



## Original Research Article

## Status of vitamin D in polycystic ovary syndrome: A case control study

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## ABSTRACT

**Background:** Vitamin D deficiency has been observed in many cases of Polycystic Ovary Syndrome (PCOS) and many possible links have been discovered regarding its role in the progression of pathophysiology. The aim of this study was to access and compare the level of vitamin D in PCOS patients and healthy women.

**Materials and Methods:** This was a case control study. 150 patients of PCOS and 150 age matched healthy controls were enrolled in this study. Serum level of Vitamin D was estimated by immunoassay method by using ELISA technique. The data were compared using independent t-test and chi square test wherever applicable.

**Results:** The total serum vitamin D level was found significantly ( $p < 0.0001$ ) low in PCOS patients ( $21.91 \pm 8.49$  ng/ml) compared to healthy controls ( $34.12 \pm 7.41$  ng/ml).

**Conclusion:** Hypovitaminosis D observed in PCOS cases indicated the possible involvement of vitamin D in the pathophysiological changes of the disease.

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## 1. Introduction

Polycystic ovary syndrome (PCOS) is an endocrine disease frequently seen in women of reproductive age. PCOS is characterized by polycystic ovarian morphology, hyperandrogenism, and ovulatory impairment.<sup>1</sup> Obesity, hyperandrogenemia, and insulin resistance (IR) are prevalent characteristics of PCOS.<sup>2</sup> At present, the etiopathogenesis and diagnostic criteria of PCOS are debatable. However, in addition to the menstrual disturbance and hyperandrogenism, PCOS patients demonstrate an increased prevalence of type 2 diabetes mellitus, impaired glucose tolerance, hyperinsulinemia, insulin resistance, and obesity.<sup>3</sup> Some studies have demonstrated that insulin resistance and obesity have a negative effect on serum levels of 25-hydroxyvitamin D [25 (OH) D].<sup>4</sup>

It is known that vitamin D regulates the skeletal growth and development and calcium/phosphorus metabolism. Deficiency of this vitamin is associated with insulin resistance, signs of hyperandrogenemia, ovulatory and menstrual disturbances, lower pregnancy success, and elevated cardiovascular risk factors.<sup>5</sup> Vitamin D is thought to influence the development of PCOS through gene transcription and hormonal modulation that influence insulin metabolism and fertility regulation.<sup>6</sup> It has been proposed that the connection between vitamin D and PCOS arises from the endocrine pathways affected in PCOS, such as sex hormone synthesis and insulin secretion.<sup>7</sup>

1,25-OH D increases insulin synthesis and secretion<sup>8</sup> and regulates steroidogenesis in the human ovarian tissue.<sup>9</sup> In addition, genetic PCOS related with vitamin D receptor variances have been described.<sup>10</sup> Vitamin D supplementation leads to an improvement in lean mass, regulation of insulin release, altered insulin receptor expression, and improves insulin sensitivity.<sup>8</sup>

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In the light of this information, there is a debate about whether vitamin D deficiency plays a role in PCOS pathogenesis or it is a result of PCOS. Studies comparing vitamin D levels between patients with PCOS and healthy women with normal ovulation have yielded contradictory results. Some studies have shown that vitamin D levels do not change in patients with PCOS,<sup>5</sup> while others have reported higher levels<sup>4</sup> or low levels<sup>11</sup> of vitamin D.

The present study was done to assess the level of vitamin D in patients suffering from Polycystic Ovary Syndrome and to examine if there is any considerable difference in this vitamin's concentration in comparison to healthy women.

## 2. Material and Methods

### 2.1. Study design and subjects

It was a case control study. In this study 150 patients suffering from Polycystic Ovary Syndrome were enrolled that were attending the Gynecology OPD at PBM Hospital, Bikaner. These were taken as Case Group. The diagnosis of PCOS was done using Rotterdam's criteria<sup>12</sup> in which patients fulfilling at least 2 of the 3 criteria—that is, (1) oligo- or anovulation, (2) clinical and/or biochemical hyperandrogenism, and (3) polycystic ovaries on ultrasound measurement—were recruited into the PCOS group. 150 similar age-matched healthy women were selected from society volunteers and relatives of patients and considered as Control Group.

Patients with other hormonal disorders, having similar clinical features like congenital adrenal hyperplasia, hyperprolactinemia, Cushing's syndrome, liver and renal disorders, DM, and who were taking drugs like sex steroids, vitamin D and calcium supplementation or insulin sensitizing agents etc. were excluded from the study.

### 2.2. Measurements

Blood samples were drawn from patients and controls during their early follicular phase, after 8 to 12 hours of overnight fasting. 5 ml blood was collected in plain vial and was allowed to clot for 30 minutes at room temperature and then centrifuged at 3000 rotations per minute (rpm) for 10 minutes to obtain clear non-haemolysed serum. Estimation of serum vitamin D was done by immunoassay method using ELISA technique<sup>13</sup> in the Department of Biochemistry, S. P. Medical College, Bikaner. Vitamin D deficiency is defined as 25(OH)D below 20 ng/ml and vitamin D insufficiency as 25(OH)D of 21–29 ng/ml while 25(OH)D of equal or greater than 30 ng/ml were considered as sufficiency.<sup>14</sup>

## 3. Data analysis

The results were presented as Mean  $\pm$  SD. Differences between means of various parameters were compared by

independent t-test. Categorical variables were compared by chi square test. The p value less than 0.05 was considered as statistically significant during analysis on data.

## 4. Results

The mean of age, dietary habits, marital and socioeconomic status etc. in the two groups did not show any significant difference ( $p > 0.05$ ). So, all such factors were ruled out to have any effect which may influence the serum vitamin D levels. The presence of PCOS had significant effects on vitamin D concentrations.

The mean serum vitamin D level was found to be  $34.12 \pm 7.41$  ng/ml with a range of 13.49 to 56.47 ng/ml in control subjects and  $21.91 \pm 8.49$  ng/ml with a range of 6.18 to 38.21 ng/ml in PCOS women. The results are represented in Table 1. There was a significant decrease ( $p < 0.0001$ ) in the total Vitamin D levels in women suffering with PCOS compared to healthy women.

Table 2 shows the distribution of PCOS patients and healthy women on the basis of their vitamin D levels. 75.33% of PCOS patients had vitamin D concentrations below sufficient level while only in 32% of healthy women had vitamin D concentrations below sufficient level.

The p value obtained after the chi square test is less than 0.05 indicates that insufficient level of vitamin D is significantly associated with PCOS disease (Table 2).

## 5. Discussion

Vitamin D may be involved in several aspects of PCOS including obesity, IR, ovulatory dysfunction, and metabolic syndrome.<sup>15</sup> The biological actions of vitamin D are exerted through a soluble protein — the vitamin D receptor (VDR). VDR can be found in various tissues including both the nuclei and cytoplasm of granulosa cells (GC) of human ovaries which indicates that it is responsible for the physiologic functions of 1,25(OH)2D3 in ovarian follicles.<sup>16</sup>

In human ovarian tissue, estrogen and progesterone production is stimulated by 1,25(OH)2D3, and testosterone production decreases may be by boosting of aromatase activity through vitamin D.<sup>9</sup> In the follicles of PCOS women compared to controls, aromatase gene expression decreased and LH levels had increased but follicular production of progesterone and estradiol decreased.<sup>17</sup> As a result of these effects, vitamin D deficiency may arise PCOS symptoms. Vitamin D deficiency is associated with calcium dysregulation, which participates in the development of follicular arrest in women with PCOS and results in menstrual and fertility dysfunction.<sup>18</sup>

There are evidences exist that supports a correlation between vitamin D deficiency, IR, and obesity.<sup>15</sup> First, vitamin D may have a beneficial effect on insulin action by stimulating the expression of insulin receptor

**Table 1:** Comparison of mean serum vitamin D levels in healthy women (Control Group) and PCOS women (Case Group)

Values	Normal Healthy Women (n=150)	PCOS Patients (n=150)
Mean (ng/ml)	34.12	21.91
Range	13.49 - 56.47	6.18 - 38.21
SD	7.41	8.49
SEM	0.61	0.69
DF		298
t-statistic		13.270
Significance		p < 0.0001 (Highly Significant)

**Table 2:** Distribution of cases and controls on the basis of their vitamin D Level

Vitamin D status	Healthy women (n = 150)	PCOS patients (n = 150)
Insufficiency or Deficiency (Vit. D < 30 ng/ml)	48 (32%)	113 (75.33%)
Sufficiency (Vit. D ≥ 30 ng/ml)	102 (68%)	37 (24.67%)
p-value (chi square test)		< 0.0001 (HS*)

\*HS = Highly Significant

and thereby enhancing insulin responsiveness for glucose transport.<sup>19</sup> Secondly, vitamin D regulates extracellular and intracellular calcium, which is essential for insulin-mediated intracellular processes in insulin-responsive tissues such as skeletal muscle and adipose tissue.<sup>19</sup> Finally, as vitamin D has a modulating effect on the immune system,<sup>20</sup> hypovitaminosis D might induce a higher inflammatory response, which is associated with insulin resistance.<sup>21</sup>

Of the possible explanations of the high prevalence of vitamin D deficiency in women with PCOS is related to obesity,<sup>5</sup> because vitamin D is trapped in adipose tissue,<sup>22</sup> and obese women may spend less time outdoors exposed to sunlight.

The above all explanations related to low vitamin D and PCOS are supported by the present study. Our results indicated that vitamin D levels below normal concentrations are strongly associated with the Polycystic Ovary syndrome. In this study, 75.33% of PCOS women showed vitamin D level below recommended level and there was a significant ( $p < 0.0001$ ) decrease in vitamin D concentration in women suffering with PCOS compared to healthy women.

The results of the present study were similar with findings obtained by Mazloomi et al.<sup>23</sup> Some previous studies yielded conflicting results in which Li et al.<sup>5</sup> found no change in vitamin D levels in PCOS compared to controls while Mahmoudi et al.<sup>4</sup> reported higher levels of vitamin D in PCOS women.

## 6. Conclusion

Hypovitaminosis observed in the PCOS patients of present study showed that vitamin D deficiency may be a risk factor or may play a role in the pathophysiology of PCOS. Although current evidence is limited and additional randomized controlled trials are required to confirm the potential benefits of vitamin D supplementation in PCOS

affected women. Still, vitamin D supplementation might be an element in the complex treatment of PCOS women. This intervention may also decrease the potential risk of mortality and morbidity associated with metabolic syndrome in PCOS.

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None.

## 8. Conflict of Interest

The author declares no conflict of interest.

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