin resistance, a defining feature of PCOS.

Additionally, the effect of vitamin D on insulin levels is highlighted among women with PCOS, with studies showing that low levels of vitamin D are detrimental to insulin metabolism, supporting the cause of insulin receptor sensitivity. There is a strong case for vitamin D therapy, as it has been shown to ameliorate obesity-induced insulin resistance, hormonal alterations, and dyslipidemia, which are common features in women with PCOS (11).

A thorough meta-analysis performed by Zhao et al. [12], examined the use of vitamin D as a possible treatment for PCOS, emphasizing its essential function in regulating gene expression, maintaining hormonal balance, and modulating inflammatory pathways associated with the disorder's pathophysiology. The study showed that vitamin D supplementation may positively affect total testosterone levels, inflammatory markers such as hs-CRP, and oxidative stress indicators like TAC and MDA. These findings further indicates that vitamin D alters important molecular mechanisms related to PCOS, such as insulin resistance and hyperandrogenism, which may be crucial in managing the condition. Understanding these complex molecular interactions can lead to more effective therapeutic interventions aimed at addressing the underlying abnormalities in PCOS, where the potential for personalized treatment strategies derived from individual molecular profiles presents promising opportunities for enhancing health outcomes in women affected by the condition.

6. Therapeutic Implications

Although the therapeutic role of vitamin D supplementation has immense potential in managing PCOS, much remains to be sorted out to get the full beneficial effect of its supplementation. Most existing studies have demonstrated favourable effects, primarily on improving metabolic dysfunction, however, determining the optimum dosage and duration of supplementation is still a significant challenge. Zhao et al. [12], indicated that further study was warranted to determine the appropriate supplementation protocols and long-term effects of vitamin D on the management of PCOS. This shows that large-scale RCTs must be conducted to establish standards that ensure that supplementation with vitamin D is both practical and safe for clinical practice.

Guo et al. [10], also pointed out the potential role of vitamin D in improving metabolic parameters among women suffering from PCOS. In this regard, the systematic review undertaken by these authors analysed a wide array of randomized controlled trials. It demonstrated how vitamin D improves outcomes for such patients and illustrated that using a standardized supplementation method could have valuable effects in improving such outcomes. Furthermore, Karadağ et al. [6], emphasized that treatment plans must be individualized to suit the different hormonal and metabolic variables in PCOS patients. This personalized approach ensures treatment strategies are at their best in resolving individual patient needs against variable and heterogeneous PCOS presentations.

Further, Bashir et al. [18] reiterated that vitamin D status needs to be addressed as an essential component in managing PCOS. When incorporated into clinical practice, all these help healthcare providers provide better and more personalized management to women with PCOS.

Conclusion

In conclusion, this literature review underscores the significant association between vitamin D deficiency and polycystic ovary syndrome (PCOS), highlighting the multifaceted role of vitamin D in the pathophysiology of this complex disorder. The evidence suggests that low vitamin D levels are prevalent among women with PCOS and may exacerbate key symptoms such as insulin resistance, hyperandrogenism, and menstrual irregularities. The therapeutic potential of vitamin D supplementation emerges as a promising avenue for managing these symptoms, with studies indicating improvements in metabolic health and hormonal balance. Moreover, the interplay between genetic and environmental factors further complicates the relationship between vitamin D and PCOS, suggesting that personalized treatment approaches may be necessary to optimize patient outcomes. While current research provides a solid foundation for understanding the implications of vitamin D in PCOS, further studies are warranted to elucidate the underlying mechanisms and establish standardized supplementation protocols. Ultimately, addressing vitamin D deficiency should be considered an integral component of the clinical management of PCOS. By incorporating vitamin D supplementation and lifestyle modifications into treatment plans, healthcare providers may enhance the quality of life for women affected by this condition and mitigate the risk of associated metabolic complications. Continued research in this area is essential to refine therapeutic strategies and improve the overall management of PCOS.

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