



## Poly Cystic Ovarian Syndrome and Vitamin D

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### Abstract

*Poly cystic ovarian syndrome (PCOS) is a common endocrine disorder in the women of reproductive age. The classical triad of criteria for PCOS are chronic anovulation, hyperandrogenism and polycystic ovaries. Insulin resistance and metabolic disturbances are its biochemical features. In addition to the classical role of vitamin D in the bone and calcium metabolism, it is now implicated in insulin sensitivity, diabetes mellitus type2 and gonadal functions. Vitamin D may be a missing link between insulin resistance and PCOS.*

*Vitamin D levels are low in PCOS women and supplementation of vitamin D may be of use in the treatment of PCOS. But this assumption is not proved consistently in clinical studies. A study was undertaken in a rural based medical college in south India to establish a relation between PCOS and vitamin D*

*120 women with PCOS and 60 age matched non PCOS women were evaluated for BMI and vitamin D level. It was found that 60.8% of women in PCOS group and 61.7% in control group are vitamin D deficient. Only 11.7% in PCOS group and 13.3% in control group has vitamin D >30 ng/ml. The mean vitamin D values in 120 PCOS women, 68 PCOS non obese women, 52 PCOS obese women are 18.94, 19.2, 18.6 ng/ml respectively. The mean vitamin D levels in 60 non PCOS women, 39 non PCOS non obese women, 21 non PCOS obese women are 18.4, 19.0, 17.3 ng/ml respectively. Differences in these values are not statistically significant. Hence it is concluded that, vitamin deficiency is in the community at large, not in any way specifically important in PCOS and BMI*

**Keywords:** PCOS; Vitamin D; BMI.

### Introduction

PCOS is the most common endocrine disorder in the reproductive age group. The prevalence is not clearly known, may be around 10%. Chronic anovulation/sub ovulation, clinical or biochemical hyper androgenism, polycystic ovaries on ultrasonography are its classical criteria. Presence of any two of these three criteria is diagnostic of PCOS<sup>(1)</sup>. PCOS is also a metabolic disease associated with insulin resistance, consequent

hyperinsulinemia, impaired glucose tolerance, diabetes type2, dyslipidemia, obesity. In the reproductive system, elevated Testosterone, elevated Luteinising hormone, high AMH, increased insulin like growth factor 1(IGF1), decreased insulin like growth hormone binding protein is seen. All of these factors lead to central obesity, hirsutism, oligomenorrhoea. Another group of women is non obese PCOS.

Vitamin D is a fat soluble vitamin. Cholesterol is photochemically converted in the skin by sunlight to 7-dehydro cholesterol. In the liver this is hydroxylated by 25-hydroxylase into 25-hydroxy vitamin D-25(OH)D. Second hydroxylation takes place in the kidney by 1 alpha hydroxylase into 1,25(OH)2D, which is the active metabolite of vitamin D. The half life of 25(OH)D is 2,3 weeks and the half life of 1,25(OH)2D is 4-6 hours, so serum level of 25(OH)D is taken as indicative of vitamin D status. 1,25(OH) 2D in circulation binds with Vitamin D receptors(VDR). Beyond the role of vitamin D in calcium and bone metabolism, vitamin D is having many more metabolic functions. Alpha1 hydroxylase and VDR is identified in the beta cells of pancreas and reproductive organs<sup>(2)</sup>. VDR complex regulates over 300 genes, including genes of gonadal function, glucose and lipid metabolism<sup>(3)</sup>. Clinical studies have shown that low vitamin D is associated with insulin resistance, type2 diabetes, hypertension, endothelial dysfunction and erectile dysfunction<sup>(4)</sup>.

In view of commonality of insulin resistance in both vitamin D and PCOS, studies are undertaken to examine the link between vitamin D and PCOS. Vitamin D is proposed as a possible missing link between insulin resistance and PCOS. Women with < 30 ng/ml of vitamin D have higher body fat, BMI, and testosterone. Conversely, in BMI matched PCOS and non PCOS, it was found out that women with PCOS had more vitamin D deficiency than non PCOS women. It was observed that in PCOS women with vitamin D deficiency, supplementation of vitamin D resulted in –a decrease in insulin resistance and increased insulin sensitivity; decrease in total testosterone and increase in SHBG; decrease in plasma glucose in Oral Glucose Tolerance Test<sup>(5)</sup>. These values didn't change significantly in non PCOD women vitamin D deficiency.

Vitamin D and fertility: In obese PCOS women, addition of vitamin to weight loss intervention resulted in improvement in menstrual status<sup>(6)</sup>. In PCOS women with vitamin D deficiency, there is

lower chance of ovulation and have 40% decrease in live birth rate, compared to women with PCOS without vitamin D deficiency.

Do vitamin D, PCOS have a cause-effect relationship or are they co existent conditions of a metabolic disease is not established. Different groups of studies did not show the relationship of vitamin D and PCOS consistently. So, we attempted an observational study of Obesity, vitamin D and PCOS.

### **Aim and Objective**

To know the relationship between PCOS and Vitamin D levels in obese and non obese women and comparing the values with those of control women

### **Material and Methods**

The study was conducted at a rural based medical college and its attached tertiary care hospital in the state of Pondicherry, India. Clearance from the ethical committee and written consent of all the participants of the study was obtained. The study was initiated in April 2018 and concluded in November 2019, after the requisite number of PCOS cases and controls was completed.

Women attending the Gynaecology outpatient department, in the age group of 18-40 years, with clinical examination suggestive of PCOS, regardless of their marital, fertility or sterilisation status are the subjects of study. Pregnant women; women who had treatment for PCOS in the past three months; who had hormonal intervention in the past three months; who had treatment for infertility in the past three months; who are on oral contraceptives; who had an acute medical condition in the past three months; who had vitamin D supplementation in the past six months and a lone woman with unilateral oophorectomy earlier –are excluded from the study.

Women employees (and also their dependant female family members), who are working in the medical institution and its affiliated offices, in the age group of 18-40 years, who came for their routine annual medical check up , who had regular

menses are the controls. The same exclusion criteria as applied to cases was applied to the controls also. The controls were age matched to the cases.

Age, marital status, menstrual history, fertility status, sterilisation status and history of their general medical diseases were enquired. Height, weight were recorded. Clinical examination specially directed at hirsutism, acne, acanthosis nigricans, galactorrhoea and goitre was done. USG examination abdominally for unmarried women and transvaginally for married women to detect PCOS was performed on all. In addition to the routine investigations like fasting blood sugar, lipid profile, LFT, serum creatinine, TSH- serum total testosterone and vitamin D estimation was done to all. Along with these tests-for PCOS women who are subjects for infertility treatment later AMH, hormone tests were done in first three days of menses; but not done for controls.

BMI was calculated with the formula. PCOS was diagnosed using Rotterdam criteria. The results were tabulated and statistical analysis was done to obtain P value.

### Results

A pool of 167 women with a clinical provisional diagnosis of PCOS were investigated biochemically and ultrasonographically to obtain 120 confirmed cases of PCOS. A pool of 83 control women with regular menstruation and no clinical signs of PCOS were investigated biochemically and ultrasonographically to obtain 60 non PCOS women, who are age matched to the cases.

BMI less than 25 was taken as non obese and BMI of more than 25 was taken as obese. Vitamin D was measured in Nano grams/ Milli litre. Vitamin D levels less than 20 ng/ml were categorised as deficiency for vitamin D; levels of 20-30 ng/ml were considered insufficiency for vitamin D; levels > 30 ng/ml were taken as normal levels for vitamin D

**Table 1**

parameter	Cases : PCOS	Controls : Non PCOS
N=	120	60
Unmarried	11 (9.2%)	6 (10%)
Married	109 (90.8%)	54 (90%)
Age <20 years	18 (15%)	9 (15%)
Age 20-30 years	69 (57.5%)	34 (56.7%)
Age 30-40 years	33 (27.5%)	17 (28.3%)
BMI <25	68 (56.7%)	39 (65%)
BMI >25	52 (43.3%)	21 (35%)

In the PCOS women, 15% are less than 20 years of age, 57.5% are in 20-30 years age group and 27.55% are in 30-40 years age group. Age matched non PCOS control women were selected, hence the percentage of women in the control group and in PCOS group are 15% vs 15%; 57.5% vs 56.7% & 27.5% vs 28.3%. In the women in PCOS group, 11(9.2%) are unmarried and the remaining 109 (90.8%) are married. The corresponding figures in the non PCOS group are 10% and 90%. In the PCOS group 43.3% of women had BMI >25 and in non PCOS group 35% of women had BMI >25.

Huge majority of women in both case and control group are vitamin D deficient or insufficient. Only 11.7% of PCOS group and 13.3% in non PCOS group are having vitamin D levels >30 ng/ml. 60.8% of women in PCOS group and 61.7% in non PCOS group are vitamin D deficient. The mean vitamin D value in PCOS group is 18.94ng/ml with a standard deviation of 7.4 and the mean vitamin D value in non PCOS group is 18.40 ng/ml with a standard deviation of 8.4. The mean vitamin D values in PCOS non obese women is 19.2 ng/ml and in PCOS obese women is 18.6 ng/ml. The corresponding values for non PCOS non obese is 19.0 ng/ml and non PCOS obese is 17.3 ng/ml.

Table 2

Vit.D in ng/ml	PCOS Non Obese	PCOS Obese	PCOS	Non PCOS Non Obese	Non PCOS Obese	Non PCOS
<20	41 (60.3%)	32 (61.5%)	73 (60.8%)	24 (61.5%)	13 (61.9%)	37 (61.7%)
20-30	19 (27.9%)	14 (26.9%)	33 (27.5%)	10 (25.6%)	5 (23.8%)	15 (25%)
>30	8 (11.8%)	6 (11.5%)	14 (11.7%)	5 (12.8%)	3 (14.3%)	8 (13.3%)
N=	68 (100%)	52 (100%)	120(100%)	39(100%)	21 (100%)	60 (100%)
Mean Vit.D	19.2 ng/ml	18.6 ng/ml	18.94 ng/ml	19.0 ng/ml	17.3 ng/ml	18.40 ng/ml
SD	7.4	6.9	7.9	7.1	7.6	8.4
N=	68	52	120	39	21	60

### Discussion

Vitamin D levels in case and control women did not show consistent results in various studies. Wher et al reported vitamin D values of 27.5 ng/ml for PCOS women and 32.0 ng/ml for controls<sup>(7)</sup>. Panidis et al<sup>(8)</sup>, Li HW et al<sup>(9)</sup>, Thomson R et al<sup>(10)</sup> reported the levels of vitamin D in PCOS women and controls is almost same. In the present study, the mean vitamin level in PCOS women is 18.94 ng/ml and in controls it is 18.40 ng/ml, which is insignificant. Laxman LR et al reported vitamin D levels of 15.45 +/-7.88 in women with PCOS and 12.83+/-5.76 in controls<sup>(11)</sup>. Xin-Zhuan Jia et al in a meta analysis indicated that, the level of 25(OH)D were notably lower in PCOS group than in control group and is

statistically significant<sup>(12)</sup>. Y.H.M. Krul-Poel et al confirmed the low serum 25(OH) D status in PCOS women when compared to fertile women. They reported the median 25(OH)D as 49.0 nmol/litre in PCOS women compared to 64.5 nmol/l in control women<sup>(13)</sup>. Ujjval Parikh et al reported that in PCOS women, 54% had vitamin D deficiency, 32% had vitamin D insufficiency and only 14% have vitamin D >30 ng/ml. They categorised PCOS women into obese and non obese women. 46% of women with PCOS are non obese and 54% of PCOS women are obese. The mean vitamin D levels in obese women is 14.52ng/ml when compared with 21.54 in non obese PCOS women<sup>(14)</sup>.

Table 3

Mean Vit.D values in ng/ml	Mean Vit.D values in ng/ml	P value
PCOS N=120 18.94 SD 7.9	Non PCOS N=60 18.40 SD 8.4	0.65*
PCOS Non obese N=68 19.2 SD 7.4	PCOS Obese N=52 18.6 SD 6.9	0.65**
Non PCOS Non obese N=39 19.0 SD 7.1	Non PCOS Obese N=21 17.3 SD 7.6	0.40**
Non obese PCOS N=68 19.2 SD 7.4	Non obese Non PCOS N=39 19.0 SD 7.1	
Obese PCOS N=52 18.6 SD 6.9	Obese Non PCOS N=21 17.3 SD 7.6	

\*There is no statistically significant difference in mean vitamin level between case and control group

\*\*Independent sample t test revealed there is no statistically significant difference in mean vitamin level between obese vs non obese group in case and control group respectively compared at 5% level of significance.

In the present study in PCOS women 57% have BMI <25, where as in non PCOS women 65 % have BMI <25. BMI was more than 25 in 43% of PCOS women and 35% of control women. In the present study, the percentage of vitamin D deficient women in PCOS group is 60.8 % and

61.7% in non PCOS group. When fractionated into obese and non obese women- vitamin D deficient women are 60.3%, 61.5%, 61.5%, 61.9% in non obese PCOS; obese PCOS; non obese non PCOS and obese non PCOS respectively, which is not statistically significant. The mean vitamin D

values in PCOS women was 18.94 ng/ ml compared to 18.40 ng/ ml in non PCOS women. When fractionated into obese and non obese women, the mean vitamin D values were 19.2, 18.6, 19.0, 17.3 ng/ ml in non obese PCOS; obese PCOS; non obese non PCOS and obese non PCOS respectively. These are not of any statistical significance. Similar findings were observed by Laxman LR et al<sup>(11)</sup>. Our findings were different from the studies of Hahn s et al<sup>(15)</sup>, Tildizhan et al<sup>(16)</sup>, Savastanos S et al<sup>(17)</sup> who showed that vitamin D levels were higher in non obese women when compared with obese women.

### Conclusions

Majority of the PCOS and non PCOS women are vitamin D deficient. There is no significant difference in the mean vitamin D level in PCOS and non PCOS women. There is no significant difference in the mean vitamin D level in obese and non obese women. The low vitamin D levels in all the groups of women is a reflection of vitamin D status in the community and don't have any linkage to PCOS and BMI status of women.. Further large scale, multi centric studies involving different groups of people and different communities of people in India is necessary to establish the relationship of PCOS, vitamin D and BMI

**Conflict of interest:** Nil.

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