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Original Research Article

Comparative study of vitamin D3 levels in polycystic ovarian syndrome vs non-polycystic ovarian females

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age and has a strong genetic component with a prevalence of 6–10% in the general population. Metabolic disturbances are common in women suffering from PCOS: 30–40% have impaired glucose tolerance and IR with compensatory hyperinsulinemia, and as many as 10% will have type 2 diabetes mellitus by their fourth decade. Recently, vitamin D deficiency has been proposed as the possible missing link between IR and PCOS. Polycystic ovarian syndrome (PCOS) and hypovitaminosis D are the two most common endocrine disorders in young women leading to many adverse metabolic consequences. This study aims to estimate vitamin D3 levels in patients of polycystic ovarian disease and compare it with non PCOS females and to study correlation between Vitamin D3 levels and polycystic ovarian syndrome.

Methods: The present patient population case control study was carried out in Department of Obstetrics and Gynaecology of Jaipur Golden Hospital diagnosed involving cases of PCOS and controls of non PCOS (48 each) by random sampling method from September 2019 to June 2021. History, general examination, systemic examination and Vitamin D levels was taken for each patient.

Results: Mean vitamin D value of cases was 14.57 ± 6.86 ng/ml and that in controls was 29.31 ± 6.53 ng/ml. When we compared the mean vitamin D value of both the groups, there was statistically significant difference found between the two groups. . We found significant negative correlation found between vitamin D value with age and BMI.

Conclusions: Hypovitaminosis D is very common in PCOS patients and exacerbates the metabolic abnormalities. It is essential to screen all the PCOS patients for 25OHD deficiency and institute appropriate replacement therapy to prevent the adverse consequences.

Keywords: Polycystic ovarian syndrome, Vitamin D, Vitamin D deficiency

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, with a prevalence of 6-10% in the general population. PCOS is characterized by- i) ovulatory dysfunction resulting in oligo- and/or anovulation, ii) hyperandrogenism and/or

hirsutism and iii) the presence of polycystic ovarian morphology.¹

PCOS is by far the most common cause of anovulatory infertility and has been reported to be associated with insulin resistance (IR), hyperinsulinemia, dyslipidaemia and central obesity which are all risk factors for the

metabolic syndrome, type 2 diabetes mellitus and cardiovascular diseases.²⁻⁴

Women with PCOS had higher LDL-cholesterol and non-HDL- cholesterol levels, regardless of BMI. ⁴ Current evidence suggests that IR has a central role in the pathogenesis of PCOS, contributing to both metabolic and reproductive disturbances.³ Many studies have been conducted to clarify the mechanism of metabolic disturbances, in particular IR, in women affected by PCOS. In part, IR might be due to obesity. However, a substantial number of lean women affected by PCOS have IR as well, independent of obesity.^{5,6}

Recently, vitamin D deficiency has been proposed as the possible missing link between IR and PCOS. This assumption is supported by the finding that the active vitamin D–vitamin D receptor (VDR) complex regulates over 300 genes, including genes that are important for glucose and lipid metabolism as well as blood pressure regulation.⁷ Moreover, there is an association between poor vitamin D status and IR in patients with type 2 diabetes mellitus.⁸⁻¹² Still, it remains unclear whether vitamin D and IR are causally interrelated or whether they constitute two independent characteristics in women with PCOS.

The prevalence of vitamin D deficiency in women with PCOS is about 67-85 per cent, with serum concentrations of 25 (OH) D <20 ng/ml.¹³

Many observational studies suggest a possible role of vitamin D in an inverse association between vitamin D status and metabolic disturbances in PCOS, but it is still hard to draw a definite conclusion in the causal relationship due to inconsistent findings from various individual studies and from a recent meta-analysis report of a systematic review.¹⁴ The present study with the objective to estimate vitamin D3 levels in patients of polycystic ovarian disease and compare it with non PCOS females.

METHODS

A case control study was planned with patients with PCOS as cases and controls as patients without PCOS. The patient population recruited from the outpatient Department of Obstetrics and Gynaecology of Jaipur golden hospital diagnosed with PCOS. With power as 80%, alpha error of 5% and taking mean values of cases and controls as 11.96±6.94 ng/ml and 16.04±7.19 ng/ml respectively, the sample size came out to be 48 in each group. Thus, the total sample was of 96 patients.¹⁵

Inclusion criteria

All newly diagnosed women with age group of 15-45 willing to given written informed consent were included in the study.

Exclusion criteria

Any diagnosed case of PCOS who was on and had history of taking vitamin D and calcium supplement within period of one year or any diagnosed cases of PCOS who was under treatment and recovered with treatment were excluded.

Total 48 women who were diagnosed with PCOS on basis of Rotterdam's criteria were labelled as PCOS group and 48 women with any other gynaecology complaint (except ovulation dysfunction and hyperandrogenism) were selected randomly and labelled as controls. History, general examination, systemic examination and vitamin D levels was taken for each patient.

According to endocrine society clinical practice guidelines vitamin D levels as¹⁶ vitamin D deficiency as levels of 25OHD D <20ng/mL, vitamin D insufficiency as 25OHD between 21 and 29 ng/mL, vitamin D sufficient as 25OHD level more than 30 ng/mL. Patient with BMI > 25 kg/m² was considered as obese. The Ferriman-Gallwey scale was used for hirsutism. A score of 1 to 4 is given for nine areas of the body. A total score less than 8 is considered normal, a score of 8 to 15 indicates mild hirsutism, and a score greater than 15 indicates moderate or severe hirsutism. A score of 0 indicates absence of terminal hair.¹⁷

Statistical analysis

Data was analysed by using SPSS 24.0 version IBM USA. Qualitative data was expressed in terms of proportions and quantitative data was expressed in terms of Mean and Standard deviation. Association between two qualitative variables was seen by using Chi square/ Fischer's exact test. Comparison of mean and SD between two groups was done by using unpaired t test to assess whether the mean difference between groups is significant or not. A p value of <0.05 was considered as statistically significant whereas a p value <0.001 was considered as highly significant.

RESULTS

We included 48 age matched cases i.e., PCOS women (cases) and non PCOS women (controls) in our study. Out of total 48 cases in each group, majority were from 21-30 years age group i.e. 23 (47.9%) followed by 14 (29.2%) from 31-40 years, 8 (16.7%) from less than 20 years and remaining 3 i.e. 6.3% from above 40 years age group. Out of 48 cases, 29 (60.4%) were married and 19 (39.6%) were unmarried whereas out of 48 controls, 35 (72.9%) were married and 13 (27.1%) were unmarried. Prevalence of infertility in cases was 37.5% and in controls was 25%. (p>0.05). Table 2 shows Prevalence of overweight in cases was 29.2% and in controls was 35.4%. Table 3 shows assessment of vitamin D revealed that it was deficient in 34 cases i.e. 91.7% and in 22 controls i.e. 45.9%. Deficiency of vitamin D was found in significantly greater number of cases as compared to controls. (p<0.05).

Table 1: Age and marital status of cases and controls.

Variables		Cases (48)	Controls (48)
		Number (%)	Number (%)
Age group	< 20	8 (16.7)	9 (18.8)
	21-30	23 (47.9)	23 (47.9)
	31-40	14 (29.2)	12 (25.0)
	> 40	3 (6.3)	4 (8.3)
Marital status	Married	29 (60.4%)	35 (72.9%)
	Unmarried	19 (39.6%)	13 (27.1%)

Table 2: BMI category of cases and controls.

BMI category	Cases	Controls
	Number (%)	Number (%)
Underweight	1 (2.1)	3 (6.3)
Normal	3 (6.3)	10 (20.8)
Overweight	14 (29.2)	17 (35.4)
Obesity class 1	19 (39.6)	13 (27.1)
Obesity class 2	9 (18.8)	4 (8.3)
Obesity class 3	2 (4.2)	1 (2.1)
Total	48 (100)	48 (100)

Table 3: Comparative distribution according to vitamin D levels.

	Cases	Controls
	Number (%)	Number (%)
Deficient	27 (56.3)	8 (16.7)
Insufficient	17 (35.4)	14 (29.2)
Normal	4 (8.3)	26 (54.2)
Total	48 (100)	48 (100)

Chi square test-23.46, p-0.00001(<0.001), highly significant

Table 4 Correlation of vitamin D with other variables showed that there was statistically significant negative correlation found between vitamin D value and age, vitamin D value and BMI. Mean vitamin D value of cases was 14.57±6.86 ng/ml and that in controls was 29.31±6.53 ng/ml. When we compared the mean vitamin D value of both the groups, there was statistically significant difference found between the two groups. It means mean vitamin D value of cases was significantly lower than controls (p<0.05). Mean BMI of cases was 36.56±5.61 and that in controls was 28.43±4.37. When we compared the mean BMI of both the groups, there was statistically significant difference found between the two group.

Table 4: Correlation of vitamin D with other variables.

Vitamin D value (ng/ml)		Age (yrs)	BMI (Kg/m ²)
		Pearson correlation	-.286*
	p value	0.049	0.001
	Inference	Negative correlation	Negative correlation

DISCUSSION

In our study, mean vitamin D value of cases was 14.57±6.86 ng/ml and that in controls was 29.31±6.53 ng/ml. When we compared the mean vitamin D value of both the groups, there was statistically significant difference found between the two groups. It means mean vitamin D value of cases was significantly lower than controls. (p<0.05). Sukul et al reported that 25(OH) vitamin D in their study was significantly lower (p<0.001) in PCOS cases (9.04±2.60 ng/ml) compared to the control group (20.06±3.28 ng/ml).¹⁸ Around 84% of PCOS cases were severely vitamin D3 deficient (<12 ng/ml), whereas in the control group, 56% were showing insufficient vitamin D3 levels. In the study reported by Wehr et al vitamin D levels were compared in a large number of women in PCOS (n=545) to the controls (n=145), and they were found to be 25.7 ng/ml versus 32.0 ng/ml, respectively.¹⁹

Li et al found highly variable 25(OH) vitamin D levels in both PCOS patients and ovulatory controls ranging from less than the detection limit to as high as 128 nmol/l. Majority 72% of PCOS subjects were found to be vitamin D deficient with 44% severely deficient levels.²⁰ In a contradictory study done by Kim et al women with PCOS showed no differences in the levels of 25(OH)D3 or the prevalence of vitamin D deficiency though majority had mean D3 <20 ng/dl (19.6±6.6 ng/ml) and 92% of PCOS subjects show vitamin D insufficiency.²¹ In interventional studies done by Selimoglu et al and Rahimi-Ardabili et al found that mean serum vitamin D increased from 16.9±16 ng/ml to 37.1±14.6 ng/ml and 7±2.80 to 22.9±6.14 ng/ml, respectively, after administration of vitamin D3 orally in PCOS cases.^{22,23}

CONCLUSION

Mean vitamin D value of cases was 14.57±6.86 ng/ml and that in controls was 29.31±6.53 ng/ml. When we compared the mean vitamin D value of both the groups, there was statistically significant difference found between the two groups. It means mean vitamin D value of cases was significantly lower than controls. (p<0.05). Hypovitaminosis D is very common in PCOS patients and exacerbates the metabolic abnormalities. We found significant negative correlation found between vitamin D value with age and BMI. Therefore, improvement of vitamin D3 levels at a younger age can contribute to prevention of PCOS. It is essential to screen all the PCOS patients for 25OHD deficiency and institute appropriate replacement therapy to prevent the adverse consequences. Each and every patient of PCOS should be screened by measuring the level of serum vitamin D3.

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