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► **To cite this version:**

S. Kharb, S. Gaur, A. Aparna, I Rajni, S. Nanda. Role of Vitamin D in Polycystic Ovarian Syndrome Patients. *Annals of Clinical and Laboratory Research*, 2021, Role of Vitamin D in Polycystic Ovarian Syndrome Patients, 09 (05), pp.1-4. 10.36648/2386-5180.9.5.351 . hal-04109334

**HAL Id: hal-04109334**

**<https://hal.science/hal-04109334>**

Submitted on 2 Jun 2023

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DOI: 10.36648/2386-5180.9.5.351

## Role of Vitamin D in Polycystic Ovarian Syndrome Patients

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**Citation:** Kharb S, Gaur S, Aparna, Rajni, Nanda S (2021) Role of Vitamin D in Polycystic Ovarian Syndrome Patients. Ann Clin Lab Res. Vol.9 No.5:351

### Abstract

**Background:** Polycystic Ovary Syndrome (PCOS), common cause of ovarian dysfunction. Vitamin D plays a physiologic role in reproduction including ovarian follicular development and luteinisation and its role in PCOS is not very clear.

**Aim and Objective:** To analyse the serum levels of vitamin D among patients with PCOS and healthy controls.

**Materials and Methods:** This cross-sectional study recruited 120 participants with PCOS and 120 healthy controls. After assessing the socio-demographic characteristics of the patients and their control, blood samples were drawn to carry out routine biochemical investigations and serum vitamin D.

**Results:** Mean serum vitamin D levels in study group were lower as compared to controls. Vitamin D deficiency was present in 95.8% of women in study group and 85% of women in control group.

**Conclusion:** Finding of lower vitamin D levels in PCOS women lends support to possible role of vitamin D in pathogenesis of PCOS. Screening for vitamin D deficiency in women with PCOS may provide better insight of its role in PCOS.

**Keywords:** PCOS; Serum Vitamin D levels

**Received:** April 20, 2021, **Accepted:** May 24, 2021, **Published:** May 31, 2021

### Introduction

PCOS is a heterogenous, multisystem endocrinopathy in women of reproductive age group affecting 5 to 21 percent of women [1]. The mechanistic links between obesity, hyperinsulinemia and anovulation have been investigated to a larger extent, still the pathogenesis of PCOS remain unclear.

Vitamin D deficiency is prevalent even in India owing to use of sunscreen and indoor lifestyle since its synthesis is reduced and impaired metabolism due to liver and kidney disease, acquired and heritable disorders of vitamin D metabolism and in responsiveness. Studies indicate that there might be an involvement of vitamin D in the pathophysiology of PCOS [2].

Vitamin D affects insulin and glucose metabolism by enhancing insulin synthesis, insulin release and increasing insulin receptor expression or suppression of proinflammation cytokines. Low vitamin D levels exacerbate the symptoms of PCOS, such as menstrual irregularities, infertility, hyperandrogenism, obesity and increased cardiovascular risk, insulin resistance [3].

Status of vitamin D is still not clear. The present study was designed to compare the serum level of vitamin D in PCOS women and healthy controls and explore the role of vitamin D in pathogenesis of PCOS.

### Materials and Methods

The study included 240 subjects of age group (15-35years) from same socioeconomic attending the Gynaecology OPD with diagnosis of PCOS. They were divided into two groups: Group A (study) comprised of 120 patients with confirmed diagnosis of PCOS, before starting any treatment and group B (control) comprised of 120 healthy volunteers.

#### Exclusion criteria

Women on multivitamin/mineral supplements for last 2 months or hormonal drugs/OCPs in past 6 weeks, thyroid/renal/liver disorder, diabetes mellitus, pregnant and lactating women were excluded from the study.

#### Methodology:

Detailed history from all the women was taken followed by complete general physical and systemic examination and informed consent was obtained. Blood samples were drawn before starting any treatment, for estimation of serum vitamin D from antecubital vein aseptically. Routine investigations namely Hb, lipid profile, fasting blood glucose and thyroid profile were

**Table 1:** Demographic and Biochemical Parameters (Mean  $\pm$  SD).

Variable	Control group (n=120)	Study group (n=120)
Age (in years)	24.71 $\pm$ 3.65	24.33 $\pm$ 4.53
BMI (kg/m <sup>2</sup> )	23.43 $\pm$ 2.44**	26.07 $\pm$ 3.99
Hemoglobin (g/dl)	12.71 $\pm$ 1.09**	10.99 $\pm$ 1.38
TSH (mIU/L)	3.61 $\pm$ 1.03	3.46 $\pm$ 2.70
RBS (mg/dl)	108.68 $\pm$ 6.55*	112.06 $\pm$ 10.23
Cholesterol (mg/dl)	175.71 $\pm$ 23.00	181.59 $\pm$ 45.41
HDL (mg/dl)	43.43 $\pm$ 8.62	41.94 $\pm$ 9.64
LDL (mg/dl)	135.73 $\pm$ 14.33	140.92 $\pm$ 27.61
Triglycerides (mg/dl)	123.70 $\pm$ 22.98	128.53 $\pm$ 39.53
** p<0.01 significant as compared to the control *p<0.05 significant as compared to the control Rest not significant		

**Table 2:** Serum vitamin D levels (Mean  $\pm$  SD).

Serum vitamin D (ng/ml)	Control group (n=120)	Study group (n=120)
Mean vitamin D levels (ng/ml)	19.57 $\pm$ 8.52	19.29 $\pm$ 5.86
Deficient (<30 ng/ml)	102 (85%)	115 (95.8%)
Normal (30-100 ng/ml)	18 (15%)	5 (4.2%)

done as per standard methods on autoanalyzer and serum vitamin D levels were estimated via Radioimmunoassay. Vitamin D levels <20ng/ml were considered as vitamin D deficient.

The quantitative parameters were expressed as (mean  $\pm$  SD) in both the groups and were done using student t-test and chi-square test. p<0.05 is considered statistically significant using SPSS version 20.

## Results

Table 1 shows clinical characteristics of both the groups (control and study).

In the present study, blood glucose levels were higher in the study group as compared to controls (p<0.05). BMI was higher in study group (p<0.01). TSH levels were lower in study group as compared to the controls (p=0.571). Serum cholesterol levels were higher in PCOS group as compared to controls (p=0.169). On the other hand, serum HDL levels were lower in PCOS group as compared to controls (p=0.210).

Vitamin D deficiency was noted in 95.8% of women in study group. In control group, 85% of women had vitamin D deficiency and the difference statistically significant (p=0.007). In the present study, serum vitamin D levels were lower in PCOS group. Only 4.2% women had serum vitamin D levels in normal range. The odds of having PCOS was 1.4 times in vitamin D deficient individuals with confidence interval of 1.45-11.32, though this association was not statistically significant. The correlation between vitamin D levels with Hb, TSH and BMI was not significant (r=0.033, -0.141, -0.058 respectively). There were 59 overweight PCOS women (BMI>24.99kg/m<sup>2</sup>) and their serum vitamin D levels were positively correlated with BMI as compared to those with BMI (18.5-24.99 kg/m<sup>2</sup>) though it was not significant (p=0.353). Forty-four PCOS women had infertility and their vitamin D levels were lower as compared to parous women though the difference was not significant (17.18  $\pm$  6.01 vs 18.27  $\pm$  4.98 ng/ml; p=0.991). Same was the case with hirsutism (p=0.769) (Table 2).

## Discussion

In the present study, the age group recruited was between 15-35 years of age to ensure comprehensive analysis which was similar to studies conducted by many workers [1,2,5-7].

In the present study, blood sugar levels were higher among study group as compared to controls and was comparable to the study of Kumar et al [4] indicating its role in pathogenesis of PCOS to IR (insulin resistance), and these women may progress to long term risks of type II DM (diabetes mellitus). The women with PCOS should be screened for DM on regular basis. TSH levels were higher in study group and LDL and triglycerides levels were higher and HDL levels were lower in PCOS group though the difference was insignificant. In contrast Bahecci et al. [5] observed that after oral fat tolerance test, triglycerides, cholesterol and VLDL levels were higher in PCOS women.

In the present study, incidence of vitamin D deficiency was higher in women with PCOS. It was noted that 95.8 % of study group and 85% of control group were found to be vitamin D deficient and these findings were comparable to study of Wehr E et al. [6].

In the present study, serum vitamin D levels in study group and control group 19.2  $\pm$  5.86 ng/ml and 19.5  $\pm$  8.52 ng/ml respectively and difference was statistically not significant. The results of present study were similar to study of Figueroa et al. [7].

Wher et al has reported vitamin deficiency in 72.8% PCOS women and Kim et al. [1] reported no difference in the level of serum 25-(OH) vitamin D in PCOS women when compared with controls [8]. Whereas, Kumar et al. [4] reported decreased levels of serum 25-OH vitamin D in PCOS women in comparison to controls.

Many observational studies suggested a possible role of vitamin D in metabolic disturbances in PCOS [9]. A recent study in PCOS has demonstrated no significant beneficial effect on insulin kinetics and cardiovascular risk factors after vitamin D supplementation [10].

Similarly, others have reported significantly lower vitamin D concentration in PCOS patients than in control [4,11].

No significant difference was found in the serum vitamin D level of the different phenotypes of PCOS by Eftekhar et al. [12].

Yilmaz et al observed a positive correlation in 25-(OH) D and SHBG (sex hormone binding globulin) levels and concluded that PCOS has been associated with hypovitaminosis D [13]. In this present study, SHBG were not done so no comparison was possible.

High prevalence of vitamin D deficiency has been reported to be associated with metabolic syndrome and this may have great impact on public health [14,15].

These findings suggest that screening for vitamin D deficiency may be useful in early diagnosis in of PCOS for preventing it's the progression to type II diabetes mellitus. Exploration of vitamin D role in pathogenesis of PCOS on higher scale can provide an area of interest for further clinical trials and can give insight into possible role of vitamin D in PCOS pathophysiology and management. Vitamin D has potential influence on glucose homeostasis. Vitamin D response element is present in human insulin gene promoter and vitamin D receptors are present in pancreatic beta cells, skeletal muscles. The conflicting results of vitamin D deficiency in PCOS in present study as compared to those in various population could be due to various degrees of gonadotrophic and metabolic abnormalities determined by interactions of multiple genetic and environment factors. Vitamin D inverse relationship with metabolic disturbances in PCOS as evident by already discussed correlation with blood sugar, lipid profile, BMI, TSH in preceding section.

Vitamin D supplementation can lower abnormally elevated serum AMH levels and anti-inflammatory soluble receptors for advanced glycation end products in vitamin D deficiency in PCOS women [16-18] and even calcium supplementation along with metformin can have beneficial effects on menstrual regularity and ovulation [19] though no significant effect of vitamin D supplementation on insulin kinetics and cardiovascular risk has been reported [20-22].

## Conclusion

Low vitamin D has been reported in PCOS and genes involved in vitamin D are candidate gene for susceptibility to PCOS. Due to wide heterogeneity of signs and symptoms of PCOS, which may be predisposed by different genetic and environmental factors future studies involving VDR SNPs and PCOS and vitamin D polymorphism and metabolic disturbances in PCOS are necessary to clarify the relationship of vitamin D metabolism with insulin resistance and polymorphism in VDR gene have been correlated and reported to play a role in insulin secretion and sensitivity in PCOS women and VDR polymorphism is protective against type II diabetes mellitus.

## Availability of data and materials

The data associated with this paper is available as dissertation and hard copy can be accessed by the editorial board if required, no weblink is available yet.

## Consent for publication

The corresponding author gives the Consent for Publication.

## Conflict of interest

None

## Acknowledgement

Residents, lab technicians, women participating in the study.

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