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Effect of Vitamin D Supplementation on Sex Stimulating hormone in Polycystic Ovary Women

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Abstract: Polycystic ovarian syndrome (PCOS) is the most frequent form of persistent anovulation caused by androgen excess, affecting 5 to 10% of women of reproductive age. PCOS is defined by a metabolic disease in which hyperinsulinaemia is a major hallmark, in addition to its reproductive consequences. Polycystic ovary syndrome (PCOS) is a complex condition having implications for reproductive, metabolic, and psychological characteristics. The fundamental cause of the condition is an anomaly in the ovaries; however other factors such as weight and environmental factors influence the development of particular symptoms. PCOS has been identified as a risk factor for diabetes. Despite the fact that PCOS signs and symptoms appear before those of insulin resistance, it is thought that insulin resistance, rather than the other way around, may have a role in the development of PCOS.

Aim to our study to investigate the impact of Vit D supplementation on the plasma glucose, lipid and other metabolic and endocrine parameter follicular stimulating hormone (FSH),sex hormone binding globulin(SHBG),and total testosterone(TT)

also to evaluate the therapeutic effect of Vit D and how improve hormonal levels in patients with PCOS.

From January 5th through June 10th, 2025, a follow-up research was conducted in Kirkuk. There were 80 PCOS women in the research, both married and unmarried, ranging in age from 15 to 45 years old. These patients were hospitalized to Azadi Teaching Hospital's obstetrics and gynecology section.in the present study, 80 PCOS was diagnosed based on the presence of two of the Rotterdam criteria: oligo and/or anovulation, clinical and/or biochemical signs of hyperandrogenism, and polycystic ovaries in ultrasound, which were defined as the presence of 12 or more follicles measuring 2-9 mm in diameter in each ovary and/or ovarian volume greater than 10 cm3. All 80 PCOS patients were given a comprehensive medical examination as well as anthropometric measurements such as weight and height, as well as a generic questionnaire to fill out. The formula for calculating the Body Mass Index (BMI) was weight (kg)/height2 (m2).

The mean of BMI for PCOS patients were 28.2 (Kg /m²) and mean for age 30 years our study. serum level of FSH in PCOS patients after three months vitamin D administration was increased with not significant at P value (0.1547),while the correlation between vitamin D and FSH over three months vitamin D administrate, was no correlation, and serum testosterone level in PCOS patients after three months vitamin D intake was increased significant at P value (< 0.0001) and give no correlation between vitamin D and testosterone level ,while SHBG level was not significant at P value (0.0767) and there is no correlation between vitamin D and SHBG . By our study insulin level decreased significantly at P value (0.0045) with statically no

correlation between vitamin D and insulin after three months of vitamin D administrate , while insulin resistance level was reduced significantly at P value (< 0.0001) with negative correlation between vitamin D and insulin resistance ,while serum FSB level was raised significantly at P value < (0.0001).
The majority of women with PCOS that enrolled in this study were within the child bearing age, and the majority of PCOS women were overweight, Vitamin D was most deficient in PCOS women, in PCOS women hirsutism, acne, and irregularity of menstrual cycle were more frequently occur. There are significantly reduced of cholesterol, triglyceride, LDL and VLDL with VIT.D in PCOS patients, while HDL with VIT.D in PCOS patients is significantly increased, there is raised significantly of testosterone with no significant of SHBG in PCOS patients and no significant reduced of FSH in PCOS patients.

Keywords: Vitamin D ; anti-Müllerian hormone; androgens

Introduction

Polycystic Ovary Syndrome is a complex, heterogeneous, multifaceted endocrine disorder that affects 4 to 18 percent of women of reproductive age with significant collateral negative effects on reproductive health metabolic, and psychological characteristics. Hyperandrogenism, ovulatory dysfunction, and polycystic ovary morphology are all symptoms of this condition. It has lifelong implications with increased risk for metabolic syndrome, type 2 diabetes mellitus, and possibly cardiovascular disease **[1][2][3]**.

Vitamin D refers to a group of fat-soluble a fat- soluble biomolecule, which was first discovered in 1919–1924 discovered in 1922 by McCollum as an antirachitic agent. synthesized in the skin by the action of ultraviolet irradiation from the sun related to bone metabolism and skeletal integrity as well. Currently, vitamin D, and especially its most reactive metabolite, 1,25(OH)2D3 (calcitriol), is considered a hormone involved in complex endocrine systems and modulating growth and differentiation of cells from various lines [4]**.**

Reduced 25(OH)D levels have been linked to insulin resistance, ovulatory and menstrual abnormalities, lower pregnancy success rate, hirsutism, hyperandrogenism, obesity, and increased cardiovascular disease risk factors in observational studies. Vitamin D controls gene transcription via nuclear VDRs found throughout the body, including the bones, parathyroid glands, and ovaries. The effects of VDRs on LH and SHBG levels have been connected to the pathophysiology of PCOS. testosterone levels, Insulin resistance and insulin levels in the blood. It's been proposed that a combination of vitamin D deficiency and dietary calcium inadequacy may be to blame for the PCOS-related menstrual irregularities. However, a recent study indicated that a reduced calcium consumption was related with increased blood testosterone concentrations in women with PCOS **[5][6][7][8].**

Low calcium consumption may also have a role in the hormonal imbalance seen in PCOS, according to the study. Vitamin D receptors are vital in the generation of oestrogen in the ovary. Vitamin D influences oestrogen production by controlling the expression of the aromatase gene and maintaining calcium homeostasis outside the cell. According to several research, there is a link between vitamin D levels in the blood and obesity, as well as other metabolic parameters, in women with PCOS [9][10][11].

We aimed to investigate the impact of Vit. D supplementation on the endocrine parameter (FSH, total testosterone, SHBG) with PCOS and to study the correlation of vitamin D with endocrine parameter.

Materials and Methods:

From January 5th through June 10th, 2022, follow-up research was conducted in Kirkuk. There were 80 PCOS women in the research, both married and unmarried, ranging in age from 15 to 45 years old. These patients were hospitalized to Azadi Teaching Hospital's obstetrics and gynecology section.

Study population

80 PCOS was diagnosed based on the presence of two of the Rotterdam criteria: oligo and/or anovulation, clinical and/or biochemical signs of hyperandrogenism, and polycystic ovaries in ultrasound, which were defined as the presence of 12 or more follicles measuring 2-9 mm in diameter in each ovary and/or ovarian volume greater than 10 cm3. All 80 PCOS patients were given a comprehensive medical examination as well as anthropometric measurements such as weight and height, as well as a generic questionnaire to fill out. The formula for calculating the Body Mass Index (BMI) was weight (kg)/height (meters2). Specific laboratory tests exclude out patients with metabolic or endocrinology disorders such as thyroid disease, diabetes, hypertension, and hyperprolactinemia from the research. Ovulation induction agents, antiandrogens, antidiabetic, anti-obesity, hormonal drug and current or previous use were also excluded. For all 80 PCOS patients vitamin D administrated and measurement were repeated after three months.

Statistical Analysis

(Wilcoxon)T test Statistic was used in a computerized statistical study. Possibility P values less than 0.05 were deemed statistically significant, whereas P values larger than 0.05 were regarded statistically non-significant.

Results and Discussion

By this study we obtained that FBS level was raised significantly after three month VIT.D administration. P value (< 0.0001) and (5.962, 6.125) mean of FBS resistance pre and post respectively as showed in table (4-7).

Table (4-7) level of FBS in PCOS women before and after VIT.D administrate

Variable	Patient				*P.* value
	Pre		Post		
	Mean	SD	Mean	SD	
FBS	5.962	1.569	6.125	1.504	< 0.0001*

*Significant

By this study we obtained no significant raised SHBG after three months VIT.D administration. Value (0.0767) and (17.04, 21.63) mean of SHBG pre and post respectively as showed in table (4-8)

Table (4-8) level of SHBG in PCOS women before and after VIT.D administration

Variable	Patient				*P.* value
	Pre		Post		
	Mean	SD	Mean	SD	
SHBG	17.04	9.04	21.63	14.35	0.0767*

*No-significant

By this study we obtained there is no significant correlation between vitamin D and SHBG in PCOS patients over three months VIT.D administration as showed in figure (4.3 A and B).

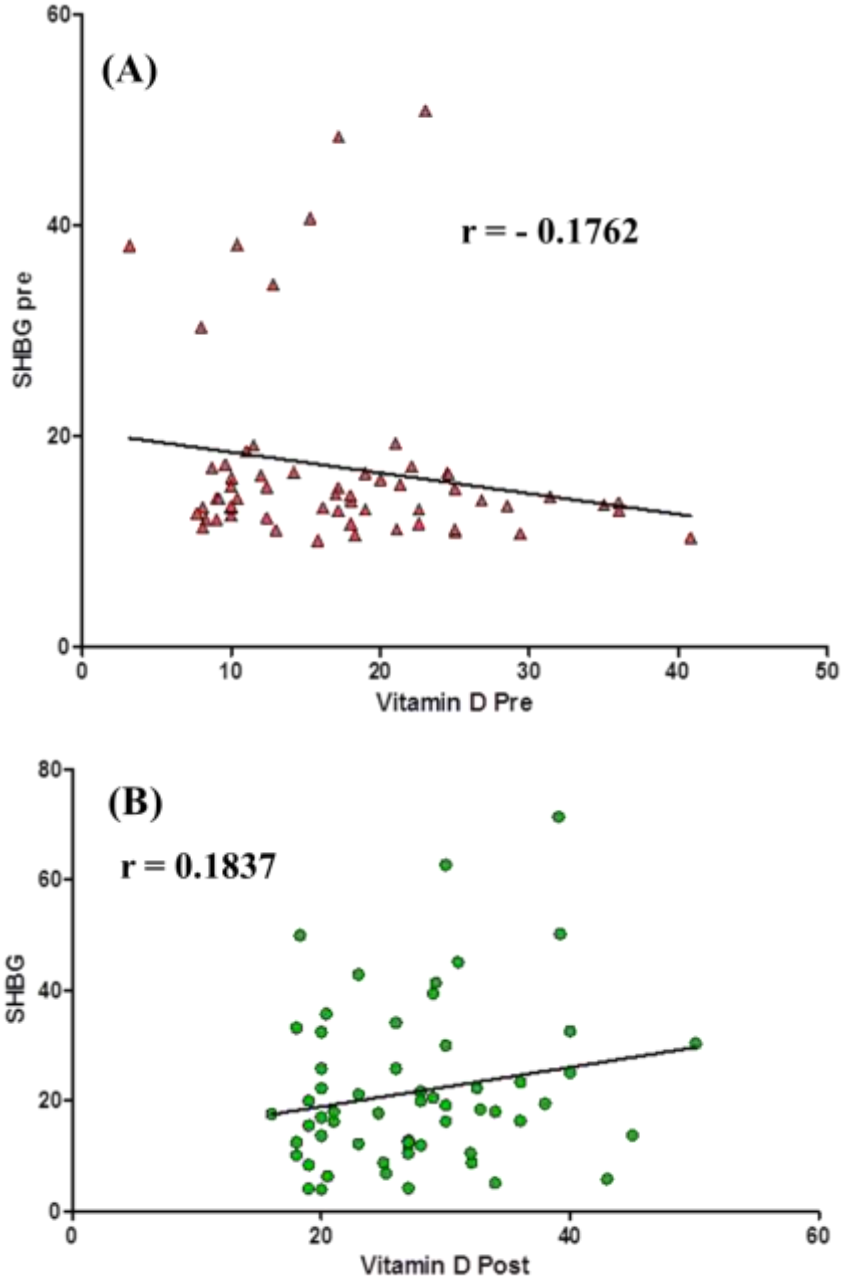

Figure (4.3) Correlation between VIT.D and SHBG in PCOS patient's (A) pre and (B) post VIT.D administration over three month's interval.

By this study we obtained significant slight elevation testosterone after three months VIT.D administration. P value (< 0.0001) and (0.7152, 0.798) mean of testosterone pre and post respectively as showed in table (4-9) .

Table (4-9) level of testosterone in PCOS women before and after VIT.D administration

Variable	Patient				*P.* value
	Pre		Post		
	Mean	SD	Mean	SD	
Testosterone	0.7152	1.105	0.798	1.123	< 0.0001*

* Significant

By this study we obtained there is no significant correlation between vitamin D and testosterone in PCOS patients over three months VIT.D administration showed in figure (4.4 A and B).

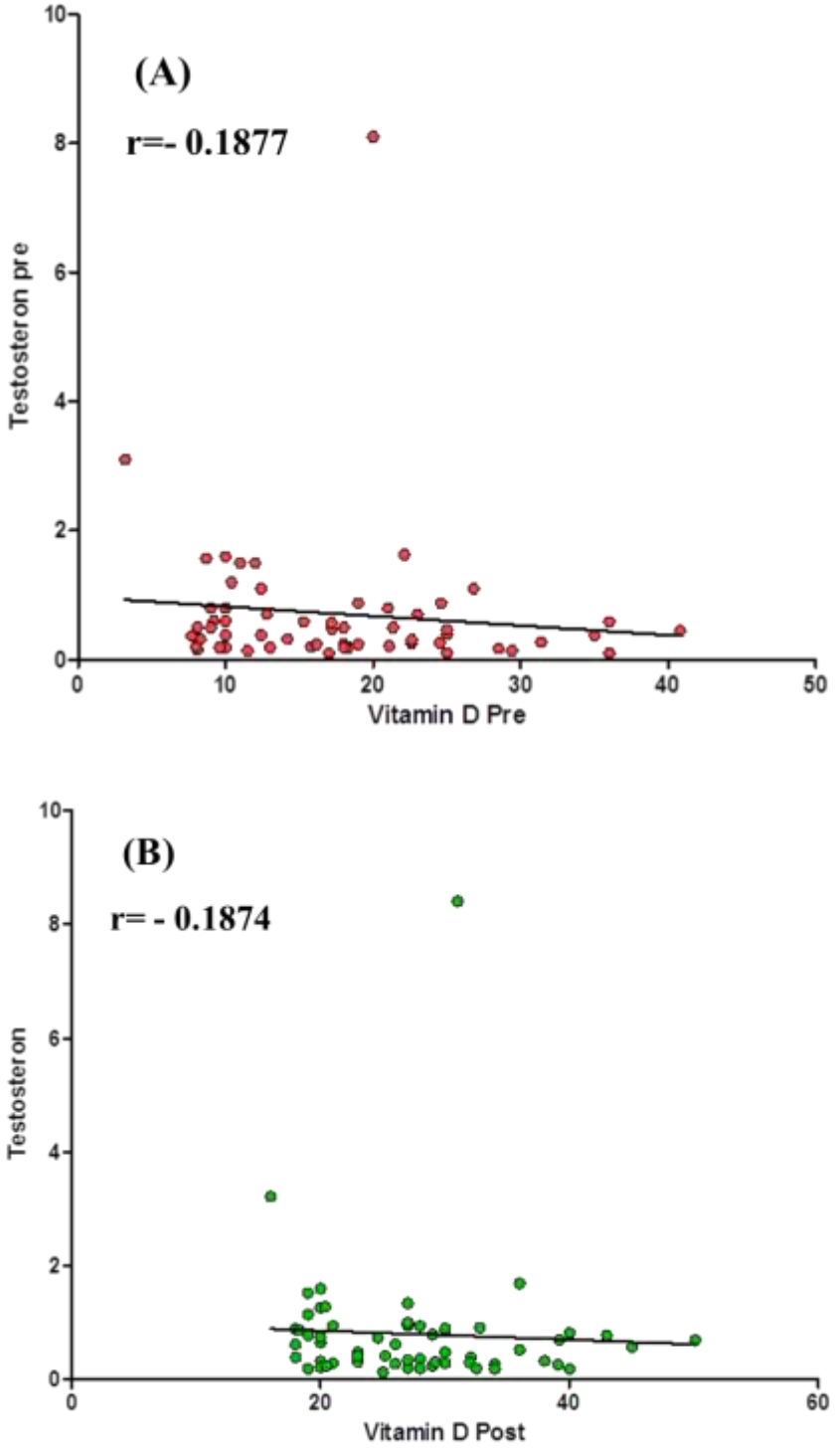

Figure (4.4) Correlation between VIT.D and testosterone in PCOS patient's (A) pre and (B) post VIT.D administration over three month's interval.

By this study we obtained no significant raised FSH after three months VIT.D administration. P value (0.1547) and (5.049, 5.135) mean of FSH pre and post respectively as showed in table (4-10)

Table (4-10) level of FSH in PCOS women before and after VIT.D administration

Variable	Patient				*P*. value
	Pre		Post		
	Mean	SD	Mean	SD	
FSH	5.049	3.593	5.135	3.532	0.1547*

*No significant

By this study we obtained there is no significant correlation between vitamin D and FSH in PCOS patients over three months VIT.D administration as showed in figure (4.5 A and B)

Discussion

Our study showed that serum level of FSH in PCOS patients after three months vitamin D administration was increased with not significant at P value (0.1547),while the correlation between vitamin D and FSH over three months vitamin D administrate, was no significant no correlation, this study is in agreement that Vitamin D levels were not associated with ovarian reserve in a large group of infertile women with a high prevalence of diminished ovarian reserve [12]. Jukic, [13] found that Vitamin D is inversely related to FSH. This is consistent with literature relating low vitamin D with lower anti-Müllerian hormone. Prospective studies should investigate whether low levels of vitamin D contribute to decreased ovarian reserve.

Our study showed that serum testosterone level in PCOS patients after three months vitamin D intake was slight elevation significant at P value **(**< 0.0001) and give no significant no correlation between vitamin D and testosterone level, while SHBG level was increased with no significant at P value (0.0767) and there is no significant no correlation between vitamin D and SHBG. The study by Ahmed M Kabel, [14] found that polycystic ovaries develop when excessive amount of male hormones (androgens) this agreed

with our study, particularly testosterone is produced by the affected ovary, this occurs by either the release of high levels of insulin in the blood. Obesity is associated with decreased testosterone level, mediated by reduced SHBG level due to insulin resistance. Lower testosterone also causes obesity. On the other hand, vitamin D is fat soluble and is sequestered into fat tissue. A previous study revealed that a higher BMI caused decreased 25(OH)D level but a lower 25(OH)D did not cause increased BMI. These observations suggest a complex role of BMI in the relationship between testosterone and vitamin D. Testosterone and vitamin D have been implicated in various medical conditions, such as osteoporosis, cardiovascular diseases, metabolic syndrome and mortality [15][16]. The results of this study suggest that the overlapping influence of testosterone and vitamin D could be caused partly by the interlacing relationship between the two factors.

1. By our study insulin level decreased significantly at P value (0.0045) with statically significant no correlation between vitamin D and insulin after three months of vitamin D administrate , while insulin resistance level was reduced significantly at P value (< 0.0001) with negative correlation between vitamin D and insulin resistance ,while serum FSB level was raised significantly at P value < (0.0001), many studies have been conducted clarify these finding especially the mechanisms involved in metabolic disorder in women with PCOS. Vitamin D deficiency associated with impaired glucose tolerance , insulin secretion, and IR and compensatory hyperinsulinaemia were found to be common features in women with PCOS. PCOS women are risky for the development of Type 2 diabetes [17][18][19]. Thomson *et al* [20] found that vitamin D deficiency may exacerbate symptoms of PCOS, insulin resistance,

ovulatory and menstrual irregularities, lower pregnancy success, hirsutism, hyperandrogenism, obesity and elevated cardiovascular disease risk factors and there is some ,but limited ,evidence for beneficial effect of vitamin D supplementation on menstrual dysfunction and insulin resistance in women with PCOS. The possible effects of vitamin D on glucose metabolism are stimulation of insulin secretion, suppression of PTH and different effects on insulin sensitivity on receptor levels [21]. The presence of VDR and vitamin D binding globulins (VDBG) in pancreatic islets and the relationship of certain allelic variations in the VDR genes with glucose tolerance and insulin secretion suggest a role of vitamin D in the pathogenesis of Type 2 diabetes. Vitamin D may stimulate pancreatic insulin secretion, administration of calcitriol to vitamin D deficient rats increases insulin secretion and decreases blood glucose response to intravenous glucose loading test. These stimulatory effects of vitamin D on insulin secretion may be obvious when calcium levels are adequate, and the intracellular calcium may play a role in insulin secretion. Vitamin D deficiency mostly causes secondary hyperparathyroidism, increased PTH activity is associated with reduced insulin sensitivity . Another effect of vitamin D on glucose metabolism is on peripheral tissue glucose uptake via VDR receptors. The skeletal muscle is a key component in the IR and may be involved in pathogenesis since VDR have been identified in this tissue [22]. Vitamin D is thought to regulate gene transcription through vitamin D receptors (VDRs), which are widely distributed throughout body tissues, including the ovaries. Genetic polymorphisms associated with VDRs have been linked to SHBG, testosterone, and insulin serum luteinizing hormone (LH) levels.

Polycystic ovaries develop when excessive amount of male hormones (androgens) this agreed with our study, particularly testosterone are produced by the affected ovary ,this occur by either the release of high levels of insulin in the blood (hyperinsulinaemia), Despite the limitations in the study, such as small sized study population and short treatment duration, the fact that the vitamin D replacement therapy has a favorable effect on IR in women with PCOS was demonstrated in the study. Due to its favorable effect, the patients with PCOS may be advised to undergo vitamin D replacement therapy in order to prevent the development of IR and Type 2 diabetes and Prospective studies with larger patient groups and longer study period are needed to address these possible favorable effects of vitamin D supplementation in obese and insulin-resistant women with PCOS [23][24][25].

Conclusion

This study shows that vitamin D supplementation can exert favorable effects on specific metabolic and endocrine parameters in vitamin D-deficient women with polyscystic ovary syndrome (PCOS), but its effect on hormonal biomarkers are different. The studies showed a notable reduction of insulin levels, insulin resistance, fasting blood sugar as well as lipid profile suggesting that supplementation with vitamin D may also help to improve metabolic regulation in women who have PCOS. Moreover, there was no significant effect of vitamin D on follicle-stimulating hormone (FSH) and sex hormone-binding globulin (SHBG), nor association between 25(OH)D3 concentrations and these endocrine parameters. Overall, these findings indicate that the metabolism benefits of vitamin D are more apparent than reproductive hormonal reversal. The suggested inclusion of supplemental vitamin D in PCOS management protocol is clinically justified by the effect of vitamin D supplementation on insulin resistance and metabolic derangement, particularly in women with vitamin D deficiency, which could delay the evolution to type 2 diabetes and other obesity-linked morbidities. However, the clearly lower hormonal response and the limited sample size and comparatively short follow-up make careful interpretation of our results advisable. Larger multicenter RCTs are warranted with extended intervention periods and incor

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