



## COMPARISON OF VITAMIN D STATUS IN POLYCYSTIC OVARIAN SYNDROME WOMEN WITH NON- POLYCYSTIC OVARIAN SYNDROME WOMEN

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**ABSTRACT** The role of vitamin D in pathogenesis of PCOS is largely unknown and deficiency of vitamin D may play a key role in development of PCOS. The study was conducted in Kasturba Hospital in the Department of Obstetrics and Gynaecology, Delhi. Study consisted of 160 patients, 80 PCOS women and 80 non-PCOS women. The main outcome measures were the difference in vitamin D status between PCOS and non-PCOS women. The study also correlated vitamin D levels with BMI, hirsutism and LH levels in PCOS patients. The study showed that serum vitamin D level was significantly lower in PCOS women as compared to non-PCOS women (mean vitamin D level of  $10.90 \pm 7.56$  ng/ml versus  $15.30 \pm 10.26$  ng/ml). Amongst PCOS group, 55% were obese with lower vitamin D levels as compared with 45% lean PCOS ( $10.26 \pm 6.67$  ng/ml versus  $11.68 \pm 8.56$  ng/ml). The vitamin D levels significantly correlated negatively with BMI, mFG score and LH levels (the correlation coefficient (r) of BMI versus Vitamin D levels was -0.17 and p value 0.02; mFG score for hirsutism with r value -0.23 and p value <0.01; the correlation coefficient of LH versus vitamin D level was -0.24 and p value >0.01).

**KEYWORDS :** vitamin D, PCOS (Polycystic Ovarian Syndrome), BMI (Body mass index), LH (luteinizing hormone), mFG score (modified ferriman gallwey score), p value, hirsutism

Polycystic ovary syndrome (PCOS) is the most common endocrinopathy in women of reproductive age, with a prevalence up to 10% [1]. It is characterized by ovulatory dysfunction, hyperandrogenism and/or polycystic ovarian morphology [2]. Metabolic disturbances are present in a majority of the women suffering from PCOS i.e. 30–40% have impaired glucose tolerance and insulin resistance with compensatory hyperinsulinemia and as many as 10% will develop type 2 diabetes mellitus during their fourth decade [3]

Vitamin D deficiency has been proposed as the possible missing link between insulin resistance and PCOS [4]. Since many years, a role for vitamin D has been suggested outside the calcium and bone homeostasis, due to the identification of the VDR, and the enzyme 1 alpha-hydroxylase in many more tissues, including the pancreatic beta-cells, immune cells [5] and reproductive organs in both genders [4]. Moreover, this assumption is supported by the finding that the active vitamin D-vitamin D receptor complex regulates over 300 genes, including genes that are important for glucose and lipid metabolism as well as gonadal functions [6].

So far, the role of vitamin D in pathogenesis of PCOS is largely unknown and deficiency of vitamin D may play a key role in development of PCOS. Therefore we have performed this study to examine vitamin D status in PCOS and non-PCOS women and to study the correlation of vitamin D with BMI, mFG score (marker of degree of hirsutism) and LH levels in PCOS patients.

### MATERIALS AND METHODS

This study included 80 PCOS women and 80 non-PCOS women, which are further mentioned throughout the manuscript as case and control women respectively. PCOS women who were screened for anovulatory infertility at the outpatient clinic of Kasturba hospital and subsequently diagnosed with PCOS according to the ESHRE criteria 2018 were eligible for inclusion in this study. First, a thorough general medical, reproductive and family history was taken. Second, anthropometric measurements were performed, including height, weight, body mass index (BMI), waist circumference, hip circumference, systolic and diastolic blood pressure, and the level of hirsutism measured with the use of the modified Ferriman-Gallwey (mFG) score. Subsequently, a transvaginal / transabdominal ultrasonography was performed to assess ovarian volume and the follicle number per ovary (FNPO). Finally, an extensive metabolic and endocrine profile was assessed. Age and BMI matched females (n=80) without PCOS coming to gynaecology OPD were enrolled as controls.

### INCLUSION CRITERIA

Women with age 16–40 yrs with complaints of irregular menses (oligomenorrhoea, amenorrhoea), hirsutism, alopecia or acne, were diagnosed as PCOS according to ESHRE guideline 2018 into one of the four phenotypes.

**Phenotype A.** androgen excess + ovulatory dysfunction + polycystic ovarian morphology

**Phenotype B.** androgen excess + ovulatory dysfunction

**Phenotype C.** androgen excess + polycystic ovarian morphology

**Phenotype D.** ovulatory dysfunction + polycystic ovarian morphology

### EXCLUSION CRITERIA

Disorders with similar clinical presentation such as Congenital adrenal hyperplasia, Cushing's syndrome, Androgen secreting tumors, Hyperprolactinemia, Idiopathic and familial hirsutism, PCOS patients on treatment, Patients who had received any medication affecting metabolism for last 3 months before study, Women who used any contraception, were pregnant or lactating, Thyroid dysfunction.

### Assessment of Metabolic Profile and Vitamin D

Venous blood samples were drawn at examination and stored at  $-80^{\circ}\text{C}$  after centrifugation at 3000 rpm for 10 min at  $20^{\circ}\text{C}$ . Serum 25(OH)D was measured using the electrochemiluminescence. The measurement of serum 25(OH)D was carried out by the biochemical laboratory of the Kasturba Hospital, Delhi.

### STATISTICAL ANALYSIS

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean  $\pm$  SD and median. Normality of data was tested by Kolmogorov-Smirnov test. If the normality was rejected then non parametric test were used.

### Statistical tests were applied as follows-

1. Quantitative variables were compared using Unpaired t-test/Mann-Whitney Test (when the data sets were not normally distributed) between the two groups.
2. Qualitative variables were compared using Chi-Square test /Fisher's exact test.
3. Pearson correlation coefficient/Spearman rank correlation coefficient was used to correlate quantitative variables with each other.

A p value of <0.05 was considered statistically significant. The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

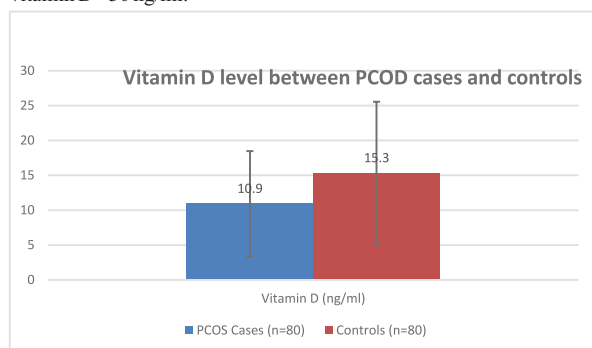
### RESULTS

#### Vitamin D status in PCOS and control women

A total of 80 PCOS women and 80 non-PCOS women were included in the analyses. The mean age was 25.06 years and 25.90 years. Overall mean serum vitamin D was 10.90 ng/ml in PCOS women versus 15.30 ng/ml in non-PCOS women. The vitamin D deficiency was present in 71 (88.8%) women out of 80 PCOS women, 4 (5%) women had a serum vitamin D level between 21 ng/ml – 29 ng/ml and 5 (6.2%) women had a serum vitamin D >30 ng/ml. In the control group 58 (72.5%) women had a serum vitamin D  $\leq$  20 ng/ml, 12 (15%) women

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### Vitamin D and its negative correlations

The mean BMI of PCOS and non-PCOS women was 25.75 kg/m<sup>2</sup> and 21.99 kg/m<sup>2</sup> respectively. Amongst 80 PCOS women 55% were obese (BMI >23 kg/m<sup>2</sup>) & 45% were lean (BMI <23 kg/m<sup>2</sup>). Vitamin D levels were compared between lean and obese PCOS patients and the mean Vitamin D level was lower in obese PCOS (10.26 ± 6.67 ng/ml) as compared to lean PCOS (11.68 ± 8.56 ng/ml). Out of 80 PCOS women 61 (76.2%) of PCOS women had hirsutism with mFG score >6. The ratio of waist circumference with hip circumference is known as WHR and WHR > 0.85 is a marker of abdominal obesity. The mean Waist to hip ratio (WHR) of all the PCOS women was 0.93 ± 0.11 and that of controls was 0.83 ± 0.05. The Vitamin D levels significantly correlated negatively with BMI (r -0.17 p value 0.02), degree of hirsutism - mFG score (r -0.23 p value < 0.01) and LH levels in PCOS women (r -0.24 and p value > 0.01).

### CONCLUSION

Our study concluded that vitamin D deficiency was significantly more common in women with PCOS than non-PCOS women (88.8% versus 72.5%). The mean vitamin D levels were lower in obese PCOS women with higher BMI as compared to lean PCOS women with lower BMI (10.26 ng/ml versus 11.68 ng/ml), suggestive of negative correlation of BMI with vitamin D. Similarly lower vitamin D levels were seen in PCOS patients with higher mFG score indicating a negative correlation of mFG score (marker of hirsutism) with vitamin D. Lastly, lower vitamin D levels were seen in PCOS patients with higher LH levels suggesting a negative correlation between LH levels and vitamin D.

Next to the linkage of vitamin D to the pathogenesis of PCOS, vitamin D may also effect fertility outcomes in PCOS [7]. Vitamin D supplementation may improve ovulatory dysfunction and thereby fertility in PCOS women [8, 9]. For future research large randomized controlled clinical trials are necessary to explore whether this association has a causal linkage. Large scale interventional studies are also required to investigate the effects of vitamin D supplementation in PCOS patients.

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