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REVIEW ARTICLE

OVERVIEW OF VITAMIN D ROLE IN POLYCYSTIC OVARIAN SYNDROME

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Summary

Vitamin D inadequacy is widespread in females with polycystic ovarian syndrome (PCOS), with blood values of 25-hydroxy vitamin D (25OHD) down to or less than 20 ng/ml in two-third of PCOS patients. Decreased 25OHD concentrations have been linked to insulin resistance, ovulatory and period abnormalities, lower pregnancy outcomes, and other indications of PCOS, according to epidemiological studies. There might be some, but inadequate, research that vitamin D supplements can help women with PCOS with menstruation disruption and insulin sensitivity. Vitamin D inadequacy may bestow to the exacerbation of PCOS, and vitamin D intake may be helpful in the treatment of this condition. However, the present evidence is insufficient, and further experimental investigations are in need to establish vitamin D supplementation's potential advantages in this population. Many investigators claimed a pertinency between vitamin D concentrations and PCOS, nevertheless, these researches bear rattle factors of conjoined with other disorders or ailments, such as obesity, diabetes, and hirsutism. In the view of this, the present review detailed the role of vitamin D inadequacy and related biomolecule abnormalities, including sex hormones, and insulin and we listed their psychological and cardiovascular encounter. We concluded that the correlation between vitamin D intake and mended PCOS prominence is dubious and no definite findings attained by studies conducted across multicentral laboratories.

Key words: PCOS; Vitamin D; Calcium; Androgen; Reproduction

1. INTRODUCTION

Polycystic ovarian syndrome (PCOS) is one of the prevailing endocrine ailments in females of child-bearing age; affecting approximately 18% of the population (1). The patients symptoms commenced with menstrual distortion, laboratory discovery proved elevated androgen levels, and clinically with hirsutism and acne, these clinical outcomes were proved by the existence of polycysts in the ovaries by ultrasonography (2). Additionally, PCOS patients repeatedly show increased incidence of cardiac diseases and metabolic ailments (obesity, hyperlipidaemia, insulin resistance, and diabetes mellitus), these metabolic ailments collectively suggest the presence of PCOS when coexists in any patient (3).

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The human body obtains vitamin D either from endogenous or exogenous sources. Exogenously from dietary products, while endogenous sources include few steps; starting from cholesterol to 7-dehydrocholesterol photochemical conversion in the skin by sunlight followed by hepatic or renal hydroxylation. Back to the skin, Photolysis of dehydrocholesterol in the skin resulted in the formation of vitamin D3 by UV light. The vitamin D3 molecules are then extorted to two hydroxylation stages, the first in the liver to 25OHD through D3-hydroxylase and the second in the kidney to 1,25-dihydroxy vitamin D3 which promulgate in the circulation by binding to vitamin D binding protein to whirl the vitamin to wield its effects on the receptors (4, 5).

Recently, researchers have divulged that vitamin D concentrations are closely cognate to the presence of PCOS(6) (7, 8, 9), however, there is no consent about this statement; because the conjoined between plasma concentrations of vitamin D and the occurence of PCOS is not always reciprocal to each other, since there is confirmation that the amount of vitamin D is the same in women regardless of presence/absence of PCOS (6, 10). Nevertheless, higher and lower plasma vitamin D amount have been demonstrated in PCOS patients correlated to healthy normal subjects (11, 12, 13, 14). Collectively, these studies have reported an average value of vitamin D of less than 20ng/ml. Correspondingly, the general population shows a generalized decline in the level of vitamin D down to 20ng/ml without any health problem; this further complicates the explanation to identify the link between vitamin D and initiation or progression of the disease status (15, 16).

A research piloted by Mahmoudi et al., (17) found that control has a lower level of vitamin D than PCOS patients whereas Li et al., (10) and Wher et al., (11) reported lower D3 level in PCOS-patients contrasted to control healthy women (11). It seems that the results are conflicting with each other. In the current study, we are highlighting a detailed difference in the associated symptoms in PCOS patients and their correlation with plasma vitamin D3 levels.

2. Vitamin D3 and metabolic parameters in PCOS patients

2.1. Insulin resistance

The postulated mode that links vitamin D and insulin is still unclear. The proposed mechanisms include, vitamin D boost insulin release, upregulate insulin receptors, inhibiting the production of pro-inflammatory cytokines responsible for mediating insulin resistance. Additionally, improved calcium levels might also mediate the reduction of insulin resistance and improve insulin secretion (18). However, recent researches have confirmed that there is no interrelation between insulin sensitivity and vitamin D unless otherwise associated with obesity (19). These discrepant results need further large-scale studies to confirm the outcome. Some studies have confirmed the accord between insulin detention and the concentration of vitamin D only when overweight is present and once obesity disappeared the relationship was negatively associated with each other (6, 9). Nevertheless, a separate report has confirmed that PCOS patients with very low vitamin D levels were conjoined with insulin resistance and they were normal BMI (7). Another statistical study (9) confirmed that the link between vitamin D and insulin in PCOS patients is unallied of BMI. Most of these aforementioned studies carry the limitation of being cross-sectional; necessitating conducting randomized controlled intervention trials. There are considerable scanty randomized controlled clinical trials; the outcome of these studies confirmed that administration of vitamin D improved insulin release and sensitivity in PCOS patients confirmed by reduced fasting glucose level (20, 21, 11).

2.2. Androgen levels

Several studies have linked the elevated level of androgen with precursors of vitamin D plasma levels (25OHD). Low plasma concentrations of vitamin D have been manifested in hirsute females with/without PCOS in comparison to normal control (22), however, non-hirsute females with PCOS show normal values of vitamin D (9). Moreover, PCOS patients have shown a positive association between plasma vitamin D3 level with sex-hormone-binding globulin (SHBG) (7, 9, 10) and a negative correlation with testosterone level (8). Additionally, SHBG is reciprocally correlated to a shallow level of vitamin D in PCOS patients (7, 10). To further confirm these links and joining between vitamin D and androgen in PCOS, vitamin D supplemented to PCOS women to restore the normal concentration of vitamin D; acne in these women has disappeared (23).

2.3. Body weight and body mass index (BMI)

Studies conducted in PCOS patients reported a converse relationship between BMI and the plasma concentrations of vitamin D in PCOS patients (6, 8, 19). Recent reports confirmed that the precursors of vitamin D are declined in overweight females with PCOS (19). These could clarify that the deficiency of vitamin D in PCOS is primarily linked to obesity (10). Taking into consideration the lipophilic nature of vitamin D which render it cloister in adipose tissue in high concentration in overweight individual (24). Correspondingly, the utilization and metabolism of vitamin D might be different between overweight and slim subjects.

3. Vitamin D and reproductive function in PCOS patients

The power of vitamin D is inferred by the remark of vitamin D receptors (VDRs) in the reproductive system (ovaries, placenta, and endometrium) (25). Low plasma level of vitamin D results in hypocalcemia; low calcium levels have been associated with inhibition of folliculogenesis in PCOS patients. These concentrations of vitamin D resulted in menstrual irregularities and fertility impairment (26, 27). The scientific concept of vitamin D supplementation to PCOS patients was practically lean on the role of vitamin D in metabolism including the metabolism of glucose and related biomolecules (insulin, insulin receptors, and proinflammatory cytokines) (18). The influence is principally propitiated via the impression of vitamin D in the modulation of insulin detention; vitamin D propitiated vitiation in insulin resistance supervened by decline of hyperandrogenism since the reduction of insulin resistance followed by ovarian reduction of androgen production and subsequently increasing sex-hormone-binding globulin; this will conjointly weaken all complications conjoined with PCOS disease (Figure 1) (28).

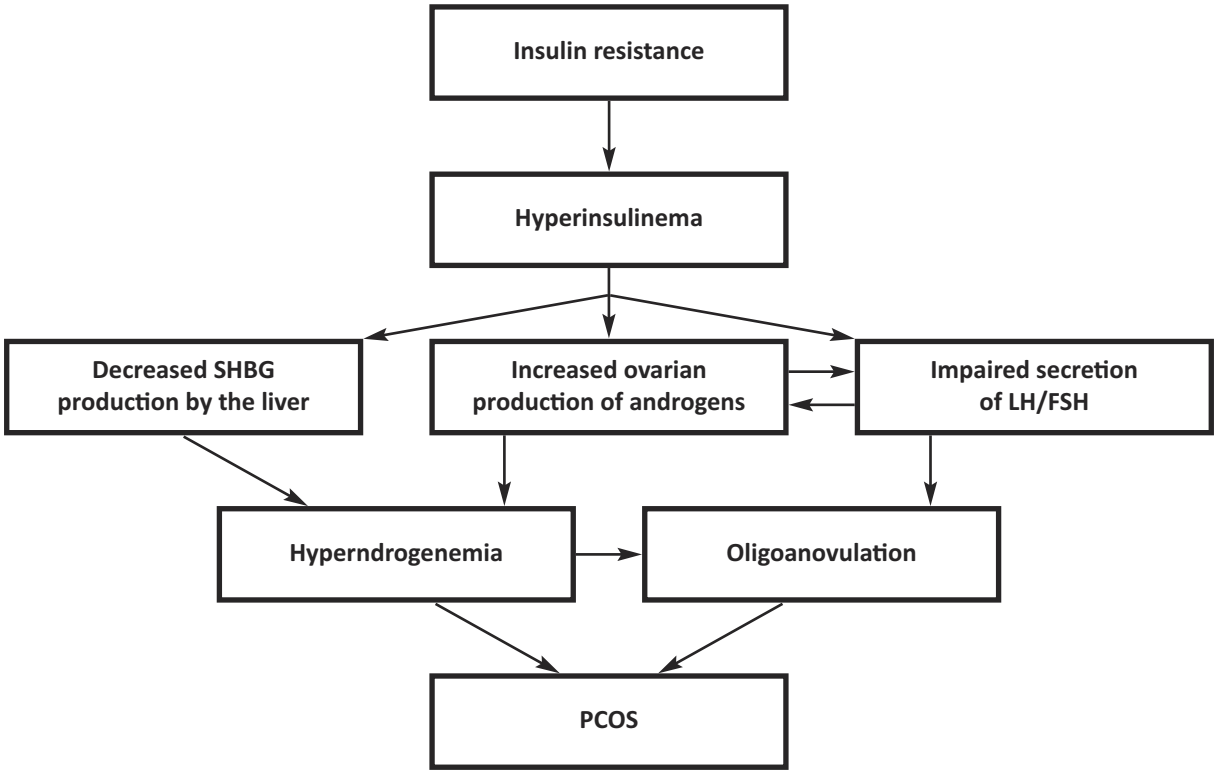

Figure 1. The link between the development of PCOS and insulin resistance.

Vitamin D influences reproduction through various molecular mechanisms which are eventually associated with improved follicular sensitivity for FSH and increased progesterone production (29).

4. Vitamin D and systemic diseases in PCOS patients

Cardiovascular diseases

The cardiovascular system is conversely compressed by inadequacy of vitamin D whereas VDR is profusely dispersed in the endothelium of vessels and heart and inadequacy of vitamin D is conjoined with augmented hazard of cardiovascular morbidity and mortality (30, 31, 32, 33). The plasma concentration of vitamin D is inversely proportional to cardiovascular risk factors of developing diseases, such as insulin resistance, spoiled glucose tolerance, dyslipidaemia, the elevation of c-reactive protein, triglycerides, high-density lipoprotein, and leptin (5). Furthermore, a few observational studies confirmed that metabolic syndrome and low vitamin D levels coexist within PCOS patients (9). Moreover, vitamin D supplementation to patients with cardiovascular diseases and metabolic disturbances has led to reduced triglyceride level, improved insulin sensitivity, and glycaemic control together with increased total cholesterol and low-density lipoprotein, however, no changes appeared with blood pressure, waist circumference, and high density (11, 21).

Psychological diseases

PCOS- associated clinical features (menstrual irregularities, impaired conceiving, hirsute, acne, and obesity) imparts a mood disturbance in women. It has been reported that these mood changes associated with PCOS are partly linked to vitamin D deficiency due to vitamin D modulated neurotransmitter release and functionality (34, 35, 36). A review published by Murphy et al., (37) reported 4 studies that confirmed the distribution of mood disturbances among patients with low plasma vitamin D levels in PCOS and these mood disorders appeared as seasonal depressive disorder, depression and low mood behaviour. Moreover, supplementation with vitamin D improved mood disorders in up to 50% of these patients and the improvement was reciprocal to improved plasma vitamin D levels (38).

5. DISCUSSION

Enormous androgen synthesis and release by the ovaries and adrenal glands are considered to be the major aberration in PCOS. PCOS is another, instinctive model for demonstrating the effect of androgen surplus on bone strength in females (39). In PCOS females, the inverse influence of amenorrhea on bone is counterbalanced by androgen overproduction (40). Insulin hyposensitivity and systemic hyperinsulinism endeavour an imperative part in the progression of the syndrome's hyperandrogenism. Insulin, in congruency with LH, initiate the synthesis of androgens by ovarian theca cells in vitro. Hyperinsulinemia, expressed as declined burning of insulin-intervened glucose, has already been declared in 10–25% of the overweight individuals in complex, dynamic insulin production investigations (41). Likewise, there's a direction indulging submerge insulin detention in slim PCOS individuals, apart from overweight individuals where these amendments are clinically worthwhile, indicating that overweight, especially adiposity, is a substantial bestowal of insulin detention in PCOS(42,43).

Bestowed on a study conveyed by Dunaif et al. (44), female with PCOS evinced vast insulin detention that is irrelevant to overweight, distorted body shape, and vitiation of glucose homeostasis. In contrast, studies revealed a considerable disparity in insulin detention between slim and overweight females with PCOS; it is advised that overweight was the component that utmost seriously compacted insulin detention and that insulin hyposensitivity(8).

Hyperinsulinemia and adiposity may both play a role in the development of PCOS. Low calcium consumption has been recognized as a possible contributor to obesity (45). On contrary, we showed no difference in calcium levels between overweight and slim females with PCOS in the current research. Serum 25-OH-D3 concentrations were substantially declined in overweight post-menopausal women compared with apparently healthy controls. The shallow concentration of 25-OH-D3 in overweight people may be due to the reduced exposure to sunlight (due to the reduced motility of obese individuals), high vitamin D accumulation in fatty tissue, and suppression of vitamin D production in the hepatic by an elevated amount of 1,25-dihydroxyvitamin D (46).

Obesity-related vitamin D inadequacy is prone to be functionally relevant, as anticipatory hyperparathyroidism was seen in overweight individuals with low 25-OH-VD concentrations (47). As in our investigation, Hahn et al. (7)

demonstrated that increasing body mass had a meaningful bad connotation with 25-hydroxyvitamin D concentrations in PCOS patients. The small level of 25-OH-VD may play a role in the development of diabetes complications (48).

Oral treatment of 1,25-dihydroxyvitamin D3 prevented slim diabetic mice from acquiring insulin-dependent diabetes, according to Zella et al.(49). Females who have PCOS are more prone to developing high blood sugar and type 2 diabetes (T2DM)(8). Women with T2DM have a significant incidence of vitamin D insufficiency (40). Vitamin D supplementation has been found to improve insulin levels (21).

6. CONCLUSION

This review has concluded that vitamin D intake is important for restoration of normal vitamin D plasma level and inadequacy could be a causative agent for initiation or progression of important diseases including PCOS.

7. RECOMMENDATION

Administration of vitamin D could be part of the entangled therapy of PCOS patients who have overweight and low vitamin D, not only to boost insulin resistance but to also decrease other vast events. Randomized, controlled, prospective studies are justified to investigate the potential beneficial impact of vitamin D administration in overweight people either with or without PCOS, particularly if vitamin D can avert type 2 and type 1 diabetes mellitus. Diabetic was shown to have an unfavourable relationship with vitamin D levels.

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Conflict of Interest

The authors have no conflicts of interest regarding the publication of this article.

Adherence to Ethical Standards

Not applicable

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